

TRABAJO DE FIN DE GRADO

Grado en Odontología

**MANDIBULAR ADVANCEMENT DEVICES
FOR OBSTRUCTIVE SLEEP APNEA**

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Abstract

Sleep disorder is a public health problem touching 1 billion of people worldwide and mandibular advancement devices therapy, as a modality to continuous positive airway pressure, is now a good alternative for obstructive sleep apnea treatment. Efficacious technic that requires a good follow up and customization. The purpose of this work was to understand the efficiency of the different appliances and their side effects compared to the CPAP, carrying out a scientific review. Mandibular advancement devices are represented by many possibilities of designs. Custom-made appliance is, by its capacity of reduction of the apnea hypopnea index of the patient, better with 6 ± 8 events per hours compared to the preformed with 11 ± 9 events per hours. Monobloc and bi-bloc appear different, monobloc allows a better reduction of the AHI but bi-bloc is preferred by the patient. The amount of protrusion is very important for the success of the treatment as the more protrusion the better it is. Adjustable appliance has greater efficacy compared to the fixed appliance. Compared to CPAP, MAD is a good alternative at all degree of severity but mainly in non-severe cases. CPAP, if tolerated, is the golden standard. MAD is also related to side effects at short and long terms meaning that a good follow-up is necessary to assess the good protrusion finding the best effectiveness / side effects ratio to avoid the withdraw of the treatment and the best outcomes of that long-life treatment.

Key words: Obstructive sleep apnea; Polysomnography; Mandibular advancement devices; Continuous positive pressure, surgery; MAD Protocol; Secondary effect; Bi-block; Mono-block; Design of MAD.

Resumen

El trastorno del sueño es un problema de salud pública que afecta a mil millones de personas en todo el mundo y la terapia con dispositivos de avance mandibular (DAM), como alternativa a la Continuous Positive Airway Pressure (CPAP), que en castellano es el tratamiento con la presión positiva continua en la vía aérea, es ahora una buena alternativa para el tratamiento de la apnea obstructiva del sueño. Es una técnica eficaz que requiere un buen seguimiento y una personalización para cada paciente. El propósito de este trabajo fue comprender la eficiencia de los diferentes dispositivos de avance mandibular y sus efectos secundarios en comparación con la CPAP a través de una revisión bibliográfica. Los dispositivos de avance mandibular están disponibles en muchas posibilidades de diseño. Los dispositivos a medida, tienen una capacidad de reducción del IAH del paciente de 6 ± 8 eventos por hora en comparación con los 11 ± 9 eventos preformados por hora. El mono-bloque y el bi-bloque parecen diferentes, el mono-bloque permite una mejor reducción del IAH, pero el bi-bloque es preferido por el paciente. La cantidad de protusión es muy importante para el éxito del tratamiento, ya que cuanta más protusión, mayor la eficacia. El aparato ajustable tiene mayor eficacia en comparación con el aparato fijo. En comparación con la CPAP, los DAM son una buena alternativa en todos los grados de gravedad, pero principalmente en los casos no graves. La CPAP, si se tolera, es el gold standard. Los DAM también están relacionados con efectos secundarios a corto y largo plazo, lo que significa que es necesario un buen seguimiento para evaluar la correcta protusión encontrando la mejor relación entre efectividad y efectos secundarios para evitar la retirada del tratamiento y conseguir los mejores resultados del tratamiento.

Palabras clave: Obstructive sleep apnea; Polysomnography; Mandibular advancement devices; Continuous positive pressure, surgery; MAD Protocol; Secondary effect; Bi-block; Mono-block; Design of MAD.

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1. Introduction

1.1. History

The History of Human Sleep starts within the Antiquity period, oldest civilizations, such as Ancient Egypt, have recorded dreams and their interpretations. Textbooks, mythological stories from anywhere in the world have sleep references. Prior to the 19th century sleep wasn't scientifically based. The tournament took place during the 19th century with the work of physicians like Humboldt and Pfluger who started to use: "The physiology and chemistry to explain sleep". Then the discovery of the Electroencephalography (EEG) over animals by the English physician Canton and over humans by Hans Berger, boosted to the scientific researches(1). The researches about sleep disorders and more particularly obstructive sleep apnea (OSA) were underlined in 1837 with the Pickwickian syndrome by Sir William Osler to describe apneic problem over obese patient. Charles Dickens book, published in 1837 also uses that term(1,2). In 1923, Pierre Robin, a dental surgeon, introduced the Oral appliance to allow the advancement of the mandible. He used a monobloc appliance as a treatment for the glossoptosis. Moreover, Meier-Ewert introduced the rigid mandibular repositioning appliance with an effective reduction of the OSA(3). In 1932, Pierre Robin pointed that pharyngeal problems could cause breathing problems during sleep in young patients with micrognathia or glossoptosis. He is one of the first to analyse the role of pharyngeal obstruction in the pathogenesis of OSA. Followed by Eberhart Sauerland who had understood the action of the pharyngeal muscles during the respiration(3). In 1965 the first polysomnography has been made, helping the diagnosis of sleep apnea syndromes. The medicine evolved, and the first sleep clinic opened at Stanford university located in California, in 1970(2). Ten years later, the first tongue-retaining device sleep oral appliance has been developed. The technique consisted in a soft plastic bulb squeezed before inserting the tongue into it to maintain it during the

night(4). Dr Sullivan started to work in 1981-83 on patients with diurnal tiredness, and thought about the non-invasive solution, the Continuous positive pressure, CPAP was born(2). In 1988 appeared the first mandibular advancement type of oral appliance: the “Boil and bite appliance” with plastic extensions behind the mandibular incisor to protrude the mandible by pressing the mandibular incisor. In 1992, the appliance of 1988 has been turned into a fixed maxillary and mandibular appliance to allow a better protrusion of the mandible. And it is in 1994 that the first custom made appliance has been developed with a full protocol of impression, bite registration and cast model(4).

1.2. Generality

1.2.1. Definition

Apnea and Hypopnea

They are the first events that characterized the OSA.

First, the apnea can be defined by the complete stop of the airflow for at least 10 seconds. There are different types of apnea: The obstructive apnea, characterized by a halt of the airflow, despite the persistence of inspiratory efforts. The central apnea, characterized by the stop of the airflow and the inspiratory muscle at the same time. The mixed apnea, characterized by an association of both starting by the central and followed by the obstructive one. Secondly, the hypopnea is not a blockage instead it is a reduction of the airflow with an oxygen desaturation of 4%(5,6).

Obstructive sleep apnea

OSA is a chronic sleep disorder in which a person frequently stops breathing during his or her sleep. Patients with OSA problems live with stops (apnea) or reductions of the breathing (hypopnea). This stop or reduction of airflow is due to a complete or partial blockage of the

upper respiratory airway. Those episodes can give hypoxemia and micro wakes up(5). The American Academy of sleep medicine define the OSA as: “OSA diagnosis is confirmed if the number of abnormal respiratory event (apnea, hypopnea, micro awaking related to an effort) with the polysomnography analysis is of at least equal to 15 events per hours or at least equal to 5 events per hours with symptoms as involuntary sleep during a waking phase, daytime drowsiness, non-reparative sleep, fatigue, insomnia, wake up with choking sensation, and description from the spouses of the snoring or of the interruption of the respiration during the sleep.”(7).

Thanks this previous definition, the OSA can be classified by severity regarding the drowsiness and the apnea hypopnea index.

According to the sleepiness the severity will be:

Drowsiness	
Mild	Unwanted drowsiness with a small repercussion on the social-professional life, and appears during non-stimulating activities (watching tv)
Moderate	Unwanted drowsiness with moderate repercussion and appears in activities that require more attention
Severe	Unwanted drowsiness affecting importantly the social and professional life and appears in a daily basis.

Table 1: Severity of Drowsiness (8).

According to the Apnea Hypopnea Index (AHI) the severity will be:

Record	Severity
AHI<5	Normal, primary snoring
5<AHI<15	Mild
15<AHI<30	Moderate
AHI>30	Severe

Table 2: Severity of the OSA according to the apnea hypopnea index(8,9).

1.3. Pathophysiology of Obstructive Sleep Apnea

The OSA corresponds to a complete upper airway (UA) collapse during the sleep due to a narrower airway. Collapsing is explained by the decreased of the intraluminal pressure and the increased of the extraluminal pressure. The obstruction is usually at the level of the oropharynx, as the structure is predominantly soft tissue with a little bone support. During the inspiration, the inspiratory muscles generate a negative pressure trying to close the pharynx. In the opposite, dilator muscles contract maintaining the patency. Dilator muscles such as genioglossus (tongue related), geniohyoid (hyoid bone related) and the Tensor Veli Palatini (palate related), are activated to keep the patency during the inspiration(10–13)(14). The sleep is constituted of cycles named Rapid-Eye-Movement (REM) and Non-Rapid-Eye-Movement (Non-REM) cycles. It is the passage of a slow-wave sleep (Non-REM phase) to a rapid eye movement phase. A cycle last normally 90 minutes(15). During the Non-REM sleep, dilator muscles keeps their normal activity. However, the tensor of the palate presents a reduction of its tonicity. In contrary, REM sleep is associated with longer and recurrent obstructions due to generalized muscle atony and the sensitivity reduction of chemoreceptors to change the partial pressure of oxygen (pO_2) and partial pressure of carbon dioxide (pCO_2) normally regulated by the ventilatory control. If there is an instability between the dilator muscles keeping the patency and the intraluminal pressure (negative) trying to close the airway during the inspiration, the closure of the upper airway will appear as the pressure of the inspiration is bigger to the force generate by the dilator muscles. This pressure necessary to explain it, is called the critical pressure (P_{crit}) (10–14). In healthy subject, the critical pressure needs to be negative to create a collapse in the opposite, in OSA patient a positive P_{crit} can collapse the upper airway. The collapse event is stopped by micro wakes up of the patient. The wakes up are due to the hypoxia and the hypercapnia, the increase in negative pressure stimulating the nasal and pharyngeal

receptor and the increasing of the respiratory effort leading to the augmentation of the pleural pressure. The micro wakes up are sufficient to activate the dilator muscles of the upper airway and make the respiration possible. The Oxyhemoglobin desaturation returns to the baseline and when the patient will return to sleep the cycles and the obstruction will repeats(10–14). The neuromuscular factor, is the neuromuscular compensation at the micro wakes up, allows the stimulation of the dilator muscles. When the patient returns to sleep, muscle tone is reduced and obstruction appears. The increase of the resistance of the upper airway for the inspiration and the expiration starts. An alteration of that compensatory reflex activating the dilator muscles in response to that resistance, can be due to a neuropathy. The neuropathy is the result of the repeated hypoxia and snoring vibrations responsible of nervous lesions reducing the responsiveness of that reflex(8,10,12,14).

1.4. Epidemiology

1.4.1. Prevalence

According to M. MELANIE LYONS et al article from 2020, 1 billion of the world's population between 30 to 69 years old have OSA(16). The prevalence will be smaller in the population <30 years old and bigger >70 years old. According to the lancet the prevalence in Spain in the population between 30 to 69 years old is 35.2%(17).

Among the population, no one is equal in front of the disease, a subgroup can have a bigger prevalence according to the risk factor they may present.

Those two prevalence shows that the obstructive sleep apnea is a public health problem.

1.4.2. Risk Factor

Risk factors	Obesity Gender Aging Alcohol Smokers Anatomic malformation Genetic Ethnicity Nasal obstruction
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Table 3 Risk factors associated to the OSA(9,10,18–21).

The obesity: is a risk factor known to be related, due to the deposit of fat in periphery of the airway, larger neck circumference, reducing the diameter of the UA and facilitate the apnea.

Some studies show that the weight loss reduces the AHI and improve the OSA condition.

The gender: Male predominance in the prevalence of OSA may be explained by different fat distributions and, the hormonal influence over the muscles. Assuming that the prevalence difference between male and female is reducing with the age, the prevalence in post-menopausal women is more important compare to pre-menopausal women.(10,20)

The age: The AHI increases with the age, however the frequency snoring seems to be reduced after 65 years old according to the study of Bixler et al (20).

The alcohol: This factor reduces the tone of the muscle and facilitate the appearance of the apnea(10,20).

Smokers: They are more susceptible to have an inflammation of the airway, which could increase the apnea (20).

Anatomic malformations: Among them macroglossia, tonsil hypertrophy, long uvula and low-lying palate. The mandibular micrognathia, retrognathia, hyoid bone to low, facilitate the collapse(10).

Genetic: Down syndrome and Marfan's syndrome are genetical anomalies facilitating the risk having OSA(10).

Nasal obstruction: Limit the airflow, even more during sleep, it increases the apnea and the oxygen desaturation produce by the OSA. Nasal obstruction can be anatomical or inflammatory such as rhinitis(22).

1.4.3. Clinical Aspect

Obstructive sleep apnea is characterized by the stop of the airflow due to the obstruction of the airway, blockages more or less important will lead to micro wakes up creating a fragmented sleep that prevent and reduce the real restful sleep for the patient. This fragmented sleep is the cause of diurnal and nocturnal symptoms(8).

Diurnal symptoms	Nocturnal symptoms
Fatigue	Snoring
Lack of energy	Nycturia
Drowsiness	Wakes up with (anxiety, palpitation)
Neurological impairment	Insomnia
Irritability	Xerostomia
Head hack	Choking
Lack of dexterity	
Lack of libido	

Tableau 4: OSA symptoms(8).

1.4.4. Outcomes

After years of episodes of apnea, snoring without treatment will result of an affectation of function. The daytime sleepiness, the fragmented sleep, provoke fatigue, low concentration, irritability, car accident, impact the social-professional life, depression. OSA gives a soft and non-recovering sleep. There are metabolic consequences such as the dyslipidemia, insulin resistance, diabetes type II, atherosclerosis. In the case of apnea symptoms, it is recommended that type 2 diabetes patients should do a screening. Then, there is an increased risk of developing diabetes type 2 in patient with OSA. Untreated OSA also appears as major determinant of

cardiovascular morbidity and mortality according to Bradley et al. and Young et al. Cardiovascular problems are, the hypertension considered as associated to OSA, Coronary artery disease, stroke, congestive heart failure, and cardiac arrhythmias(5,10,19,21–23).

1.5. How to diagnose OSA

The Diagnosis is made by professional. The anamnesis of the patient is led to know the symptoms experienced and the possible risk factors that the patients may have.

Then questionnaires can be used to asses this diagnosis of excessive sleepiness(5,19).

1.5.1. Epworth scale

The Epworth scale questionnaire uses questions related to the drowsiness, sleepiness during the day or while driving. The answers are records using a scale of 0 to 3, it allows to predict if the patient could have a sleep disorder and if the professional have to check with other diagnosis process(1,13).

Use the following scale to choose the most appropriate number for each situation	
0 = no chance of dozing or sleeping 1 = slight chance of dozing or sleeping 2 = moderate chance of dozing or sleeping 3 = high chance of dozing or sleeping	
Situation	Chance of Dozing or Sleeping
Sitting and reading	-
Watching television	-
Sitting inactive in a public place	-
Being a passenger in a car for an hour or more	-
Lying down in the afternoon to rest	-
Sitting and talking to someone	-
Sitting quietly after lunch	-
Stopped for a few minutes in traffic while driving	-
Total score (This is your Epworth score)	-
Score Results	
1-6 : You are getting enough sleep 7-8 : Your score is within the average range, however you tend to be sleepy ≥9 : You are very sleepy and should see your primary healthcare provider or a sleep specialist as soon as possible	

Picture 1: Epworth scale (9)

1.5.2. STOP-bang questionnaire

It enables to assess the risk of having the obstructive apnea and also help to follow the outcomes of the treatment. It includes four sleep related question and four additional demographic ones. It is a yes or no questions types and include: “Snoring, Tiredness, observed apnea, High blood pressure, Body Mass Idex (BMI), Age, Neck circonference, Gender”. That give the name of Stop-Bang. This questionnaire can easily be led by the dentist(9,19).

STOP-Bang Questionnaire		
<i>Please answer the following questions by checking "yes" or "no" for each one</i>		
	Yes	No
S noring (Do you snore loudly?)	<input type="checkbox"/>	<input type="checkbox"/>
T iredness (Do you often feel tired, fatigued, or sleepy during the daytime?)	<input type="checkbox"/>	<input type="checkbox"/>
O bserved Apnea (Has anyone observed that you stop breathing, or choke or gasp during your sleep?)	<input type="checkbox"/>	<input type="checkbox"/>
H igh Blood P ressure (Do you have or are you being treated for high blood pressure?)	<input type="checkbox"/>	<input type="checkbox"/>
B MI (Is your body mass index more than 35 kg per m ² ?)	<input type="checkbox"/>	<input type="checkbox"/>
A ge (Are you older than 50 years?)	<input type="checkbox"/>	<input type="checkbox"/>
N eck Circumference (Is your neck circumference greater than 40 cm [15.75 inches]?)	<input type="checkbox"/>	<input type="checkbox"/>
G ender (Are you male?)	<input type="checkbox"/>	<input type="checkbox"/>

Score 1 point for each positive response.

Scoring interpretation: 0 to 2 = low risk, 3 or 4 = intermediate risk, ≥ 5 = high risk.

Figure 1. STOP-Bang Questionnaire to assess the risk of obstructive sleep apnea.

Adapted with permission from Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology. 2008;108(5):821.

Picture 2: Stop bang questionnaire(9).

1.5.3. Berlin Questionnaire

The Berlin Questionnaire (BQ) is built with 3 categories: the snoring, the daytime somnolence and Hypertension, BMI. Giving to the patient at the first visit and scored, high risk if positives results in at least 2 categories and low risk if not scored positively(24).

CATEGORY 1

1 Complete the following:
height _____ age _____
weight _____ sex _____

2 Do you snore?
 yes
 no
 don't know

If you snore:

3 Your snoring is?
 slightly louder than breathing
 as loud as talking
 louder than talking
 very loud, can be heard in adjacent rooms

4 How often do you snore?
 nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

5 Has your snoring ever bothered other people?
 yes
 no

6 Has anyone noticed that you quit breathing during your sleep?
 nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 nearly or nearly never

CATEGORY 2

7 How often do you feel tired or fatigued after your sleep?
 nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

8 During your wake time, do you feel tired, fatigued or not up to par?
 nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

9 Have you ever nodded off or fallen asleep while driving a vehicle?
 yes
 no

If yes, how often does it occur?
 nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

CATEGORY 3

10 Do you have high blood pressure?
 yes
 no
 don't know

BMI = _____

Berlin Questionnaire Scoring:

Scoring Questions: Any answer within box outline is a positive response

Scoring Categories: Category 1 is positive with 2 or more positive responses to questions 2-6
Category 2 is positive with 2 or more positive responses to questions 7-9
Category 3 is positive with 1 or more positive response and/or a BMI >30

Final Results: 2 or more positive categories indicates a high risk of obstructive sleep apnea

Figure 1. The Berlin questionnaire for obstructive sleep apnea.[5] The questionnaire incorporates questions about snoring (category 1), daytime somnolence (category 2), and hypertension and BMI (category 3).

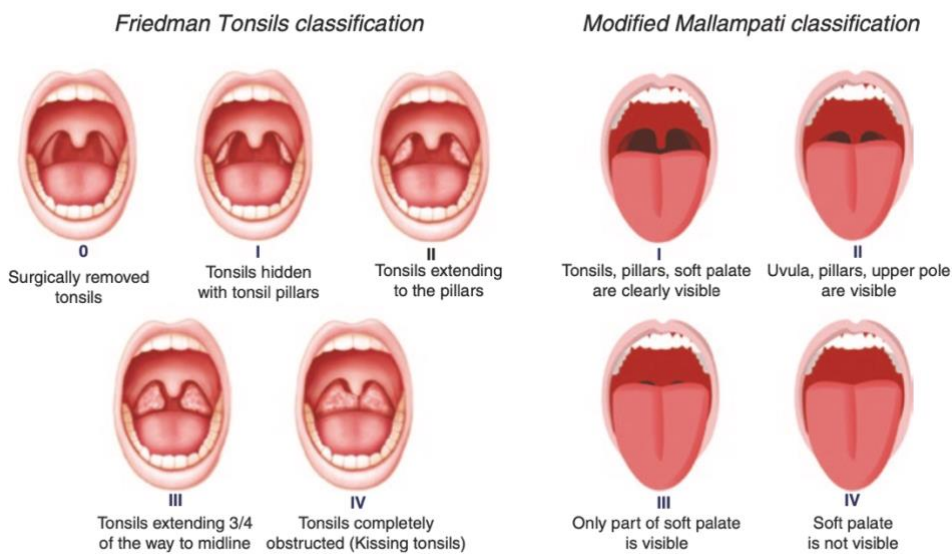
Picture 3: Berlin questionnaire(24).

1.5.4. Mallampati and Friedman scores

The possible anatomical anomalies the patient may have can be related to an increase risk having OSA. To do so a classification has been made to assess the tonsillar hypertrophy. They work as additional value in diagnosing OSA. The Mallampati is Non-invasive and cheap technique. Classified in class from 1 to 4 according to the different structure visible. It is simple to do and don't require any equipment. These scorings give clue to the dentist to identify soft tissues problems and predict the presence of an OSA and its severity(9,25).

Classification of Mallampati	Class 1: Soft palate, Fauces, Uvula, Pillars Class 2: Soft palate, Fauces, Uvula Class 3: Soft palate, Base of the uvula Class 4: Soft palate not visible
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Tables 5: Classification of the Mallampati score(25).



Picture 4 : Friedman and mallampatie classification(9).

1.5.5. Polysomnography

It is the “Gold standard” technique to diagnose the Obstructive sleep apnea. It is usually done overnight at the clinic, measuring different activities: Cerebral with an electroencephalography; Ocular with the electrooculography (EOG); Muscular with an electromyography (EMG); Cardiac with the Electrocardiography (ECG) and the recording of the cardiorespiratory signals. The apnea and hypopnea event are assessed every hours by this technique and are classified according to the severity on the apnea hypopnea index (AHI). There is four types of Sleep analysis, with different amounts of parameters assessed(9,19).

Tyoos	Description
Type 1	Laboratoty test overnight with full analysis with EEG,EOG,ECG,EMG, respiratory efforts, airflow,pulse oxymetry,and additional channels for CPAP level
Type 2	Home studies, same analysis than a type 1 test
Type3	Home studies assess at least 4 parameters, respiratory movement, airflow, cardiac variables, and oxygen saturation. Respiratory-effort-related arousals (RERAs) and Respiratory disturbance index (RDIs) cannot be detected
Type4	Only assess the airflow and Oxygen saturation

Table 6: Sleep test classification (9).

It is important to understand that Home Studies are usually recommended for adults with no comorbidities and only presenting signs and symptoms of a moderate to severe OSA(19).

1.5.6. Other diagnosis techniques

Other additional diagnosis techniques can be use to help the diagnosis of an OSA focusing on the anatomical site as the Nasopharyngoscopy, checking the internal surface of the nose and the throat, or as the acoustic rhinometry analysing the geometry of the nasal airway. Another technique is the Müller’s Maneuver which checks where the callapsing is when the patient inspires(9). After the positive evaluation of the presence of an OSA the patient should be guided to a way of treatment.

1.6. Treatment approach

1.6.1. Lifestyle

This is a very easy treatment as it is defined with the patient motivation. Patient should do lifestyle modifications. Those modifications will focused on reducing the possible daily basis risk factors as stop or drastically reduce smoking, drinking, having a healthy life, do exercises, loose weight for obese patients. The patient should also adopts a good posture avoiding the supine position which favorises the appearance of collapse during sleep. It is also important to prevent any nasal obstruction as it is a cause for OSA(8,9,19).

1.6.2. Continous Positive Airway Pressure (CPAP)

It is considered as the “Gold standard” treatment for any degree of severity of OSA and mainly for the moderate to severe OSA. CPAP works by delivering a constant pressure during the inspiration and the expiration of the patient to keep the airway patency and avoid the closure. A generator creating a constant pressure is plugged to a tube system placed on the patient face with the help of different design of masks, and allows the customization of the treatment for each patient. The evolution of this treatment is to improve the easiness of using it and the efficacy such as reducing the noise of the generator. There is also the possibility that the machine automatically adjusts the pressure for the patient. The machine adapts the pressure to the patient’s position and regarding the pressure he needs to keep the airway patency. This improves the tolerance capacity of the patient. Patient could also preferes the bilevel PAP using high pressure while the patient is inhaling and a lower pressure while he is expiring(6,10). Like almost any treatment, secondary effects can appear. They are frequent mainly at the beginning during the adaptative period. Those secondary effects are realted to the mask which can cause injuries, pain, marks, insomnia, redness, anxiety. The continous positive pressure

administered to the patient can provoke flatulence, sinus and ear pressure, xerostomy, dry eye, aerophagia. All those Secondary effects can be reduced by a good adjustment of the CPAP pressure and mask design(5,8,19).

1.6.3. Oral appliance

Three types of oral appliance are used for the OSA treatment but they don't have the same effectiveness. Depending on the action model, it allows to reduce the vibration of the palate, improve the nasal respiration and place the tongue in a good position. Those 3 oral appliances are: The mandibular advancement devices; The soft palate lifts; The tongue retaining devices(4,13).

1.6.3.1. The Soft Palate Lift (SPL)

The SPL is an appliance made to reduce the vibration of the soft tissue responsible of the snoring by elevating the soft palate and replacing the uvula in a more superior way. Not clinically used very often nowadays. This appliance is not comfortable giving gagging reaction and choking(4,6).

1.6.3.2. The Tongue Retaining Device (TRD)

The TRD, is a simple non-invasive alternative, reversible. The TRD is placed in the mouth to allow the tongue to stay in a forward position and prevent the blockage of the airway by the tongue. These appliances are made of flexible polyvinyl materials and are adapted to each patient's mouth. Noticing that the retention is made by the teeth. In front of the appliance the bulb created serves as a vacuum chamber creating a negative pressure to hold the tongue in a forward position. The advantages of that appliance is that the mandible is free and doesn't have

any rigidity. The TRD is also useful for edentulous patients as the retention is not done by teeth and also for patients with temporomandibular joint (TMJ) disorder and periodontal problems. However, it is contraindicated for patients having nasal airway obstruction because the oral ventilation will be blocked. There is some possible side effects such as sore jaw muscle, increased salivation and difficulties to chew by the morning(9,26,27).

1.6.3.3. Mandibular Advancement Devices (MAD)

1.6.3.3.1. Anatomical reminder

The upper airway has a role to drive the air into the lungs. It is composed by the nasal cavity and oral cavity. The zone involved in the collapse during apnea are mainly, the tongue, the soft palate and the pharynx. The pharynx is a muscular tube situated, posterior to the nasal and oral cavities composed of Four parts: Nasopharynx, Velopharynx, Oropharynx, Hypopharynx. Extended from the base of the skull down to the cricoid cartilage and surrounded by more than 20 muscles. Divided in different groups: the constrictor muscle on the external part of the pharynx, (Superior, Middle, Inferior constrictor muscles) and the elevator muscle, (stylopharyngeus and palatopharyngeus muscle)(28). The tongue is constituted of a fixed base at the level of the oropharynx and the body, which is free in the oral cavity. The tongue base is constituted of muscles inserted on the mandible and the hyoid bone, genioglossus which protrude the tongue and the hyoglossus retract in a low downward position(29). The soft palate is situated behind the hard palate in the velopharynx region(30).

1.6.3.3.2. MAD definition

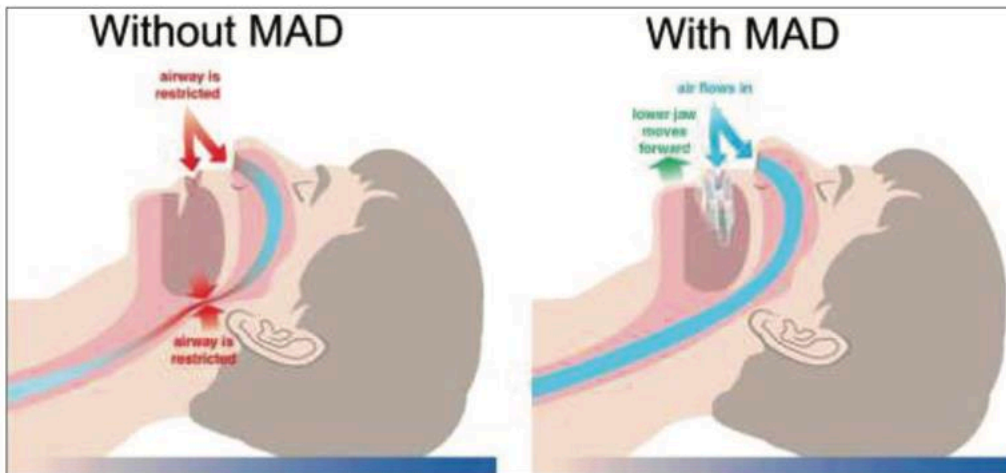
MAD is a type of appliance described as the one that advances the mandible to provoke a modification of the Airway caliber and avoids a possible collapse. The appliance will stabilize the mandible and the hyoid bone, avoiding the posterior rotation of those structures. While the patient is in supine position, the obstruction of the airway should not appear. In a study of Chan et al using the Magnetic Resonance Imaging (MRI) over patient, they showed that the MAD increases the airway volume from $16.5 \pm 0.7 \text{ cm}^3$ vs $18.1 \pm 0.8 \text{ cm}^3$, which is mainly done by increasing the velopharynx. That increase is more important in a lateral way rather than anteroposterior way. The MAD mechanism allows the modification of the structure as the increase of the lower anterior height, hyoid bone higher, parapharyngeal fat lateral displacement and anterior position of the tongue(31,32).



Picture 5 : Bi-bloc custom made MAD(32).



Picture 6 : Mono-bloc custom made(33)



Picture 7 : Airway with and without MAD in supine position(31).

1.6.3.3.3. Indications

Indication	<ul style="list-style-type: none"> → Severe OSA ((AHI>30) or 5<AHI<30 with severe drowsiness) if the patient refused or intolerance of the CPAP → Mild to moderate OSA (5<AHI<30 with mild drowsiness) without comorbidities in first treatment → Primary snoring → Obese patient (first start a lifestyle treatment therapy)
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Table 7: Indication for MAD treatment(4,7,34).

1.6.3.3.4. Contraindications

Containdication	<ul style="list-style-type: none"> Periodontal disease Edentulous patient (8 tooth minimum for good retention) TMJ disorder Mandibular protrusion < 6mm Significant obstruction Severe gag reflex Severe bruxism
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Table 8 contraindication for MAD treatment(4,35–37).

1.6.3.3.5. Differents types of MAD

MAD, as defined before, by placing the mandibule in an anterior position, improves the upper airway caliber. Differentes types and designs exist. There are the Preformed universal MAD and the Custom made MAD. Both of them can be design like mono-block or bi-block. An appliance is usually called “mono-block” when it is made as a single appliance attaching both mandible and maxilla. Unlike “bi-block appliance” corresponds to 2 separated parts (mandibular and maxillary) linked together and allows mandibular movements. The third characteristic of a MAD is if they are fixed (not adjustable) or adujastable (tritable) which means if it’s possible or not to set the mandibular position(3,4,23,37,38).

1.6.3.3.6. Preformed and Custom made MAD

The preformed MAD, (over the counter), (Boil and bite appliance) are known to be easy to make and adapt to the patient’s mouth but retention problems and instability may appear in the long term due to the thermoplastic material. They are Non-adjustable and it’s a non-expensive option. To make the appliance, you need to place the appliance in hot water. The patient has to bite on it, and let cool down the thermoplastic material already placed in the appliance. Unlike the custom made appliance is made by a professional and is known for their capacities of setting and titration. Making them better for the adaptability, confort and duration. Custom made appliances have different possibilities to advance the mandibule. There are appliances that push the mandibule forward by propulsion, the system of protrusion of the mandibule will be attached posteriorly on the maxilar and anteriorly in the mandible, this type of appliance can produce an opening of the bucal cavity as the forces are directed forward and downward reproducing the mouvement of the TMJ without compressing the articulation. At the contrary, the appliance called in traction, tracts the mandibule forward. The system of traction will be

placed posteriorly on the mandible and anteriorly on the maxilla, this type of appliance is more subject to articular pain due to the forces directed forward and upward creating a risk for the articulations(3,4,23,38–40). The recording of variables is needed to make a custom-made MAD. The use of a gauge (George gauge) to determine the centric occlusion, maximum protrusion, maximum retrusion, and protrusion range is important. During the treatment the range of protrusions is usually situated between 50 to 80% of the maximum patient protrusion(4). Two things are also important to take into account when creating a MAD. First the rigidity of the appliance, currently rigid appliances appear as better choice, they have a better adaptation and provide a better retention and confort, it's easier to modify, and allow a better appliance solidity reducing the dental movement. Unlike, a too soft appliance will not create confort for the patient wearing it. Soft appliance don't well protect the TMJ and get damages more rapidly. Secondly the dental recovery, the MAD can have a partial or a complete covering of the tooth. The partial covering should be limited in time, the partial covering of the tooth increases the risk of dental migrations because of the lack of stabilisation. They have less retention and it is easier to lose the appliance. The full covering improves that problem by stabilazing all the arches, increasing the retention and becoming less subject to the exerced forces during the nighth(40).

1.6.3.3.7. MAD realization

Custom-made monobloc and bi-bloc appliances requires clinic and laboratory steps. Monobloc need a bigger precision of the therapeutic mandibular position finding as both aligners a fixed together(41).

Bi-bloc, with free aligners allows a better movement and adaptation due to the different junction types of both arches, so it doesn't need that amount of precision. But the laboratory requires

information: Impressions of both arches, dental class, the protrusion starting from the edge to edge position, the deviation, the maximal opening and if the overbite is important, wax records are made to evaluate the interdental space. All those records will be sent to the laboratory and will allow the starting process of a good bi-block appliance to treat the obstructive sleep apnea(41). The impressions are done with alginate and the model with hard plaster for both types of appliances(41).

1.6.3.3.7.1. Fabrication of a custom-made Monobloc appliance

The construction starts with the clinical step. First the operator needs to find the therapeutic mandibular position.

- In the sagittal plan

At the beginning the appliance will be set at 50% of the maximal mandibular advancement (Maximal protrusion = (overjet + free border of the maxillary incisor) + maximal protrusion from edge to edge position) and will be increased progressively if necessary for the efficacy and also the comfort as a too big advancement could reduce the compliance(41).

- In the frontal plan

The dentist has to guide the protrusion and maintain it without deviation. If a structural deviation is present it should not be corrected(41).

- In the vertical plan

The minimal downward mandibular movement is sought during the protrusion to avoid any fatigue and mandibular retrusion. Indeed, the more the mandible is open the more it goes back. Usually it will be set at 6mm corresponding to 2mm thick for each aligner to reach a good rigidity and 2 mm to let the air pass through(41).

The material used for the records is modeling wax, really helpful with a good thickness and after the cooling the stability of the record remains. The modeling wax is heated at about 50 degrees and folds on itself to reach the good thickness.

The therapeutic mandibular position (TMP) is found first without wax with the help of the incisor as marker of the wanted TMP position. Then the patient needs to open wide and follow the lead of the dentist to reach the best position. 50% of the maximum protrusion, 6mm between the upper and lower incisor, and a good interincisal alignment. Then mounting in the articulator helping by the records.

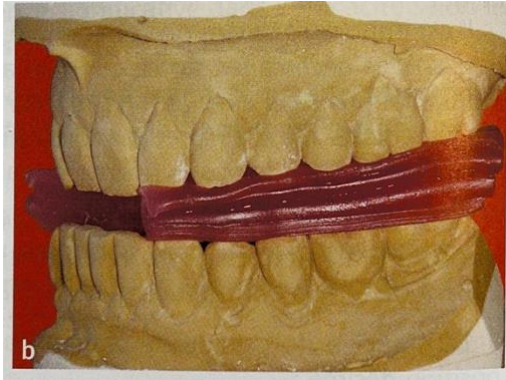


Picture 8: TMP recording with wax(41)

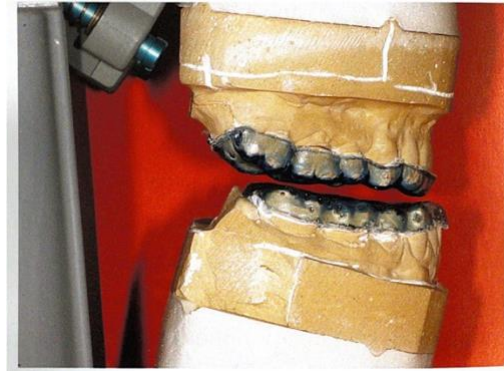
The laboratory's work starts after having recorded all the different information. The split casts are sent to the laboratory. The aligners can be made by thermoforming or by muffling.

The limitation of the aligners will be, lingually set at 3 to 4 mm below the cervical part of teeth and below the contour line in vestibular. Once the aligners are done they are mounted in the articulator and the solidarization process can start. To joined both aligners, auto-polymerizable resin is added from the canine to the last molar on both sides and the anterior zone from canine

to canine should remain free to facilitate the oral respiration. At the end the prosthetist has to polish and regularized the contour(41).



Picture 9: Casts positioning according to the record(41)



Picture 10: Aligners mounted in the articulator (41)



Picture 11: Solidarization of the aligners(41)

1.6.3.3.7.2. Fitting of the MAD

Three steps are necessary to assess: The clipping control, assessing the good retention of the appliance. The good retention is related to a good efficacy of the appliance as if the patient loses the appliance will lead to the unclipping of it and will produce the contrary effect.

If it is a bi-bloc appliance the control of the posterior contact during the protrusion is important as both arches are not in a fixed contact. In fact, the bilateral equilibrium of the upper and lower aligner is needed to avoid any compression of the temporomandibular joint. If any disequilibrium is present the operator should add or remove resin to overcome it.

The control of placing and the removing of the appliance by the patient. The patient has to be able to place and remove the appliance without difficulty(41).



Picture 12: MAD placed in the patient's mouth(41)

1.6.4. Surgery

Surgery, is an invasive treatment, indicated when other treatments failed or were not supported by the patient(5). Different surgical approaches are used depending where is located the obstruction problem: Nasal surgery with the septoplasty, the uvulopalatopharyngoplastyas example for oral surgery type, hypopharyngeal surgery procedures with the tongue reduction and stabilization, laryngeal procedures with the epiglottoplasty and for the complete airway procedure type, the maxillomandibular advancement(5,8,19).

2. Objectives

2.1. Main Objective

- Analyzed and understand the efficiency and the benefit of the Mandibular advancement devices as a treatment for obstructive sleep apnea.

2.2. Secondary Objectives

- Determined which type of Mandibular advancement devices is the more efficient for treatment of obstructive sleep apnea.
- Analyzed and determined the secondary effects created by the action of the MAD on the patient treated.

3. Methodology

3.1. The Strategy

In order to answer in the best way as possible to the written objectives, the research strategy was to use Internet and Library. In order to find all the information needed, website as Pub med, NCBI, research gate, google scholar was used during all the work as portal to access to the knowledge. Online library as the Cray Dulce accessible directly from the university was also very useful to access to books and other articles. In this work the research has been made with key words that helped to find focused information about the subject.

Key words: Obstructive sleep apnea; Polysomnography; Mandibular advancement devices; Continuous positive pressure, surgery; MAD Protocol; Secondary effect; Bi-block; Mono-block; Design of MAD.

3.2. Inclusion an Exclusion criteria

Those criteria were used to improve the research, as inclusion criteria:

- Languages, articles written in French, Spanish and English were included.
- Articles published after 2010 were included.
- Then the most important key words were used as inclusion criteria and focused even more the research.

The exclusion criteria:

- Articles that wasn't coming from academic journal, books and systematic reviews were excluded.
- Articles with a short period of follow-up were excluded.

3.3. Articles selected

All of this strategy of inclusion and exclusion criteria has driven the selection of article. More than 1780 articles related to the subject have been found. After applying the filters 1000 articles have been selected. The most relevant have been used. At the end, the total of article used for that work is: 72 articles.

4. Discussion

4.1. Mandibular advancement device efficacy among the design

4.1.1. Prefomed versus Custom-Made

Custom made and prefomed are two types of mandibulare advancement devices but they are differents by the way they are made. One is made with the help of a professional starting with an impression of the patient's mouth and the other is already made and set, the patient only has to follow the instruction of the brand to adapt it to his mouth. A systematic review from 2018 by Ama Johal et al, 3 studies has been used comparing a ready to use appliance and a custom made appliance. First the apnea hypopnea index is compared. In the study of VADERVEKEN et al the AHI reduction after placing the prefomed appliance is 11 ± 9 and the custom made is 6 ± 8 with a baseline of 13 ± 11 before treatment. In QUINNELL et al study, the baseline is 13.8 ± 6.2 after placement the prefomed group is at 10.8 ± 9.5 and the custom 9.5 ± 8.4 in the last study from the systematic review of johal et al from 13.3 ± 11.9 the AHI drop to 10.68 ± 7.4 for the prefomed and 5.39 ± 4.8 for the custom devices group. The analysis of the different result is clear, the custom made appliance obtain better results in the reduction of the AHI compared to the prefomed appliance and then have a better treatment rate. The results are the same for achieving a complete reduction ($AHI < 5$) or a partial reduction (50% reduction of AHI) of the AHI. Then in the same systemetic study, they compared the reduction of the daytime sleepiness using the Epworth Sleepiness Scale (ESS) and the result shows a significant preference for the Custom made appliance. Two of the three studies used different questionnaires to asses the quality of life (QOL), improvements of the sleepiness, energy. The differents questionnaire are the ESS, The Short Form-36 (SF-36) measuring different aspect of the QOL as the physical, emotional and social aspects, bodily pain, mental health, vitality and general health. The Functional Outcomes of Sleep Questionnaire (FOSQ), five dimensions questionnaire like

Productivity, social, vigilance, intimacy, sexual relationships, divided in 30 questions. According to the ESS score all the Studies analyzed on the systematic review have shown that both appliances reduced it. But custom made was better. From a baseline of 8 meaning, the patient is sleepy according the scale but in the average range, for VADERVEKEN et al the preformed devices group decreased the ESS to 6 ± 4 and the custom group 5 ± 4 . ESS of 11.9 for QUINNELL et al and 11 for JOHAL et al, means that the patient is very sleepy and need a treatment. The preformed appliance decreased the ESS to 8.5 ± 4 and the custom 7.7 ± 3.8 and 7 ± 5.3 and 5 ± 5.1 respectively for the other two studies. The reduction of the sleepiness is present for both appliance but the custom devices remains better. The SF 36 and the FOSQ were only assessed on the last 2 studies reviewed in the articles. The results show real benefits from custom made appliances, improving the energy and the vitality. In terms of compliance and preference of appliance the treatment finality is really related to it. Relating to the systemic study, the preference of the patient for the custom made appliance is stronger than the one of preformed appliance. The adherence and the compliance are also better in custom made devices. It means that the patient feel more confort, retention and ability to tolerate the custom appliance than the preformed. In fact this study shows that the custom made is more effective in all point of comparasion instead of the preformed one. Indeed, the preformed can't fit all patient's mouth in the best way possible (42–44).

4.1.2. Mono-bloc versus Bi-Bloc

Mono or bi-block appliances are different because bi-block devices allow more movement according to the separation between the upper and the lower part linked together by connecting rods, hooks, screws or elastics, acrylic extensions and magnets(45). The literature compares these appliances. The Zhou and al study from 2012 analyses monobloc and bi-bloc appliances

with the same amount of vertical and horizontal protrusion for a short period of time (3 months for each appliance). This study shows that even if there are not many differences between the results of both appliances, the mono-bloc one appears in all points of the study slightly better, like the SaO₂ (oxygen saturation) where the monobloc presents bigger increase. The reduction of the AHI from a baseline of 26.38 ± 4.13 drop to 6.58 ± 2.28 and 9.87 ± 2.88 for the monobloc and the bi-block devices respectively. For the sleep effectiveness, the monobloc appliance improves it more than the bi-block, there is a difference in the sleep efficacy of about 4.5% between the 2 appliances. Compared to the baseline of 80.68, the mono-bloc increases the sleep efficacy (SE) to 89.40 and the bi-block to 84.88. About the reduction of the ESS, no significant difference as been found as they both reduce the ESS in a better severity scale. With that study, at the same amount of vertical and horizontal advancement the monobloc appears as a better choice for the patient with mild to moderate OSA for the reduction of the symptoms and outcomes(46). The same conclusion has been found in the systematic review of Hiroyuki and al reviewing 2 articles comparing the mono-block vs bi-block appliances of different brands and designs. In this Systematic review both appliances show their efficiency by reducing the OSA symptoms but monoblocs remain the best option because of the results are slightly better(47). At the opposite, the randomized control trial from 2018, is comparing the bi-bloc and monobloc appliances, according to the short-term period test of the study there is no difference between the 2 types of appliances. Both reduce the AHI index correctly, both are well accepted by the patient and present similar adverse events(48). A study from 2012 of Woo Hyun Lee and al try to find which is the more effective. In that study both appliances are set at 60% of the maximal protrusion. Mono-bloc and bi-bloc appliance reduced the AHI but the monobloc appears better due to the better response rate. 77.4% in monobloc group compared to 58.3% in bi-bloc group. According to the compliance, the bi-bloc appliance appears better,

68.8% of the monobloc and 83.3% of the bi-bloc are compliant after 1 years, the outcomes are seen in the compliance according to the severity(49). Bi-bloc and mono-bloc appliance present almost no difference comparing the different studies, mono-bloc seems to be slightly more effective but the bi-bloc are more accepted by patient. Both appliances are useful to treat OSA and they are not shown any superiority from each other. Instead the result may depend on the severity of the OSA and the amount of mandibular advancement(48).



Monoblock appliance fitted(46).



Bi-bloc appliance fitted(46).

4.1.3. Adjustable vs Fixed

Comparing the possibility of the appliance being adjustable or fixed, Lettieri et al have achieved the study. The adjustable sample can modify the mandibular advancement to improve the effectiveness of the appliance. In contrast the fixed sample has to keep the same amount of protrusion during all the treatment. The study points out that the adjustable appliances are better for patient compared to fixed appliances. Adjusting the protrusion of the mandibular is important. The study shows that the fixed appliance sample gets into the treatment sooner as the protrusion is already fixed. But the adjustable appliance sample, after having adjusted the mandibular according to the patient tolerance and effectiveness over the OSA, shows a better reduction of AHI. With a baseline of 29.7 ± 24.1 and 30.1 ± 24.4 for the adjustable and fixed samples, with the treatment they drop to 7.6 ± 9.7 and 10.0 ± 12.4 respectively. Both improved

the AHI in general, but according to that study and the different severity of AHI presented, Adjustable appliance still remains a better option for all severity types. On the ESS analysis, results are looking in the same direction, the drowsiness during the day are reduced in both appliances but the adjustable treatment does it better. From a baseline of 13.2 ± 5.1 and 14.3 ± 4.5 it drops to 9.7 ± 4.1 10.6 ± 4.3 on the adjustable and fixed sample respectively. The success of the adjustable appliance of being better is the fact of having the possibility to increase the protrusion without making a new one. Thanks to that a better reduction of the AHI and ESS is possible avoiding the possible secondary effects and creating a better compliance. In the article of Mayoral et al, appliances are guided by the more the mandible is advanced the better(50,51)(52). Emel Sari et al in 2011 compare 2 appliances, one titrable and one nonadjustable. The two appliances are analysed for a period of 1 month. The difference between the two appliances is represented by the titrable one, adjustment are assessed until the patient symptoms and signs disappear. The advancement of the titrable group varied according the need of the patient compared to the non adjustable group in which the advancement is set at 75% for all the participants. The comparison shows that the titrable adjustable appliance allows the professional to set the patient in the best position of protrusion. Both of treatments are able to reduce correctly the AHI and the ESS. Even if patients find a better restful sleep in both groups, the result of the study shows, at 1 week and 1 month, a better success of treatment with the titrable appliance (83,3% for the titrable group at the end of the first month, compared to 66.7% for the non adjustable group). Comparing the different degrees of severity. In Mild OSA group both appliance show great reduction, and both can be recommended as they have reduce the $AHI < 10$ event/hours. In the opposite in the moderate group even both reduce the AHI, the titrable group expresses a better reduction compared to the non adjustable group after 1 month

of treatment (9.2 in titrable group and 13.0 in non adjustable). For those results it will be more recommended to prescribe a adjustable appliance in moderate group(33).

4.1.4. Degree of mandibular advancement and vertical opening

According to the analysis of the results from the different articles treating about either fixed or adjustable, adjustable appliance seems to be more recomendable. This adjustment of the mandible, done to improve the patient situation, is not made without thinking. The degree of advancement must be balanced with the side effects and allows the increase of the airway to a sufficient caliber to avoid the collapse. The protrusion is made by the condyle following the slope of the articular eminence. If the MAD is designed with a little protusion of the mandibule the outcomes of the treatment will be, a no or a smaller improvement of the AHI and symptoms, due to the reduced effects on the airway caliber. In contrary a too increased protrusion will cause TMJ disorder and a limitation of the effectiveness of the treatment(52). The protrusion of the mandubile done by the MAD should be assessed to permit the opening of the airway. Every patient is different and might need a different amount of protrusion which will increase the caliber of the airway. In a study of Piskin et al from 2015, differents degrees of protrusion (0%, 50%,75% and vertical opening (5mm and 10mm) were studied. The result of the study showed that 75% of protrusion and 10mm of vertical opening, have a mean of pharyngeal area among the patient of $770\text{mm}^2 \pm 154$. The difference with the same protrusion and a vertical opening of 5mm is not different ($769\text{mm}^2 \pm 154$). Knowing that, with no splint the mean pharyngeal area is $698 \pm 137\text{mm}^2$, settings the protrusion of the mandibule at 75% from the maximm protrusion is more effective compared to the 50% protrusion group. According to this, the more mandibule protrusion the more airway opening there is(53).

The vertical dimension opening, is important to take into account while creating a MAD. If it increase too much, it will provoke the postero-rotation of the mandibule, creating a diminution of the maximum propulsion possible and a posterior position of the mandibule augmented. According to Mayoral et al, comparing different protrusions at different vertical opening settings, the study shows that if the vertical opening increases of 1mm, it will produce a protrusion reduction of 0.3mm. Then the mandibule will go in a more retrusive posture. During the MAD construction, the recommendation of keeping the Vertical dimension to the minimum helps to avoid the retrusion and maintain the good protrusion, which is effective to treat the OSA(52).

4.2. MAD effectiveness compared to golden standard treatment.

Continous positive airway pressures have always being the first line treatments for moderate to severe OSA as the good reduction of the OSA variables shows. However the MAD is currently a good alternative for the Moderate to severe OSA when the patient is not able to tolerate the CPAP treatment. Both reduce the OSA outcomes(37).

4.2.1. Efficacy on the apnea hypopnea index (AHI).

The efficacy for the apnea and hypopnea index is very important as it is the reducton of the abnormal respiratory event per hour. In the study of Craig L et al, CPAP and MAD are compared over 108 patients. At the end of the treatment a polysomnograph is made to record the outcomes of both treatment. This sample is constituted mainly of patients with moderate to severe OSA. The reduction of the AHI is greater in CPAP group. From a baseline of 25.6 events/h the CPAP group drops to 4.5, the MAD to 11.1 events/ hours. The treatment positive response of the CPAP is almost the double of the MAD response(54). Schwartz et al study, a

systematic and meta analysis review have found the same conclusion as Craig et al study. In the 11 Study Reviewed an heterogeneity of the result has been found between the treatment putting the CPAP in first position for the treatment(55). According to this two articles results the efficacy of MAD is smaller compared to the gold standard treatment. In the study of Doff et al, he compares the MAD and CPAP over 2 years follow up. According to the severity, non severe (mild moderate) OSA the amount of succesfull treatment at 2 month is 4% better for the MAD (84%) vs 80% for the CPAP. At 1 years follow up both treatments obtain the same rate of success. At 2 years, the CPAP was better by 4%. So, Mild to moderate OSA treatment, both of the treatments are equivalent and good choice. In that case, the patient has the choice for equal results. However, in the case of severe OSA, results are different. CPAP shows at every follow up periods a better result on succesful treatment as it reduce more the AHI(56). The efficacy of the health outcomes joins the AHI efficacy analysis as the favor is for the CPAP treatment for a severe OSA but according to a mild to moderate OSA the MAD and CPAP don't have any significant differencies in success.

4.2.2. Efficacy on the Quality of Life

The quality of life of the treatment is assessed by different questionnaires which help to understand the improvement of the daily life signs and symptoms with the treatment and also the sleep efficiency. In Craig et al study, after both treatments, for ESS, no differences have been noticed from 9.1 baseline drop to 7.5 CPAP and 7.2 MAD. In the FOSQ analysis, no differences have been noticed between the two treatment, from a baseline of 16.3 both treatments have reach 17.3. But for the SF 36 the MAD is better from a baseline of 82.3, the CPAP reaches 83.7 and MAD 84.7 according to a better improvement in all the domains of the SF36 questionnaire(54). The study of Gagnadoux et al, compares a titrated MAD and CPAP

treatments and shows that both treatments are similar in terms of daytime sleepiness and ESS. He uses the Quality of life helping by the Nottingham Health Profile questionnaire assessing the physical mobility, social isolation, pain, emotional reactions, energy and sleep. Both treatments improve the QOL, and MAD appears as having reduced even more the baseline of the patients and so improved more the QOL. CPAP appears as reducing more only one characteristic of the Nottingham Health Profile (NHP) which is the energy(57). Again, for the QOL, MAD and CPAP are two treatments very useful to enhance the patient's quality of life treated by ameliorating signs and symptoms.

4.2.3. Efficacy on the cognitive performance

In the study of Gagnadoux et al, a cognitive test has been done to assess the attention and the concentration, named Trail Making Test. According to the results there is no differences with the test A but a difference with the test B. The test B is seen with a better result in CPAP group. The small differences in the test B, between MAD and CPAP are not very relevant to explain a better reduction on the cognitive performance problems from one treatment compare to the other.(57)

4.2.4. Efficacy on the SaO₂ and oxygen saturation

The raise of SaO₂ provoked by the MAD reduces the Hypoxia. According to the B.Fleury et al study, MAD increase the oxygene saturation but the CPAP increases it more when we compared them(58).

4.2.5. Efficacy on the blood pressure

In the Graig et al study the results show that in the no hypertensive group both of the treatments don't lower the blood pressure. At the opposite, among the hypertensive group, a reduction of blood pressure is noticed but without underlining a treatment as better than another(54). In the systematic review of Daniel J. Bratton et al, 51 studies have been reviewed. The results show no differences between the reduction of the Systolic and diastolic blood pressure as both reduced it compared to no treatment(59). In J.C Meurice et al articles, a study with 299 patients, they have had the evaluation of their blood pressure before treatment and during the follow up period. The diastolic and systolic blood pressure are significantly reduced if the patient is hypertensive compare to a non-hypertensive patient where the blood pressure is remaining the same. So the MAD is effective by treating the OSA and also reducing the blood pressure for hypertensive patient(60).

4.2.6. Efficacy on the cardiovascular morbidity

Untreated OSA, increase the risk for cardiovascular mortality. As the CPAP shows a superior efficiency in severe OSA and comparable to MAD in mild to moderate OSA the risk of cardiovascular event should be reduced by both treatments. In the systematic review of Daniel J. Bratton et al 51 studies have been reviewed(59). Anil Anandam et al study from 2013 is compared the MAD and the CPAP in the reduction of the cardiovascular mortality. Over 669 patient have been observed in different groups as: non OSA, MAD treated, CPAP treated and non treated group. The results at the end of the screening show that CPAP and MAD treatments samples, allow a reduction of the cardiovascular mortality. CPAP (0.56 dead per 100 persons/year) and MAD (0.61 dead per 100 persons/year) treated samples have closed results from the non OSA group (0.28 dead per 100 persons/year) and a big difference is noticed with

the untreated OSA group which have 2.1 dead per 100 persons/year. That study spotlights that the non treatment of OSA leads to an increased risk of death by cardiovascular problems. MAD and CPAP instead are reducing that risk by treating the OSA(61).

4.2.7. Compliance

As the MAD can not record the data automatically compared to CPAP having the possibility to obtain objective compliance data. The patient needs to assess his self the report of compliance. Following the study of Graig L et al, the self-report compliance is compared between the MAD and CPAP. Self-report, shows that 51% of the patients prefer the MAD instead the CPAP with only 23,1% of positive answers(54). In an other study, from Schwartz et al systematic analysis, the self report from the patient put in favor the MAD, as the difference of hours per nighth of wearing the appliance is lower in the CPAP by 1,1 hours per nighth(55). Objective compliance in MAD can be assessed with a microsensor reacting to the temperature and fixed to the appliance. It is considered that patient wear the appliance when the temperature is above 35°C(62). A study from Grietje et al assesses the objective compliance using the microsensor on the MAD. Results are offsetting the idea that MAD compliance is better. The study shows that at 3 and 12 months the objective compliance is not significantly different. 7.4 hours/night for the mad and 6.8 h/nighth for the CPAP at 3months and 6.9 hours/nighth and 6.8 hours/night at 12 months. In this study patients haven't been blinded and they are aware of being recorded to assess the compliance. This limitation could lead to an increased of the wearing rate from the patient part. To concluded, the fact that the patients are not blinded, the increase of the compliance can be effectively accorded to the hypothesis, if the patients accept the treatment, the compliance of it will be better(63). The results in the compliance are still confusing as studies assesing the compliance by self report from the patients give the favor to MAD. The

study using the objectives compliance recording by microsensors in MAD gives no favor for both treatments as the results are not significantly different while using the direct report from the patient MAD seems to be better. The study of F. Gagnadoux et al, where the result for the reported compliance is placing MAD as preferred by the patient as the results are better in term of hours and of night use. CPAP is used about 1 hours less compared to the MAD (6.0 (4.0–7.0) and 7.0 (6.0–8.0) hours per night respectively) and 90% night used for CPAP and 98% of the night used in MAD(57).

4.2.8. Mean Disease Alliviation concept (MDA)

It is a concept found in Vanderveken et al. study(62). It is mean comparing the total efficacy and the compliance of the treatment. This means disease alleviation is represented with the surface of a rectangle. The MAD treatment relates to a better compliance and a smaller effectiveness. When comparing MDA rectangles, both treatments have the same amount of surfaces, CPAP has better efficacy but smaller compliance. This concept underlines that both treatments are equal to treat OSA(64).

4.3. Secondary effect

It is impossible to predict patient's secondary effect. There are two types of secondary effects, the short term and the long term secondary effects. It is important to assess those side effects as the MAD and CPAP treatments are considered lifelong treatments. In fact knowing the possible side effects is important because it can produce a reduction of the efficacy(35).

4.3.1. Short term secondary effects

They are frequent and it is possible to identify them over the compliance and the withdraw of the treatment. Easy to manage them, if the patient has a good follow up by a professional. If not, this can lead to give up the treatment(35). Those short term adverse effects include: increasing salivation, xerostomy, tooth pain, irritation of the gum, headaches, and TMJ discomfort and myofascial pain(51). CPAP also presents short time side effects such as eye irritation, nasal congestion, rhinorrhea and choking sensation(65). According to the study of Christian Vacher et al including 40 patients, 57% of them relates transitory secondary effects of tooth pain and TMJ discomfort during less than 30 minutes. These transitory effects can be explained by the biomechanics of the appliance(66). B. Fleury et al, describes that TMJ discomfort appears in 20% to 44% of the patients after some weeks or months of MAD treatment. TMJ discomfort are related also to muscular discomfort where 10% to 36% experienced it. According to B. Fleury et al's articles patients experience also tooth pain, modifications of the occlusion mainly at the awaking after removing the appliance(58). MAD treatment is related to this short appearance side effects, it is caused by the beginning of the treatment because the patient is not accustomed to the appliance. Those side effect are resolved after the patient get used to it and also after some adjustments of the appliance as the protrusion adjustments to palliate the TMJ, muscle and tooth discomfort or the appliance relines to palliate the gingival pain(64).

4.3.2. Long term secondary effect

Long term side effects are more important in term of gravity as they can be irreversible they are mainly related to craniofacial changes, overbite and overjet and TMJ disorder, occlusion. If they are serious for the patient it can lead to the discontinuation of the treatment(35,67). Long term side effects can be also found in CPAP as a decrease of the overbite and the overjet, and a retrusion of the maxillary incisor and a retrude position of the chin. Those effects still remain less important compared with MAD. In CPAP group it is mainly due to the mask pressure(65).

4.3.2.1. Dental and skeletal effect

Assessing side effects needs cephalometric analyses, with the help of landmarks, the long-term therapy craniofacial modifications can be seen. The study of Doff et al from 2010 reviewing the MAD and CPAP side effects after a follow up of 2 years. The patient's analysis revealed some changes. Two-degree reduction of the angle of the maxillary plane and the upper incisors line showing a retroclination, and an increase of 3.7 degrees of the mandibular plane and the lower incisors line showing a proclination is seen(68). This retroclination and proclination are related to a modification of the overjet reduction of 1.7mm and overbite of 1.0mm. The forces created by the MAD are involved, when the patient place the appliance, the mandible try to return to its normal position. As the mandible have to be advanced, the force will be labially directed giving the proclination of the lower incisors. At the opposite, the force against the maxilla is palataly directed being an anchorage point for facilitate the protrusion explaining the retroclination of the maxillary incisor. The amount of protrusion could explain the adverse effects of overjet and overbite reductions as the for being effective mild to moderate group of patients need less advancement and so the group will have less side effect compared to the severe group where more protrusion should be applied to be effective(68). Doff et al, explains

also a reduction of 0.7 (± 1.6) mm the line between the Sella nasion–perpendicular line and the menton line. It is explained by a more backward and downward mandible rotation guided by the incisal guidance. The dental changes induced by the MAD, result of an increase of the lower facial height 0.8 (± 1.5) mm. Comparing the MAD results to the CPAP treatment, none of those modifications has been found. But if changes occurred at the dental or skeletal level it will be mainly due to the mask pressure over the mouth of the patient(68). This reduction of the overbite and overjet is related to the amount of protrusion as more protrusion will provoke more pressure(69). Dental changes can be related to the number of teeth present in the mouth. Missing tooth is a contraindication in MAD treatment. The lack of tooth can be a factor in the force distribution leading to a bigger movement of the incisor(70). A different study from Julia Anne Margarethe Uniken Venema et al, doesn't use the cephalometry but casts to assess the side effects. She also assesses the angle classification with the right and left cuspid and 1st molar. The angle classification changes much more in the MAD group compared to the CPAP group. Class III angle patient increases over the time more in MAD than in CPAP. This changes over a class III angle is due to the reduction of the overbite and the overjet done by the appliance over the time. Because of that it leads to possible open bite(65). In the study of Julia A.M. Uniken Venema et al patient passed from angle class I to class II or class II to class I or III due to the reduction of the overjet and the overbite leading to a mesial shift of the occlusion(71). At the opposite of the Doff et al study, in the CPAP group of that study reduction of the overbite and overjet is assessed, and related to the pressure of the mask over the patient mouth(65).

4.3.2.2. TMJ disorder

Another long-time effects can be seen, temporomandibular disorder during mandibular advancement treatment or CPAP. TMJ disorders, includes masticatory muscles and temporomandibular joint. MAD by protruding the mandible place it in a non-natural position (forward and downward).

According to the study of Doff et al from 2011, 103 patients were included in that study comparing MAD and CPAP and the TMJ side effects. Compared to the baseline of the study and after 2 month an increase of TMD is seen, 5% in CPAP and 10% in MAD. After that follow-up the TMD have diminished and returned near to the baseline occurrence. Showing at the initial stage in increase of occurrence bigger in MAD compared to the CPAP, MAD results also to a bigger pain over the study compared to CPAP without giving restriction in the TMJ complex. The pain assessed by the MAD group at 2 months follow up could be related to the capsular ligament and the muscle of the TMJ. As the Mandible during the sleep is not in the normal resting position, the tension produces over the muscles and ligaments and the retrodiscal tissues can lead to pain. This pain according to the study is present during a short period of time and will decreased with the time to return. While the patients are wearing the appliance, they adopt a new vertical dimension. This vertical dimension can also lead to pain but as the pain reduce over the time, patient seems to be able to adapt to a new vertical dimension. The dentist should prescribes to the patient mandibular exercises during the treatment, with that, the compliance of the patient can be improved at the initial phase where the pain is more present(72).

5. Conclusion

1. The results of this bibliographic review indicate that treatment of OSA with MAD on adults has positive effects and its effectiveness is comparable with the gold standard treatment (CPAP) for mild and moderate patients. The CPAP remains the first-choice treatment for severe cases unless it is refused or contraindicated, in this cases MAD will be an indicated treatment.
2. MAD types effectiveness are related to the amount of protrusion as all types are able to treat the signs and symptoms. But the custom made and the adjustable appliances have better efficiency. The good titration of the appliance is necessary as the protrusion of the mandible is related to the success of the treatment.
3. The appearance of secondary effects is unpredictable and appear at short-term, adaptation of the patient and some adjustments are necessary to overcome them. And long-term side effects, give dento-skeletal problems due to the pressure applied by the appliance and TMJ disorder, related to the non-natural position of the mandible due to the appliance. The sides effects appear more often in MAD and are more important compared to the CPAP according to researches. For this reason, a strict control of the MAD's patients by the dentist have to be done to avoid or reduce side effects.
4. Future clinical studies are needed that focus on measuring long-term adverse effects, the use of a standardized protocol could help the data analyses, so that an exhaustive and complete comparison with CPAP therapy can be conducted.

6. Social responsibility

The mandibular advancement devices are related to the economic sustainability. It is different among the countries, but in general it is a cheaper and an effective solution compare to CPAP. Countries define OSA as a public health problem. And treatment need to be affordable to the population affected by this disorder. States are creating plans to reduce the cost of the appliance for the patient. If the cost effectiveness ratio of MAD is high the economic sustainability is better.

Environmental sustainability: As it requires less component compare to the golden standard treatment (CPAP), MAD is very simple to make. It is done at the laboratory with substances used over decades and it respects more the environment as it doesn't need elements that pollutes the environment. It is not done by industries unlike the CPAP using electronic parts coming from around the world. MAD is a useful alternative to CPAP, being almost as effective in terms of reduction of OSA symptoms and has a lower energy consumption in the conception.

The social sustainability of the MAD is very important, OSA is in the daily life of many people. OSA gives a lot of social problems affecting occupational and private people's life. MAD reduces the symptoms, helps the patients to recover their restful sleep, reduces the mortality rate of patient with comorbidities. Even if the MAD is responsible of side effects the increase of the quality of life is overcoming them. Furthermore, MAD is easier to wear for the patient and more pleasant for the spouse compare to the CPAP. It is less cumbersome facilitating the transport and so it is simpler to feel serene in all the different postures (at the hotel, friend's house).

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Michel Billiard
Editors

Sleep Medicine

A Comprehensive Guide
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 Springer

THIRTY YEARS OF CPAP

A brief history of OSA

Is 30 years a long time or a short time in medical science? Have we come a long way, or is our understanding of OSA still in its infancy? Whichever way you look at it, Sullivan et al's 1981 paper brought a revolutionary treatment to light.

OSA has been observed since ancient times, and there are records of its symptoms, such as heavy snoring, dating back over 2,000 years. The term 'Pickwickian syndrome' was adopted in the late 19th century to describe apneic symptoms, but research concentrated on the patients' obesity rather than on disordered breathing during sleep. In 1965 the first polysomnograph recorded apneas during sleep. Further research in the 1960s established that obesity was not essential for OSA, but that there were other comorbidities associated with sleep-disordered breathing.¹

In 1970 the first sleep clinic was established at Stanford University, California, USA by William Dement. In 1972 Christian Guilleminault joined the clinic, concentrating on respiratory disorders during sleep.

The period 1975–80 saw an intense amount of research into sleep and apnea, with 319 articles appearing in medical literature. In 1978 JE Remmers et al resolved the key question of where airway obstruction occurred during an apnea, showing that the locus of airway closure lay in the oropharynx, not the larynx.²

In Toronto, Canada, Eliot Phillipson started investigating respiratory control in dogs in 1970. He was joined in 1976 by Colin Sullivan on a post-doctoral research fellowship from Sydney University, Australia. Sullivan worked with the dogs in the laboratory, studying effects such as hypoxia, hypercapnia, control mechanisms during REM and non-REM sleep, arousal and laryngeal stimulation. In 1979 Sullivan returned to Sydney and devised a mask that would fit over a dog's snout to deliver air or an experimental gas.

Until this time the experiments on the dogs had been conducted via a tracheotomy. Similarly, people who were severely affected by OSA were given tracheotomies to bypass the blockage in the upper airway and allow unimpeded breathing. However, this was a dramatic solution for the problem, and could in itself have serious consequences for the patient. Sullivan was moving towards an alternative non-invasive treatment for OSA.

He applied his experimentation on dogs to humans, using masks that were created for each patient. A plaster cast would be made of their nose and fibreglass moulded over the cast. The resulting fibreglass shape would be fitted with air inlets and outlets and attached to the patient's face each night with silicone adhesive. Tubes to the therapy device were attached to the mask, providing the patient with a source of continuous positive airway pressure that could be regulated.

Sullivan used his observations of five patients using this technology for his 1981 paper. He describes the patients as having long histories of noisy snoring and excessive daytime

From the Editor



It is 30 years since Colin Sullivan et al's groundbreaking paper, 'Reversal of obstructive sleep apnoea by continuous airway pressure applied through the nares' was published in *The Lancet*.¹ To mark its anniversary, in this edition of *ResMedica* we have interviewed one of the sleep technicians from Dr Sullivan's first sleep unit; a long-time practitioner in sleep-disordered breathing; a long-time user of continuous positive airway pressure (CPAP); and one of the people deciding the future direction of CPAP. These interviews take us from the source of Dr Sullivan's paper to the present day and beyond.

The global significance of Professor Colin Sullivan's work was acknowledged when he was profiled in *The Lancet* in April this year.²

We thank everyone interviewed for this edition of *ResMedica* for generously giving us their time and sharing their thoughts and passion about the treatment of obstructive sleep apnea (OSA).

Once again we extend an invitation to you to contribute your thoughts to *ResMedica* by sending an email to theeditor@resmed.com.au

We look forward to your comments.

Sleep well,

Alison Hansford,
Global Editor

1. Sullivan CE, Berthon-Jones M, Issa FG, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1981; 862–5.

2. Kirby, T. Profile: Colin Sullivan: inventive pioneer of sleep medicine. *Lancet* 2011; 377:1485

sleepiness to the point where their lives were seriously affected. Two had lost their jobs as a result of falling asleep at work, and one, a 13-year-old boy, was unable to stay awake at school and had consequently been categorised as 'mentally retarded'. Sullivan notes that three of the five had been offered, but refused a tracheotomy. He conducted three all-night sleep studies on each patient, using CPAP on the third night. He writes: 'Continuous positive airway pressure completely prevented the upper airway occlusion in each of the five patients. The upper airway occlusion could be turned off and on simply by increasing or reducing the level of positive airway pressure.'

Sullivan had shown that the occurrence of obstructive sleep apnea could be reversed by the application of CPAP to provide 'a pneumatic splint for the nasopharyngeal airway'. Acceptance of this treatment did not come immediately, and application of his findings to a wide audience was even slower.

> CONTINUED PAGE 2

History of Dental Sleep Medicine

Robert R. Rogers, DMD, DABDSM¹; John Remmers, MD²; Alan A. Lowe, DMD, PhD, ABDSM³; Peter A. Cistulli, MD, PhD⁴; Jeff Prinsell, DMD, MD, DABDSM⁵; Donald Pantino, DDS, ABDSM⁶

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As this inaugural issue of *The Journal of Dental Sleep Medicine* debuts, it is my pleasure to recount the historical highlights of the development of Dental Sleep Medicine over the past 25 years. The youthfulness of this nascent field allows us the luxury of calling on some of the original pioneers for their direct recollection and comment in this regard. I have chosen to let each submission stand essentially on its own to reflect the individual author's unique, personal take on the subject. As such, there may be some redundancies in the content and a difference in writing style. I am hoping this adds to the depth and texture of the presentation.

The basic underpinnings of Dental Sleep Medicine are the critical roles sleep and breathing play in the maintenance of overall health and well-being and indeed, life itself. Presently, it is well known that sleep deprivation and sleep disorders are highly prevalent and are intimately related to adverse social, health, and occupational problems. Snoring is no longer thought to be benign, and obstructive sleep apnea is viewed in epidemic proportion worldwide. Fortunately, continuous positive airway pressure (CPAP) has been found to prevent upper airway collapse, normalize nocturnal sleep and breathing, alleviate daytime hypersomnolence, and decrease associated medical comorbidity. However, despite the benefits positive airway pressure intervention can provide, adherence remains a significant issue and effective treatment options are needed.

The impact of tongue and mandibular positioning on upper airway patency has been well known for over 100 years and remains the functional basis of the "jaw thrust" during CPR maneuvers. In the early 1900s, surgeons occasionally treated micrognathic infants by suturing the tongue to the lower lip in a forward position attempting to open and stabilize the upper airway during sleep. By 1930, helmets and chin straps were utilized by physicians for mandibular repositioning in an effort to accomplish the same goal. The first described use of an intra-oral mandibular repositioning device is generally attributed to Pierre Robin, a French pediatrician, in 1923.¹ Since then, surgical advancement of the maxilla and mandible has been reported and, in 1982, Charles Samuelson, a Chicago psychiatrist, designed a tongue retaining device that was shown to be effective.²

Substantial progress has been documented in the expanding literature. A milestone review appeared in the 1995 literature summarizing the efficacy of oral appliance therapy (OAT) for the first time and suggested clinical practice parameters.^{3,4} In 2005, these two documents were revised to reflect the newer data in this growing field,^{5,6} and the scientific literature is replete today with investigations supporting OAT. Most recently, the American Academy of Sleep Medicine has, for the first time, published guidelines for the evaluation, management, and long-term care

of obstructive sleep apnea in adults that cites OAT as an effective option for management of sleep disordered breathing.⁷

Today, Dental Sleep Medicine represents a synergistic blend of medicine and dentistry as dentists bring their unique skills associated with the stomatognathic system to bear on the problems that physicians face attempting to create and maintain a patent airway during sleep.

—Robert R. Rogers

DENTISTS, DENTISTRY, AND SLEEP APNEA: AN UNINHIBITED HISTORY AND PERSONAL PERSPECTIVE

For a physician and non-historian to write on the historical role of dentists in sleep science might be presumptuous or folly depending on your viewpoint. I will attempt to mitigate concerns by restricting my comments to sleep apnea.

Dentistry was pivotal in the earliest elucidation of sleep apnea. In 1932 the well-known French dental surgeon, Pierre Robin, described a breathing impairment during sleep caused by pharyngeal obstruction in children with micrognathia and glossoptosis.¹ This was the first clear demonstration that oral-pharyngeal anatomic abnormalities can induce a narrowing of the pharyngeal airway that obstructs breathing during sleep. In this seminal contribution, Robin laid the groundwork for understanding the role of pharyngeal obstruction in the pathogenesis of sleep apnea. Arguably, the entire field of sleep disordered breathing was founded by a dentist who discovered that anatomic abnormalities of the pharynx lead to obstruction of breathing during sleep.

Thirty-eight years later, another dental scientist, Eberhart Sauerland, provided a complimentary insight to Robin's when he discovered the respiratory action of pharyngeal muscles. While not formally educated as a dentist, "Ebo" was a dental academician at the UCLA Dental School. In 1970, he reported that during inspiration, humans displayed a burst of EMG activity in the genioglossus muscle, thereby dilating and stiffening the pharynx when subatmospheric intraluminal pressure acts to narrow it.⁸ In 1976 with Ron Harper, he extended this finding by showing that the rhythmic respiratory bursting of the genioglossus is exhibited by normal humans during sleep.⁹ Thus, the contributions of two dental scientists, Robin and Sauerland, laid the foundation for our understanding of that pharyngeal structure and function engage in a complex neural-anatomical interaction that maintains pharyngeal airway during wakefulness and sleep.

In the early 1970s, Sauerland and I serendipitously moved to the same institution, the University of Texas Medical Branch,

Oral Appliances for Snoring and Obstructive Sleep Apnea



Samuel A. Mickelson, MD, FACS, FABSM

KEYWORDS

- Sleep oral appliance • Mandibular advancement device (MAD)
- Oral appliance therapy (OAT) • Primary snoring • Obstructive sleep apnea syndrome
- OSAS

KEY POINTS

- The efficacy of a mandibular advancement device is less than that of continuous positive airway pressure (CPAP) but mandibular advancement devices have similar effectiveness, with a self-reported compliance rate of approximately 80%, and typically are preferred over CPAP.
- Due to improved compliance, mandibular advancement devices are reasonable second-line treatments of patients who refuse or fail positive airway pressure (PAP) and potentially first-line treatment options.
- Mandibular advancement devices are effective in reducing apnea-hypopnea index via a nonlinear dose-dependent relationship with degree of advancement, and greater protrusion often results in better outcomes.
- Relative contraindications for a mandibular advancement device include loose teeth, significant dental carries or periodontitis, severe bruxism, upcoming dental work or braces, temporomandibular joint (TMJ) pain, significant nasal obstruction, and findings of TMJ crepitation or popping, or inadequate mandibular protrusion.
- Side effects of mandibular advancement devices are common but typically can be managed by slowing protrusion of the appliance. TMJ or dental pain is the most common problem associated with these appliances followed by occlusal changes and shifting of the teeth.

OVERVIEW AND HISTORY OF ORAL APPLIANCE THERAPY

The first mandibular advancement type of oral appliance for sleep apnea was developed in 1988, designed as maxillary boil-and-bite fixed appliance with a plastic extension behind the mandibular incisors and intended to protrude the mandible by pressing on the mandibular incisors. The appliance was soon found to cause anterior displacement of the mandibular incisors and also had problems with retention on the

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L'apnée du sommeil

Le syndrome d'apnée du sommeil (SAS) est une affection fréquente et un réel problème de santé publique, concernant 2 à 5 % de la population adulte. L'officiel, professionnel de santé de proximité, peut jouer un rôle de dépistage, de suivi et de conseil auprès des personnes concernées.

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L'apnée du sommeil se définit par un arrêt de la respiration au cours du sommeil d'au moins 10 secondes, répété au moins cinq fois par heure. On observe un relâchement des muscles du pharynx et le blocage partiel ou total de la trachée provoquant des interruptions (apnées) ou des réductions (hypopnées) de respiration, souvent liées à des ronflements. La mauvaise oxygénation du cerveau entraîne des "micro-réveils", d'où un sommeil saccadé et d'une qualité affectée, responsable de nombreux symptômes.

Le dépistage

Le syndrome d'apnée du sommeil (SAS) attire de plus en plus l'attention des professionnels de santé mais son dépistage et son diagnostic au quotidien restent compliqués. Il se révèle souvent à la suite d'un accident de la route ou du travail. À l'officine, un interrogatoire ciblé est nécessaire, évaluant ronflements, pauses respiratoires

constatées par le conjoint, maux de tête au réveil, libido diminuée, fatigue, somnolence, irritabilité, déprime et difficultés de concentration. La connaissance du terrain est également importante : obésité, âge (45-64 ans), sexe masculin (plus exposé), anomalies ou antécédents ORL, prise d'alcool ou de sédatifs, hypertension artérielle (HTA). Enfin, une évaluation de la somnolence peut être réalisée avec l'échelle de somnolence d'Epworth qui permet d'effectuer un dépistage et d'orienter le patient vers son médecin (encadré 1).

Les complications

Certains facteurs aggravent le syndrome d'apnée du sommeil mais en sont aussi les conséquences. Il est alors questions de comorbidités. **Le manque répété d'oxygène a des conséquences immédiates sur la fonction cardiaque, entraînant un sommeil léger et non récupérateur responsable d'une somnolence diurne.** Avec le temps, cela accroît

le risque cardiovasculaire : HTA, insuffisance coronaire (diminution du débit sanguin avec risque d'infarctus) et accident vasculaire cérébral. **La somnolence excessive en journée a des incidences sur la vie socioprofessionnelle : fatigue, baisse de la concentration, irritabilité, dépression, risques sécuritaires (accidents du travail, de la vie domestique et de la route).**

Le diagnostic

Le diagnostic de l'apnée du sommeil repose, en premier lieu, sur la consultation médicale : bilan des troubles ressentis par le patient

Définitions

- ◆ **Apnée** : arrêt du flux d'air aérien pendant une durée ≥ 10 secondes.
- ◆ **Hypopnée** : diminution du flux respiratoire de moins de 50 % associée à une désaturation en hémoglobine $> 4\%$.

Encadré 1. Échelle de somnolence d'Epworth

Dans les situations suivantes, quelle est la probabilité que vous somniez ou que vous assoupissiez ? (0 jamais ; 1 minime ; 2 modérée ; 3 importante) :

- vous êtes assis et vous lisez ;
- vous regardez la télévision ;
- vous êtes assis, inactif, dans un lieu public (salle de réunion, cinéma...);
- vous êtes passager d'une voiture ou d'un autobus qui roule depuis une heure sans faire d'arrêt ;

- vous êtes assis dans une voiture pendant plus d'une heure sans interruption ;
- vous vous allongez pour vous reposer dans la journée lorsqu'il vous est possible de le faire ;
- vous êtes assis et vous bavardez avec quelqu'un ;
- vous êtes assis tranquillement après avoir pris votre repas du midi, sans avoir consommé de l'alcool ;

- vous êtes au volant d'une voiture immobilisée quelques minutes dans le trafic ou à un feu rouge.

Le score total : 8 somnolence normale ; 8-10 somnolence moyenne ; 11-15 somnolence élevée ; 16-20 somnolence sévère ; 21-24 somnolence excessive.

Le patient est orienté vers son médecin si les éléments recueillis évoquent la suspicion d'une apnée du sommeil.

Série aérosolthérapie

Dispositifs d'inhalation, conseils d'utilisation et précautions d'emploi
L'apnée du sommeil

L'oxygénothérapie : appareillage, manipulations, indications et précautions d'emploi

Valérie BATTU

Mots clés

- Micro-réveil
- Pression positive continue
- Respiration
- Syndrome d'apnée du sommeil

Updates on Definition, Consequences, and Management of Obstructive Sleep Apnea

JOHN G. PARK, MD; KANNAN RAMAR, MD; AND ERIC J. OLSON, MD

On completion of this article, you should be able to (1) identify patients who may have obstructive sleep apnea (OSA), (2) recognize the implications of untreated OSA, and (3) review and apply different treatment options for management of OSA.

Obstructive sleep apnea (OSA) is a breathing disorder during sleep that has implications beyond disrupted sleep. It is increasingly recognized as an independent risk factor for cardiac, neurologic, and perioperative morbidities. Yet this disorder remains undiagnosed in a substantial portion of our population. It is imperative for all physicians to remain vigilant in identifying patients with signs and symptoms consistent with OSA. This review focuses on updates in the areas of terminology and testing, complications of untreated OSA, perioperative considerations, treatment options, and new developments in this field.

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AASM = American Academy of Sleep Medicine; AHI = apnea-hypopnea index; APAP = automatically adjusting positive airway pressure; CMS = Center for Medicaid and Medicare Services; CompSAS = complex sleep apnea syndrome; CPAP = continuous positive airway pressure; OSA = obstructive sleep apnea; PAP = positive airway pressure; PSG = polysomnography; RDI = respiratory disturbance index

Obstructive sleep apnea (OSA) is a disorder in which a person frequently stops breathing during his or her sleep. It results from an obstruction of the upper airway during sleep that occurs because of inadequate motor tone of the tongue and/or airway dilator muscles. In the United States, the prevalence of OSA is estimated to be 3% to 7% in men and 2% to 5% in women.¹ Among patients with a body mass index (calculated as the weight in kilograms divided by height in meters squared) greater than 28, OSA is present in 41%.² The prevalence of OSA can be as high as 78% in morbidly obese patients who present for bariatric surgery.³ Up to 93% of women and 82% of men may have undiagnosed moderate to severe OSA,⁴ emphasizing the importance of vigilant evaluations for signs and symptoms of OSA. These may include a spouse's report of disruptive snoring, daytime sleepiness, obesity, and large neck circumference (>42 cm in men)⁵ (Table 1).⁶ Not all patients, however, present with typical findings. For example, patients with heart failure and OSA may not present with daytime sleepiness.⁷ Likewise, a patient may not be aware of snoring or apneic episodes. Thus, it is important to obtain collateral sleep history and recognize associated medical comorbid conditions that may implicate OSA as an underlying diagnosis. This article is intended as an update to the 2003 Concise Review for Clinicians covering OSA.⁸

TERMINOLOGY AND TESTING

Diagnosis of OSA usually requires overnight polysomnography (PSG) to detect the frequency of apneic and hypopneic events⁹ (Table 2). Traditionally, this is done as a standardized, facility-based PSG, with multichannel recordings that help determine sleep time, sleep stages, respiratory effort, airflow, cardiac rhythm, oximetry, and limb movements.⁹ The apnea-hypopnea index (AHI) is the average number of disordered breathing events per hour. Other definitions of sleep-related breathing disorders are highlighted in Table 2. Typically, OSA syndrome is defined as an AHI of 5 or greater with associated symptoms (eg, excessive daytime sleepiness, fatigue, or impaired cognition) or an AHI of 15 or greater, regardless of associated symptoms.⁹

Overnight, facility-based, and attended PSG remains the criterion standard for diagnosis of OSA. Recently, the Center for Medicaid and Medicare Services (CMS) approved the use of portable PSG to diagnose OSA.¹⁰ The American Academy of Sleep Medicine (AASM) recommends considering this route in patients with a high pretest likelihood for moderate to severe OSA without other substantial comorbid conditions.¹¹ The portable monitors include at least 3 sensors that detect respiratory events in the home setting. Because these monitors cannot determine the actual sleep time, AHI cannot be determined (because AHI is an index of apnea and hypopnea per hour of sleep). Rather, the resultant index is known as the respiratory disturbance index (RDI), which represents the frequency of apnea and hypopnea per hour of recording time. Because the total recording time often exceeds the actual sleep time of the patient, RDI from portable monitors often underrepresents the severity of OSA. Hence, a negative result from a portable

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HAUTE AUTORITÉ DE SANTÉ

RÉVISION DE CATÉGORIES HOMOGENÈS DE DISPOSITIFS MÉDICAUX
ÉVALUATION ÉCONOMIQUE

Évaluation clinique et économique des dispositifs médicaux et prestations associées pour la prise en charge du syndrome d'apnées hypopnées obstructives du sommeil (SAHOS)

Volet 1 : Volet médico-technique et évaluation clinique

Date de validation par la CNEDiMTS : 15 juillet 2014

APNÉE OBSTRUCTIVE DU SOMMEIL

et autres troubles respiratoires du sommeil

Guide d'exercice

du Collège des médecins du Québec



MARS 2014

Orthodontics in Obstructive Sleep Apnea Patients

A Guide to Diagnosis,
Treatment Planning,
and Interventions

Su-Jung Kim
Ki Beom Kim
Editors

Obstructive sleep apnea syndrome: natural history, diagnosis, and emerging treatment options

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Abstract: Sleep apnea is an entity characterized by repetitive upper airway obstruction resulting in nocturnal hypoxia and sleep fragmentation. It is estimated that 2%–4% of the middle-aged population has sleep apnea with a predilection in men relative to women. Risk factors of sleep apnea include obesity, gender, age, menopause, familial factors, craniofacial abnormalities, and alcohol. Sleep apnea has been increasingly recognized as a major health burden associated with hypertension and increased risk of cardiovascular disease and death. Increased airway collapsibility and derangement in ventilatory control responses are the major pathological features of this disorder. Polysomnography (PSG) is the gold-standard method for diagnosis of sleep apnea and assessment of sleep apnea severity; however, portable sleep monitoring has a diagnostic role in the setting of high pretest probability sleep apnea in the absence of significant comorbidity. Positive pressure therapy is the mainstay therapy of sleep apnea. Other treatment modalities, such as upper airway surgery or oral appliances, may be used for the treatment of sleep apnea in select cases. In this review, we focus on describing the sleep apnea definition, risk factor profile, underlying pathophysiologic mechanisms, associated adverse consequences, diagnostic modalities, and treatment strategies.

Keywords: positive airway pressure, obstructive sleep apnea, cardiovascular disease

Introduction

Obstructive sleep apnea (OSA) is a condition characterized by repetitive episodes of complete or partial collapse of the upper airway during sleep resulting in complete cessation (apnea) or reduction (hypopnea) of airflow leading to arousal and hypoxia.¹ Apnea is defined as complete cessation of oronasal airflow for at least 10 seconds. Alternatively, the definition of hypopnea requires (1) a drop of $\geq 30\%$ of oronasal airflow from baseline associated with $\geq 4\%$ decrease in oxyhemoglobin saturation, (2) a drop of $\geq 50\%$ of oronasal airflow from baseline and $\geq 3\%$ decrease of oxyhemoglobin saturation, (3) a reduction in airflow as above along with an associated electroencephalographic arousal. In sleep study monitoring, the frequency of apneas and hypopneas per hour of sleep (apnea–hypopnea index [AHI]) is the key measure to define and stratify the severity of OSA, although inherent limitations to this metric include not taking into consideration degree of accompanying hypoxia, length of respiratory events, etc. AHI levels of 5, 15, and 30 have been used as cutpoints to define mild, moderate and severe OSA, respectively.¹ Apnea can be distinguished as obstructive vs central based upon presence or absence of thoracoabdominal effort.²

Symptoms of OSA may include daytime sleepiness, impaired concentration and mood, morning headaches, snoring, and witnessed breathing pauses during sleep

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REVUE GENERALE

Le syndrome d'apnées-hyponées obstructives du sommeil (SAHOS)

The obstructive sleep apnea-hyponea syndrome (OSAHS)

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SUMMARY

Obstructive sleep apnea syndrome (OSAS), due to upper airway collapse, is frequent but still underestimated. It is associated with an increase in cardiovascular risk and with a decrease in sustained attention that may cause traffic accidents or occupational accidents.

The functional symptoms of OSAS are well tolerated in long term. The snoring is very sonorous, bothering the entourage more than concerned person, intersected by the pauses and the reprises of noisy respiration, constituted principal clinical signe. The excessive hypersleepiness of the day is well evocative for OSAS. It is associated with tired sensation, whether permanent or perceiving at walkup in morning. The technical diagnosis of OSAS is based on polysomnography or polygraphy registries permitting an easy access to diagnosis which might be done in ambulatory.

The reference treatment of OSAS is still continuous positive airway pressure (CPAP). The use of continuous positive airway pressure have made in progress the management of obstructive sleep apnea syndrome. It is indicated when apnea-hyponea is more than 30/h associated with evocative clinical symptom. The management is also considered severity of respiratory and sleep disorders and concomitant diseases such as systemic hypertension, coronary diseases, and cerebral vascular events.

KEYWORDS: OSAS, hypersleepines, apnea-hyponea, CPAP, AHI

RESUME

Le syndrome d'apnées obstructives du sommeil (SAOS), dû à un collapsus des voies aériennes supérieures, est une maladie fréquente mais encore sous-estimée. Cette maladie est associée à une augmentation du risque cardiovasculaire et à une baisse des capacités d'attention soutenue pouvant être responsables d'accidents de conduite et d'accidents professionnels.

Les signes fonctionnels du SAOS sont souvent tolérés longtemps. Le ronflement très sonore, gênant l'entourage beaucoup plus que l'intéressé, entrecoupé de pauses avec reprise ventilatoire bruyante, constitue le signe clinique principal. L'hypermomnolence diurne excessive est très évocatrice du SAOS. Il s'y associe une sensation de fatigue soit permanente, soit perçue surtout le matin au réveil. Les techniques diagnostiques du SAOS sont basées sur l'enregistrement polysomnographique ou polygraphique permettant un accès plus aisé au diagnostic qui peut être fait en ambulatoire.

Le traitement de référence du SAOS reste la pression positive continue (PPC). L'utilisation de la pression positive continue a révolutionné la prise en charge du syndrome d'apnées obstructives du sommeil. Elle est indiquée quand l'index d'apnées-hyponées (IAH) est supérieure à 30/h et une symptomatologie clinique évocatrice. Le traitement tient compte aussi bien de la gravité des troubles de la respiration et du sommeil que d'éventuelles affections concomitantes telles que l'hypertension artérielle, les maladies coronariennes, et les accidents vasculaires cérébraux.

MOTS CLES: SAOS, hypersomnolence, apnées-hyponées, PPC, IAH

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Physiopathologie du syndrome d'apnées-hypopnées obstructives du sommeil et de ses conséquences cardio-métaboliques

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■ Points essentiels

Le syndrome d'apnées-hypopnées obstructives du sommeil (SAHOS) correspond à la succession d'apnées et d'hypopnées au cours du sommeil, par collapsus complet ou incomplet des voies aériennes supérieures (VAS). Les mécanismes contribuant au collapsus des VAS durant le SAHOS sont complexes et multifactoriels.

Différents facteurs influencent le calibre et la stabilité des VAS durant le sommeil incluant des anomalies anatomiques des tissus mous, du squelette osseux du massif maxillo-facial, une infiltration graisseuse liée à l'obésité et des mouvements liquidiens au cours du sommeil *fluid shift*. Au cours du sommeil, il existe une augmentation des résistances des VAS et de la collapsibilité pharyngée du fait d'une diminution de l'activité des muscles des VAS et d'une altération du réflexe protecteur du pharynx.

Le SAHOS principalement sévère est associé à un risque cardiovasculaire et métabolique élevé. Les épisodes répétés d'apnées-hypopnées via l'hypoxie intermittente et la fragmentation du sommeil vont activer les principaux mécanismes intermédiaires (activation sympathique, stress oxydant, inflammation tissulaire locale et systémique, variation des pressions intra-thoraciques) qui seront à l'origine des conséquences cardio-métaboliques.

Le SAHOS sévère est associé à une augmentation de l'incidence des événements cardiovasculaires létaux (infarctus du myocarde et accident vasculaire cérébral [AVC]) et non létaux (hypertension artérielle [HTA], infarctus du myocarde, AVC, pontage aorto-coronarien et angioplastie coronarienne).

Le SAHOS est associé au diabète de type 2 et à son mauvais contrôle à la dyslipidémie et à la stéatopathie métabolique.

Le dépistage du SAHOS chez les patients cardio-métaboliques et le traitement intégré du SAHOS et de ses co-morbidités cardio-métaboliques sont donc essentiels dans la prise en charge clinique.



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**ESTUDIO SOBRE EL USO DEL APARATO
INTRAORAL DE AVANCE MANDIBULAR
ORTHOAPNEA PARA EL TRATAMIENTO DEL
SÍNDROME DE APNEA-HIPOPNEA
OBSTRUCTIVA DEL SUEÑO**

Tesis Doctoral

Pablo Valiente Samalea

Málaga, 2017

Obstructive sleep apnea: current perspectives

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Abstract: The prevalence of obstructive sleep apnea (OSA) continues to rise. So too do the health, safety, and economic consequences. On an individual level, the causes and consequences of OSA can vary substantially between patients. In recent years, four key contributors to OSA pathogenesis or “phenotypes” have been characterized. These include a narrow, crowded, or collapsible upper airway “anatomical compromise” and “non-anatomical” contributors such as ineffective pharyngeal dilator muscle function during sleep, a low threshold for arousal to airway narrowing during sleep, and unstable control of breathing (high loop gain). Each of these phenotypes is a target for therapy. This review summarizes the latest knowledge on the different contributors to OSA with a focus on measurement techniques including emerging clinical tools designed to facilitate translation of new cause-driven targeted approaches to treat OSA. The potential for some of the specific pathophysiological causes of OSA to drive some of the key symptoms and consequences of OSA is also highlighted.

Keywords: pathophysiology, sleep-disordered breathing, arousal, upper airway physiology, control of breathing, precision medicine

Introduction

Obstructive sleep apnea (OSA) is an increasingly common, chronic, sleep-related breathing disorder.^{1–3} OSA is characterized by periodic narrowing and obstruction of the pharyngeal airway during sleep. Untreated OSA is associated with long-term health consequences including cardiovascular disease,^{4,5} metabolic disorders,⁶ cognitive impairment,⁷ and depression.⁸ Common symptoms include excessive daytime sleepiness, fatigue, non-refreshing sleep, nocturia, morning headache, irritability, and memory loss.^{9,10} Untreated OSA is also associated with lost productivity and workplace and motor vehicle accidents resulting in injury and fatality.^{11–13} The costs of untreated OSA and sleep loss are substantial.^{14,15} Recommended therapy can relieve symptoms^{16,17} and reduce some of the associated sequelae.^{18,19} However, many people with OSA struggle with the first-line therapy, continuous positive airway pressure (CPAP), for which adherence rates remain unacceptably low.^{20,21} Non-CPAP therapies (e.g., oral appliance therapy and upper airway surgery) are beneficial in many cases but have variable and unpredictable efficacy.^{22–25} Thus, new approaches to treat OSA are required.

Indeed, most people with OSA are undiagnosed and untreated.^{26–28} In some cases, this may be attributed to, at least in part, a lack of awareness of the disorder.²⁹ Other potential barriers to seek treatment include stigma related to some of the features of the disease such as snoring, access to polysomnography (PSG) and diagnostic services

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REVIEW

Open Access

Daily rhythms of the sleep-wake cycle

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Abstract

The amount and timing of sleep and sleep architecture (sleep stages) are determined by several factors, important among which are the environment, circadian rhythms and time awake. Separating the roles played by these factors requires specific protocols, including the constant routine and altered sleep-wake schedules. Results from such protocols have led to the discovery of the factors that determine the amounts and distribution of slow wave and rapid eye movement sleep as well as to the development of models to determine the amount and timing of sleep. One successful model postulates two processes. The first is process S, which is due to sleep pressure (and increases with time awake) and is attributed to a 'sleep homeostat'. Process S reverses during slow wave sleep (when it is called process S'). The second is process C, which shows a daily rhythm that is parallel to the rhythm of core temperature. Processes S and C combine approximately additively to determine the times of sleep onset and waking. The model has proved useful in describing normal sleep in adults. Current work aims to identify the detailed nature of processes S and C. The model can also be applied to circumstances when the sleep-wake cycle is different from the norm in some way. These circumstances include: those who are poor sleepers or short sleepers; the role an individual's chronotype (a measure of how the timing of the individual's preferred sleep-wake cycle compares with the average for a population); and changes in the sleep-wake cycle with age, particularly in adolescence and aging, since individuals tend to prefer to go to sleep later during adolescence and earlier in old age. In all circumstances, the evidence that sleep times and architecture are altered and the possible causes of these changes (including altered S, S' and C processes) are examined.

Keywords: Adolescence, chronotype, circadian rhythm, endogenous component, exogenous component, old age, sleep homeostat, time awake

Review

Sleep in adults

Most adults take a consolidated 7-hour sleep during the night [1]. The reasons for sleeping at night are partly because the environment is quiet and also it would be unconventional to arrange meetings or meet friends at this time. Moreover, we are diurnal creatures and after a normal day when we have been awake and active for some time, we feel tired in the evening and ready for sleep. It is possible to sleep at other times, as is evident from the lifestyle of night workers but, even in a quiet environment, daytime sleep tends to be more fragmented and shorter than nocturnal sleep. That is, the ability to get to sleep and sleep uninterrupted for long enough shows a daily rhythm. This rhythm of ease of getting to sleep (sleep propensity) is clear if individuals

miss a night's sleep; they feel tired during the night but, in spite of having had no sleep, they then feel less tired as the new day dawns and, during the afternoon, will feel surprisingly alert. However, by the evening, the sensation of fatigue increases markedly and becomes increasingly difficult to resist. This result indicates that there is an increasing drive to sleep as the amount of time awake continues to rise but that it is mixed with a rhythmic component that varies during the course of the 24 hours.

A good sleep is recuperative and removes the feelings of fatigue (and also produces an improvement in cognitive ability); individuals then feel ready to face the rigors of a new day. Intuitively, the concept of increasing 'sleep pressure' with increasing time awake is not difficult to appreciate (even if the detailed nature of sleep pressure is not understood). However, the presence of daily rhythms in the desire to sleep, staying asleep and waking up might be less easy to understand. In fact, when repeated measurements are made over the course of

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INVITED REVIEW SERIES:

NEW FRONTIERS IN SLEEP-DISORDERED BREATHING

SERIES EDITORS: MATTHEW NAUGHTON, PETER A. CISTULLI AND PHILIP DE CHAZAL

Global burden of sleep-disordered breathing and its implicationsM. MELANIE LYONS,^{1,2}  NITIN Y. BHATT,¹ ALLAN I. PACK³ AND ULYSSES J. MAGALANG¹¹Division of Pulmonary, Critical Care, and Sleep Medicine, The Ohio State University Wexner Medical Center, Columbus, OH, USA; ²School of Nursing, University of Pennsylvania, Philadelphia, PA, USA; ³Division of Sleep Medicine/Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA**ABSTRACT**

One-seventh of the world's adult population, or approximately one billion people, are estimated to have OSA. Over the past four decades, obesity, the main risk factor for OSA, has risen in striking proportion worldwide. In the past 5 years, the WHO estimates global obesity to affect almost two billion adults. A second major risk factor for OSA is advanced age. As the prevalence of the ageing population and obesity increases, the vulnerability towards having OSA increases. In addition to these traditional OSA risk factors, studies of the global population reveal select contributing features and phenotypes, including extreme phenotypes and symptom clusters that deserve further examination. Untreated OSA is associated with significant comorbidities and mortality. These represent a tremendous threat to the individual and global health. Beyond the personal toll, the economic costs of OSA are far-reaching, affecting the individual, family and society directly and indirectly, in terms of productivity and public safety. A better understanding of the pathophysiology, individual and ethnic similarities and differences is needed to better facilitate management of this chronic disease. In some countries, measures of the OSA disease burden are sparse. As the global burden of OSA and its associated comorbidities are projected to further increase, the infrastructure to diagnose and manage OSA will need to adapt. The use of novel approaches (electronic health records and artificial intelligence) to stratify risk, diagnose and affect treatment are necessary. Together, a unified multi-disciplinary, multi-organizational, global approach will be needed to manage this disease.

Key words: economics, global burden, obesity, obstructive sleep apnoea, risk factors.

INTRODUCTION

Approximately 1 billion of the world's population of 7.3 billion people, between the ages of 30 and 69 years, are estimated to have the most common type of sleep-disordered breathing, obstructive sleep apnoea (OSA).¹ OSA prevalence is rising and affects all countries. The increase in prevalence is driven by the global increase in obesity, the major risk factor for OSA.²⁻⁶ In this review, we examine contributing factors, the burden of disease, approaches and challenges in addressing the global burden of OSA.

GLOBAL POPULATION RISK FACTORS: ACCOUNTING FOR DIFFERENCES IN CHARACTERISTICS

In a pivotal study using state-of-the-art statistical modelling techniques, Benjafield *et al.* revealed a heterogeneous distribution of OSA across 193 countries, estimating greater than 936 million people as having OSA, defined by an apnoea-hypopnoea index (AHI) of ≥ 5 events/h, and, importantly, of which 425 million people as having moderate-severe OSA, defined by an AHI ≥ 15 events/h.¹ The prevalence of OSA ranged from 7.8% (Hong Kong) to as high as 77.2% (Malaysia) for mild OSA, and from 4.8% (Ireland and Israel) to 36.6% (Switzerland) for moderate-severe OSA.¹ This prevalence of OSA was neither associated with the state of economic development within countries nor limited to specific continents. In this study, the 10 countries with the highest OSA prevalence estimates with an AHI ≥ 5 /h were led by China followed by the USA, Brazil, India, Pakistan, Russia, Nigeria, Germany, France and Japan.¹ The five countries with the highest OSA prevalence estimates with an AHI ≥ 15 /h were China (estimated at 66 million patients, prevalence estimate of 8.8% of population ages 30-69), India (29 million, 5.4%), Brazil (25 million, 26%), USA (24 million, 14.5%) and Russia (20 million, 25.6%).¹ This study is timely and suggests that a better understanding of the global phenotypes of OSA risk is necessary.

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Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis



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Summary

Background There is a scarcity of published data on the global prevalence of obstructive sleep apnoea, a disorder associated with major neurocognitive and cardiovascular sequelae. We used publicly available data and contacted key opinion leaders to estimate the global prevalence of obstructive sleep apnoea.

Methods We searched PubMed and Embase to identify published studies reporting the prevalence of obstructive sleep apnoea based on objective testing methods. A conversion algorithm was created for studies that did not use the American Academy of Sleep Medicine (AASM) 2012 scoring criteria to identify obstructive sleep apnoea, allowing determination of an equivalent apnoea-hypopnoea index (AHI) for publications that used different criteria. The presence of symptoms was not specifically analysed because of scarce information about symptoms in the reference studies and population data. Prevalence estimates for obstructive sleep apnoea across studies using different diagnostic criteria were standardised with a newly developed algorithm. Countries without obstructive sleep apnoea prevalence data were matched to a similar country with available prevalence data; population similarity was based on the population body-mass index, race, and geographical proximity. The primary outcome was prevalence of obstructive sleep apnoea based on AASM 2012 diagnostic criteria in individuals aged 30–69 years (as this age group generally had available data in the published studies and related to information from the UN for all countries).

Findings Reliable prevalence data for obstructive sleep apnoea were available for 16 countries, from 17 studies. Using AASM 2012 diagnostic criteria and AHI threshold values of five or more events per h and 15 or more events per h, we estimated that 936 million (95% CI 903–970) adults aged 30–69 years (men and women) have mild to severe obstructive sleep apnoea and 425 million (399–450) adults aged 30–69 years have moderate to severe obstructive sleep apnoea globally. The number of affected individuals was highest in China, followed by the USA, Brazil, and India.

Interpretation To our knowledge, this is the first study to report global prevalence of obstructive sleep apnoea; with almost 1 billion people affected, and with prevalence exceeding 50% in some countries, effective diagnostic and treatment strategies are needed to minimise the negative health impacts and to maximise cost-effectiveness.

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Introduction

Obstructive sleep apnoea is a common disorder that can present with or without symptoms and is accompanied by major neurocognitive and cardiovascular sequelae.^{1–3} At present, care of patients with obstructive sleep apnoea varies by country and depends on a patient's symptoms. In well resourced settings, considerable efforts are being made to diagnose and treat individuals with obstructive sleep apnoea, but available data suggest that most cases of obstructive sleep apnoea remain undiagnosed and untreated, even in developed countries. In developing countries, there is generally little awareness of obstructive sleep apnoea, and diagnostic and treatment options are often not available or have not been adapted for resource-poor settings.⁴ Because of the multifactorial and social consequences of obstructive sleep apnoea, the disorder is associated with a high economic and societal burden. In 2015, the cost of diagnosing and treating

obstructive sleep apnoea in the USA was approximately US\$12.4 billion.⁵ The global cost of diagnosing and treating obstructive sleep apnoea has not been estimated because information about global prevalence is required first.

Evidence suggests that obstructive sleep apnoea is an important contributor to poor health outcomes and that treatment of this condition is generally beneficial in minimising the associated adverse clinical outcomes and improving sleep-related quality of life.⁶ Thus, focusing on effective treatment of obstructive sleep apnoea might be one approach for reducing associated health-care costs and the negative impact of the condition, such as the cognitive impact of sleepiness.^{7,8} Additionally, given the shift in focus from issues around malnutrition and basic hygiene towards chronic health conditions, such as the obesity pandemic and its associated metabolic complications,^{9–12} the ageing population demographic,¹³

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Interactions Between Obesity and Obstructive Sleep Apnea

Implications for Treatment

*Abel Romero-Corral, MD, MSc; Sean M. Caples, DO;
Francisco Lopez-Jimenez, MD, MSc; and Virend K. Somers, MD, PhD, FCCP*

Obstructive sleep apnea (OSA) adversely affects multiple organs and systems, with particular relevance to cardiovascular disease. Several conditions associated with OSA, such as high BP, insulin resistance, systemic inflammation, visceral fat deposition, and dyslipidemia, are also present in other conditions closely related to OSA, such as obesity and reduced sleep duration. Weight loss has been accompanied by improvement in characteristics related not only to obesity but to OSA as well, suggesting that weight loss might be a cornerstone of the treatment of both conditions. This review seeks to explore recent developments in understanding the interactions between body weight and OSA. Weight loss helps reduce OSA severity and attenuates the cardiometabolic abnormalities common to both diseases. Nevertheless, weight loss has been hard to achieve and maintain using conservative strategies. Since bariatric surgery has emerged as an alternative treatment of severe or complicated obesity, impressive results have often been seen with respect to sleep apnea severity and cardiometabolic disturbances. However, OSA is a complex condition, and treatment cannot be limited to any single symptom or feature of the disease. Rather, a multidisciplinary and integrated strategy is required to achieve effective and long-lasting therapeutic success.

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Abbreviations: AHI = apnea-hypopnea index; CPAP = continuous positive airway pressure; HDL = high-density lipoprotein; OSA = obstructive sleep apnea

Our understanding of the implications of obstructive sleep apnea (OSA) on disease pathophysiology has been evolving rapidly. OSA is thought to adversely affect multiple organs and systems and may be especially relevant to cardiovascular disease.^{1,2} It

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has been implicated in the etiology of hypertension^{3,4} and in the progression of several established medical conditions such as congestive heart failure, atrial fibrillation, diabetes, and pulmonary hypertension.¹ However, whether OSA is causally linked to the development of these latter disease states remains to be proven.^{1,2}

In the adult population, the prevalence of OSA is estimated to be ~25%, and as high as 45% in obese subjects.⁵⁻¹⁰ Obesity predisposes to and potentiates OSA. The prevalence of OSA and its consequences are likely to increase in light of the current obesity epidemic. Recent estimates suggest that 60% of the adult population in industrialized countries is overweight (BMI ≥ 25 kg/m²) and at least 30% is obese

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Diagnosis and Treatment of Obstructive Sleep Apnea in Adults

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Obstructive sleep apnea is a common disorder that causes patients to temporarily stop or decrease their breathing repeatedly during sleep. This results in fragmented, nonrestful sleep that can lead to symptoms such as morning headache and daytime sleepiness. Obstructive sleep apnea affects persons of all ages, with an increasing prevalence in those older than 60 years. The exact prevalence is unknown but is estimated to be between 2% and 14%. There are many health conditions associated with obstructive sleep apnea, including hypertension, coronary artery disease, cardiac arrhythmias, and depression. Loud snoring, gasping during sleep, obesity, and enlarged neck circumference are predictive clinical features. Screening questionnaires can be used to assess for sleep apnea, although their accuracy is limited. The diagnostic standard for obstructive sleep apnea is nocturnal polysomnography in a sleep laboratory. Home sleep apnea tests can be performed for certain patients but are generally considered less accurate. Continuous positive airway pressure is the first-line treatment; adherence rates are variable and seem to improve with early patient education and support. Other treatment modalities include weight reduction, oral appliance therapy, and surgery to correct anatomic obstructions, although there is insufficient evidence to support these types of surgeries. Bariatric surgery can improve sleep parameters and symptoms in obese patients with obstructive sleep apnea and can result in remission in many patients. (*Am Fam Physician*. 2016;94(5):355-360. Copyright © 2016 American Academy of Family Physicians.)



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► **Patient information:** A handout on this topic, written by the authors of this article, is available at <http://www.aafp.org/afp/2016/0901/p355-s1.html>.

Obstructive sleep apnea (OSA) is a common, chronic disorder that disrupts breathing during sleep. It affects persons of all ages but especially those middle-aged and older.¹ Patients with OSA temporarily stop or decrease their breathing (apnea or hypopnea, respectively) repeatedly during sleep.²⁻⁵ This cessation or decrease in breathing is the result of repetitive partial or complete obstruction of the airway caused by narrowing of the respiratory passages.^{4,6-8} These breathing disruptions can awaken a person or prevent deep, restful sleep. The effects of fragmented sleep on daytime fatigue and sleepiness are widely recognized.^{3,6}

Prevalence

The exact prevalence of OSA is unknown, although estimates range from 2% to 14% in community-screened populations to a much higher prevalence in certain subgroups (i.e., 20% to 90% of persons referred for sleep studies).^{7,9}

Men are three times more likely than women to have OSA. It is particularly uncommon in nonobese, premenopausal women;

however, the rates of OSA in postmenopausal women not taking hormone therapy approach the rates of OSA in men of a similar age and body mass index.^{6,10,11}

The prevalence of OSA increases with age, especially in persons older than 60 years. OSA is also more prevalent among persons who are obese. Both an aging population and a growing rate of obesity contribute to the increasing rate of OSA.^{1,2,4,6}

Associated Conditions

OSA is important from a public health perspective because patients with untreated OSA have higher rates of health care use, including more frequent and longer hospitalizations and higher health care costs.^{2,4,12,13} Furthermore, OSA has been associated with higher rates of unintentional injury, including motor vehicle collisions and work-related injuries, which add to the public health burden.^{3,4,6,9,14}

OSA has been associated with increased morbidity and mortality rates^{2,8,14,15} and decreased quality-of-life scores,^{6,15} as well as numerous health problems (*Table 1*^{2,16-20}); however, a causal relationship has not been

Obstructive sleep apnea is a common disorder in the population— a review on the epidemiology of sleep apnea

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Abstract: The prevalence of obstructive sleep apnea (OSA) defined at an apnea-hypopnea index (AHI) ≥ 5 was a mean of 22% (range, 9-37%) in men and 17% (range, 4-50%) in women in eleven published epidemiological studies published between 1993 and 2013. OSA with excessive daytime sleepiness occurred in 6% (range, 3-18%) of men and in 4% (range, 1-17%) of women. The prevalence increased with time and OSA was reported in 37% of men and in 50% of women in studies from 2008 and 2013 respectively. OSA is more prevalent in men than in women and increases with age and obesity. Smoking and alcohol consumption are also suggested as risk factors, but the results are conflicting. Excessive daytime sleepiness is suggested as the most important symptom of OSA, but only a fraction of subjects with AHI >5 report daytime sleepiness and one study did not find any relationship between daytime sleepiness and sleep apnea in women. Stroke and hypertension and coronary artery disease are associated with sleep apnea. Cross-sectional studies indicate an association between OSA and diabetes mellitus. Patients younger than 70 years run an increased risk of early death if they suffer from OSA. It is concluded that OSA is highly prevalent in the population. It is related to age and obesity. Only a part of subjects with OSA in the population have symptoms of daytime sleepiness. The prevalence of OSA has increased in epidemiological studies over time. Differences and the increase in prevalence of sleep apnea are probably due to different diagnostic equipment, definitions, study design and characteristics of included subjects including effects of the obesity epidemic. Cardiovascular disease, especially stroke is related to OSA, and subjects under the age of 70 run an increased risk of early death if they suffer from OSA.

Keywords: Epidemiology; population-based; sleep apnea; prevalence

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Introduction

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of partial and complete airway obstructions during sleep with repetitive apneas and hypopneas as a result (1). The disease severity is measured using the apnea-hypopnea index (AHI), i.e., the mean number of apneas and hypopneas per hour of sleep. OSA is defined when the AHI is ≥ 5 and OSA syndrome when AHI ≥ 5 is accompanied with daytime sleepiness (1).

The American Association of Sleep Medicine defined daytime sleepiness as mild, moderate and severe in relation to impact on social life during the daytime (1). The Epworth Sleepiness Scale (ESS) is, however, the most often used measure to define daytime sleepiness (2,3). Diagnostic equipment and definitions of oxygen desaturations, apnea, hypopnea, OSA and daytime sleepiness has, changed over time, which in turn affects estimates of the prevalence of sleep apnea.



**Syndrome d'apnée-hypopnée
obstructive du sommeil : facteurs
de risque et comorbidités**

**Obstructive sleep apnea–hypopnea
syndrome: risk factors and
comorbidities**

**متلازمة انقطاع ضعف التنفس أثناء النوم : عوامل الخطر
والاضطرابات المشتركة**

A. Jniene, M. El Ftouh, M. T. El Fassy Fihry

الملخص : يشكل مرض انقطاع ضعف التنفس الأنسدادي أثناء النوم حالة شائعة لدى البالغين في منتصف العمر. ومنذ فترة طويلة كان يعتبر هذا المرض بسيط ونادر الحدوث إلا أنه الآن «يؤخذ على محمل الجد»، ويعتبر مشكلة صحية كبيرة، لأنه في حالة عدم علاجه، فإنه يسبب زيادة في نسبة الاضطرابات المشتركة وحتى في نسبة الوفيات فيما يخص جهاز القلب والأوعية الدموية (ارتفاع ضغط الدم المقاوم للعلاج الطبي، ومرض الشريان التاجي...)، وجهاز الغدد الصماء، الجهاز العصبي (السكتة الدماغية، ومرض الانسداد التجلطي...) والأمراض النفسية (الاكتئاب، وضعف الأداء الإدراكي) : ومن الناحية الفيزيولوجيا المرضية، يتميز هذا المرض بانسداد كامل أو جزئي للمجاري الهوائية العلوية عند الشهيق، وهو ناتج عن إنطواء هيكل البلعوم الشيء الذي يحدث بشكل متكرر أثناء النوم.. وهذا الانطواء ناتج عن عدد من عوامل الخطر التي يتوجب معرفتها بما أنها تسمح باستحضار المرض (الجنس الذكري، السن المتقدم، السمنة، تناول الأدوية، وأمراض أخرى كبعض أمراض الغدد الصماء، أمراض في الجهاز الهضمي، تشوهات خلقية...) ونظرا للفيزيولوجيا المرضية وتعدد عوامل الخطورة والاضطرابات المشتركة ومضاعفاته - تعتبر هذه المتلازم مرضي (عرض) يستلزم تضافر متعدد الإختصاصات.

الكلمات الأساسية : انقطاع التنفس، النوم، ضعف التنفس.

Résumé : Pathologie fréquente chez le sujet adulte d'âge moyen, le syndrome d'apnée-hypopnée obstructive du sommeil est une maladie ayant longtemps été considérée comme à la fois rare et bénigne. Aujourd'hui, elle est «prise au sérieux» et considérée comme un problème majeur de santé publique car, non traitée, elle expose à une augmentation de la morbidité voire de la mortalité cardiovasculaire (hypertension artérielle surtout résistante au traitement médical, pathologie coronarienne...), endocrinienne (syndrome métabolique), neurologique (accidents vasculaires cérébraux, maladie thromboembolique...) et psychique (dépression, déficiences des performances cognitives...).

Sur le plan physiopathologique, la maladie est caractérisée par l'obstruction complète ou partielle des voies aériennes supérieures à l'inspiration résultant d'un collapsus des structures pharyngées survenant de façon répétée au cours du sommeil. Ce collapsus est secondaire à un certain nombre de facteurs de risques primordiaux à reconnaître puisqu'ils permettent de suspecter la maladie (sexe masculin, âge avancé, obésité, prise médicamenteuse, certaines pathologies endocriniennes, malformatives, digestives...).

De part sa physiopathologie, la diversité de ses facteurs de risque, comorbidités et complications, cette pathologie est considérée comme « transversale » dont la prise en charge doit être multidisciplinaire.

Mots clés : Apnée, hypopnée, sommeil.

Abstract : A common condition in the middle-aged adults, the obstructive sleep apnea-hypopnea syndrome is a disease which has been considered both rare and benign illness. Now it is «taken seriously» and considered as a real public health problem because, if untreated, it leads to increased morbidity or even mortality concerning the cardiovascular system (hypertension particularly resistant to medical treatment, coronary artery disease ...), the endocrine system (metabolic syndrome), the neurological system (stroke, thromboembolic disease ...) and also psychologically (depression, impairment of cognitive performance ...).

As concern the pathophysiology, the disease is characterized by a complete or partial obstruction of the upper airway on inspiration due to a collapse of the pharyngeal structures occurring repeatedly during sleep.

This collapse is secondary to a number of risk factors crucial to recognize because they allow to suspect the disease (male gender, advanced age, obesity, drug taking, certain disorders as endocrinal diseases, malformation diseases, digestive diseases...)

Due to its pathophysiology, the diversity of its risk factors, comorbidities and complications, the pathology is considered as «transversal » that support should be multidisciplinary.

Keywords: Apnea, hypopnea, sleep.

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Obstructive sleep apnoea syndrome and its management

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Abstract: Obstructive sleep apnoea (OSA) is a common disorder characterized by repetitive episodes of nocturnal breathing cessation due to upper airway collapse. OSA causes severe symptoms, such as excessive daytime somnolence, and is associated with a significant cardiovascular morbidity and mortality. Different treatment options are now available for an effective management of this disease. After more than three decades from its first use, continuous positive airway pressure (CPAP) is still recognized as the gold standard treatment. Nasal CPAP (nCPAP) is highly effective in controlling symptoms, improving quality of life and reducing the clinical sequelae of sleep apnoea. Other positive airway pressure modalities are available for patients intolerant to CPAP or requiring high levels of positive pressure. Mandibular advancement devices, particularly if custom made, are effective in mild to moderate OSA and provide a viable alternative for patients intolerant to CPAP therapy. The role of surgery remains controversial. Uvulopalatopharyngoplasty is a well established procedure and can be considered when treatment with CPAP has failed, whereas maxillar-mandibular surgery can be suggested to patients with a craniofacial malformation. A number of minimally invasive procedures to treat snoring are currently under evaluation. Weight loss improves symptoms and morbidity in all patients with obesity and bariatric surgery is an option in severe obesity. A multidisciplinary approach is necessary for an accurate management of the disease.

Keywords: continuous positive airway pressure, obstructive sleep apnoea, oral appliance, positional therapy, uvulopalatopharyngoplasty

Introduction

Obstructive sleep apnoea (OSA) is a common chronic disorder affecting about 2–4% of the adult population, with the highest prevalence reported among middle-aged men [Young *et al.* 1993]. The condition is characterized by repetitive episodes of complete or partial collapse of the upper airway (mainly the oropharyngeal tract) during sleep, with a consequent cessation/reduction of the airflow [Guilleminault *et al.* 1976; Guilleminault and Quo, 2001]. The obstructive events (apnoeas or hypopnoeas) cause a progressive asphyxia that increasingly stimulates breathing efforts against the collapsed airway, typically until the person is awakened (Figure 1).

The diagnosis of OSA is made through different levels of nocturnal monitoring of respiratory, sleep and cardiac parameters (polisomnography

or nocturnal cardio-respiratory poligraphy), aimed to detect the obstructive events and the following changes in blood oxygen saturation (SaO₂) [Berry *et al.* 2012; American Academy of Sleep Medicine, 2014]. The most commonly used index to define the severity of OSA is the apnoea/hypopnoea index (AHI), calculated as the number of obstructive events per hour of sleep and obtained by nocturnal cardiorespiratory monitoring [Berry *et al.* 2012] (Table 1). The aetiology of OSA is multifactorial, consisting of a complex interplay between anatomic, neuromuscular factors and an underlying genetic predisposition toward the disease [Guilleminault and Quo, 2001; Dempsey *et al.* 2010]. Risk factors include snoring, male gender, middle age, menopause in women, obesity and a variety of craniofacial and oropharyngeal features such as a large neck circumference, retro- or micrognazia, nasal obstruction, enlarged tonsils/

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THESE

POUR LE DIPLOME D'ETAT DE DOCTEUR EN CHIRURGIE DENTAIRE

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par

Fanny GERE

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**REGLAGE AUTONOME
DES ORTHESES D'AVANCEE MANDIBULAIRE PAR LES PATIENTS
ADULTES ATTEINT DU SYNDROME D'APNEE HYPOPNEE
OBSTRUCTIVE DU SOMMEIL**

Directeur de thèse : Pr Frédéric VAYSSE

JURY

Président :	Professeur Frédéric VAYSSE
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The Berlin questionnaire screens for obstructive sleep apnea in idiopathic intracranial hypertension

Abstract

Background—Obstructive sleep apnea (OSA) may be associated with idiopathic intracranial hypertension (IIH), a disorder most commonly occurring in young obese women. Because polysomnography, the standard test for diagnosing OSA, is expensive and time-consuming, questionnaires have been developed to identify persons with OSA. The Berlin questionnaire (BQ) reliably identifies middle-aged and older persons in the community who are at high-risk for OSA. We aimed to validate the BQ as a screening tool for OSA in IIH patients.

Methods—Patients with newly diagnosed IIH completed the BQ and then underwent diagnostic polysomnography. The BQ was scored as high- or low-risk for OSA, and the diagnosis of OSA was based on polysomnography findings. OSA was defined as an apnea-hypopnea index of ≥ 5 on polysomnography.

Results—Thirty patients were evaluated [24 women; 15 white, 15 black; age 16–54 years (median 32 years) and BMI 27.3–51.7 kg/m² (median 39.8 kg/m²)]. Twenty patients (66.7%) had a high-risk BQ score and eighteen (60%) exhibited OSA. Fifteen of 20 (75%) with a high-risk BQ score had OSA, while 3 of 10 (30%) with a low-risk score had OSA (Fisher test, $p=0.045$). The sensitivity and specificity of the BQ for OSA in IIH patients were 83% and 58%, respectively, whereas the positive predictive value was 75%.

Conclusions—A low-risk BQ score identifies IIH patients who are unlikely to have OSA. Polysomnography should be considered in those with a high-risk score.

Keywords

Idiopathic Intracranial Hypertension; Obstructive Sleep Apnea; Berlin Questionnaire

Introduction

Obstructive sleep apnea (OSA) is a common condition in which there are intermittent partial (viz., hypopneas) and complete (viz., apnea) limitations in airflow, with associated hypoxia and sympathetic arousals, during sleep.[1,2] It is associated with obesity and older age, is more common in men, and, when left untreated, results in increased cardiovascular morbidity and mortality.[1–3] Polysomnography is the gold standard test for OSA diagnosis, but requires overnight evaluation.[4] The Berlin questionnaire (BQ), which includes questions about snoring, daytime somnolence, body mass index (BMI), and hypertension, is a brief and validated screening tool that identifies persons in the community who are at high risk for OSA.[5]

OSA is thought to be associated with idiopathic intracranial hypertension (IIH).[6] Although the BQ has been used as a screening tool for OSA in prior IIH studies [7], validation studies of the BQ have only been performed in middle-aged and older adults living in the community, whereas IIH most often occurs in young, obese women.[5] Because visual outcomes may be worse in IIH patients who have OSA,[3,11] we obtained diagnostic polysomnography as part of routine clinical practice on newly-diagnosed IIH patients. We concurrently administered the BQ, to evaluate the validity of the BQ as a screening tool for OSA in IIH patients.

Article

Assessment of Screening for Nasal Obstruction among Sleep Dentistry Outpatients with Obstructive Sleep Apnea

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Abstract: Oral appliances (OA), a common treatment modality for obstructive sleep apnea (OSA), are not suitable for patients with nasal obstruction. Rhinomanometry, the gold standard technique to assess nasal airway resistance, is not readily available in sleep dentistry clinics. We demonstrate the use of a portable lightweight peak nasal inspiratory flow (PNIF) rate meter to objectively assess nasal airflow and utilized the Nasal Obstruction Symptom Evaluation (NOSE) scale to subjectively assess nasal obstruction in 97 patients with OSA and 105 healthy controls. We examined the correlations between the following variables between the groups: demographics, body mass index, PNIF, NOSE scale scores, apnea–hypopnea index (AHI), minimum SpO₂ (SpO₂min), Mallampati classification, and Epworth Sleepiness Scale (ESS) scores. Patients with OSA had significantly lower PNIF values and higher NOSE scores than controls. In the patient group, PNIF was not significantly correlated with AHI, SpO₂min, Mallampati classification, or NOSE or ESS scores. Lower PNIF values and higher NOSE scores suggested impaired nasal airflow in the OSA group. As daytime PNIF measurement bears no relationship to AHI, this cannot be used alone in predicting the suitability of treatment for OSA with OA but can be used as an adjunct for making clinical decisions.

Keywords: apnea–hypopnea index; Mallampati classification; mandibular advancement devices; nasal obstruction; sleep apnea; obstructive

1. Introduction

Obstructive sleep apnea (OSA) is a condition in which oxygen levels in the brain are reduced by the cessation of breathing during sleep, resulting in sleep disturbances [1]. OSA has been associated with the onset and worsening of lifestyle-related diseases such as hypertension, myocardial infarction, and diabetes. OSA can also lead to excessive daytime sleepiness, significantly increasing the risk of accidents [2]. Continuous positive airway pressure (CPAP) therapy remains the gold standard for the

Oral appliances treatment for obstructive sleep apnea

Tahere Hossein zadeh Nik^a, Fariba Esmailnia Shirvani^b

Abstract

Obstructive sleep apnea (OSA) is a physical disorder that leads to repetitive obstruction of upper air way, causing in 30 or more apneic (the pause of airflow at the mouth and nose for more than 10 seconds) episodes during sleep. It is caused by the repeated collapse or narrowing of the pharyngeal walls due to partial or complete obstruction of the upper airway. Treatment for sleep apnea include weight loss, keeping off alcohol, positional therapy, oral appliances, continuous positive airway pressure (CPAP). Oral appliances have proven to be useful, noninvasive and easy to use. Patients prefer oral appliances and mandibular advancement appliances to CPAP. Our study concluded that oral appliances may assist in the management of OSA.

Keywords: Obstructive sleep apnea, Appliance , Treatment

Obstructive sleep apnea (OSA) is a physical disorder that leads to repetitive obstruction of upper air way¹, causing in 30 or more apneic (the pause of airflow at the mouth and nose for more than 10 seconds) episodes during sleep.² It is caused by the repeated collapse or narrowing of the pharyngeal walls due to partial or complete obstruction of the upper airway

The prevalence of OSA is fairly 3% for the middle-aged population² and in the adult working-age population of 4% for men especially overweight males and 2% for women who have an apnea-hypopnea Index greater than 5 per hour.⁴

OSA symptoms such as snoring, fatigue and sleepiness are usual. Snoring affects 35% to 40% of adults.⁵ Dental devices might be used for treatment of snoring and OSA.⁷ Another term that has been mentioned is obstructive sleep apnea hypopnea syndrome (OSAHS) that occurs as the base of the tongue contacts the posterior pharyngeal wall at intervals or partially occludes the upper airway when the patient is asleep.⁶ Some patients have multifactorial etiologies interplay between the neuromuscular system, airway and anatomical structures.⁸

Dentofacial problems that are closely related to OSA include a narrow upper airway, hypoplastic maxilla, a retrognathic mandible, steep mandibular plane angle, narrow dental arches, increased lower anterior facial height, long soft palate and high palatal vault.⁹ The head extends backwards to expand oropharynx at the tongue base and epiglottis. This head

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Oral Appliance for the Treatment of Severe Obstructive Sleep Apnea in Edentulous Patient

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Abstract Oral appliances have attracted interest for the treatment of mild and moderate obstructive sleep apnea (OSA) and the mandibular repositioning device (MRD) or a tongue-retainer device (TRD) is usually indicated to increase the upper air space. Describes a combination of MRD (with 60 % maximum mandibular protrusion) and TRD to treat severe OSA. Polysomnography (PSG) and two questionnaires: the Epworth Sleepiness Scale (ESS) and the Pittsburgh Sleep Quality Index (PSQI) evaluated the sleep pattern in two times (after and before the use of oral appliance). The initial PSG exam was compatible with diagnoses severe OSA and the Apnea–Hypopnea Index was 40.4, and 54 % oxygen saturation $-spO_2$. The ESS and PSQI scores were 11 and 6, respectively. After she began wearing the device she stopped snoring, her Apnea–Hypopnea Index decreased to 17.6, presented a sleep efficiency of 81.6 % and had a 77 % spO_2 . The ESS and PSQI scores dropped to three. MRD in association with the tongue-retainer was effective in reducing the severity of the apnea for this edentulous patient.

Keywords Sleep apnea · Oral appliance · Sleep disturbance

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Introduction

Obstructive sleep apnea (OSA) is a respiratory disorder characterized by repeated collapse of the upper airway and cessation of breathing during sleep [1]. It is usually associated with snoring. Both are caused by partial or complete collapse of the pharyngeal airway during sleep due to a combination of a reduction in muscle tone at sleep onset and structural factors such as obesity, retrognathia, tonsillar hypertrophy, and macroglossia [2]. There are three kinds of apnea: OSA (blockage of air space); central sleep apnea (there is no blockage, but the brain fails to give the muscles to the signal to breathe); and mixed apnea (a combination of these two conditions), all diagnosed by polysomnography [3].

The prevalence of OSA ranges from 9 to 28 % [4], and it is higher in the elderly population (62–81 %) [5]. In this age group, edentulous patients are common, and an atrophic mandible associated with poor retention may cause difficulty into retaining the appliance [6]. Edentulous patients present changes in facial anatomy [7, 8], and reduced upper air way [9]. They also are more likely to be affected by severe medical complications due to low oxygen saturation, such as hypertension, coronary heart disease and stroke, as a result of recurrent nocturnal hypoxemia and hypercapnia [3, 10, 11].

In recent years, oral appliances (OA) have attracted considerable interest in the treatment of snoring and OSA [12]. There are two types of OA: the mandibular repositioning device (MRD), which retains the advancing mandible, and the tongue-retainer device (TRD) which is designed to keep the tongue in an anterior position during sleep by means of negative pressure [12–15].

Edentulous patients may not be ideally suited for treatment with a MRD because they may not have enough intraoral retention to keep the appliance in the mouth

ANATOMIE DU PHARYNX

I. DEFINITION :

- Segment du tube digestif reliant la cavité orale à l'œsophage .
- conduit musculo-membraneux impair , médian et vertical .
- Situé en arrière des fosses nasales, de la cavité buccale et du larynx.
- **Carrefour aéro-digestif**

II. FONCTION :

- Déglutition
- Respiration
- Phonation

III. SITUATION :

Le pharynx est situé

➤ en arrière :

- Des fosses nasales
- De la Cavité orale
- Du larynx
- En avant: du rachis cervical
- Limite supérieure : la base du crâne
- Limite inférieure : bord inférieur du cartilage cricoïde(C6)

IV. CONFIGURATION EXTERNE

Il a la forme d'une gouttière ouverte en avant

- **Longueur:** 15 cm
- **Largeur :** 5 cm en haut et 2 cm en bas

V. CONFIGURATION INTERNE

La morphologie intérieure du pharynx permet de le subdiviser en trois segments:

- **Le rhino-pharynx**
- **L'oro-pharynx**
- **Laryngo-pharynx**

☐ 1- LE RHINO-PHARYNX:

- Appelé aussi **cavum**
- Partie supérieure du pharynx; située en arrière des fosses nasales

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Functional Anatomy and Physiology of Airway

Aslı Mete and İlknur Hatice Akbudak

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.77037>

Abstract

In this chapter, we scope the importance of functional anatomy and physiology of the upper airway. The upper airway has an important role in transporting air to the lungs. Both the anatomical structure of the airways and the functional properties of the mucosa, cartilages, and neural and lymphatic tissues influence the characteristics of the air that is inhaled. The airway changes in size, shape, and position throughout its development from the neonate to the adults. Knowledge of the functional anatomy of the airway in these forms the basis of understanding the pathological conditions that may occur. The upper airway extends from the mouth to the trachea. It includes the mouth, the nose, the palate, the uvula, the pharynx, and the larynx. This section also describes the functional physiology of this airway. Managing the airway of a patient with craniofacial disorders poses many challenges to the anesthesiologist. Anatomical abnormalities may affect only intubation, only airway management, or both. This section also focuses on the abnormal airways in obesity, pregnancy, children and neonate, and patients with abnormal facial defects.

Keywords: anatomy, airway, function, physiology, upper airway

1. Introduction

The upper airway has an important role in conducting air to the lungs. Both the anatomical structure of the airways and the functional properties of the mucosa, cartilages, and neural and lymphatic tissues influence the characteristics of the air that is inhaled [1]. The upper airways begin with the nasal cavity and continue over nasopharynx and oropharynx to the larynx and the extrathoracic part of the trachea. The structure and function of this system have a major influence upon the conduction of the air to the lower airways [1]. Functions of the airway include phonation, olfaction, digestion, humidification, and warming of inspired

Mandibular advancement device for obstructive sleep apnea: An overview

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ABSTRACT

This paper presents an overview of mandibular advancement device (MAD). The primary purpose of MAD is to move the mandible forwards relative to maxilla in order to widen the airway to prevent closure.

KEY WORDS: Mandibular advancement device, sleep apnea, snoring

Obstructive sleep apnea (OSA) is a condition wherein there is repetitive and intermittent occlusion of the upper airway (UA) during sleep.^[1] This closure occurs due to inspiratory collapse of the pharyngeal walls. If complete closure occurs, it results in apnea; if partial closure occurs, hypopnea results. Although snoring occurs in majority of population, it has significant ramifications. If repetitive apnea occurs in a patient, many times a night, for years together, there will be considerable changes in the (1) nervous system (2) myocardial and cerebral circulation (3) pulmonary and systemic circulation.

Snoring is an expression of the pharyngeal narrowing. It is due to the vibration of the soft parts of the UA, that is, the pharyngeal walls, veils of the palate and the uvula. It is the commonest symptom reported by the patient or the spouse. The nocturnal signs are xerostomia, salivation, altered sleep – patterns, suffocative feeling. The daytime signs include irritability, headache, depression gastroesophageal reflux etc.

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First description of this disorder was reported in 1965^[2] and since then many treatments have been suggested. Treatment for OSA can be (1) continuous positive airway pressure (CPAP) (2) surgery (3) oral appliances.^[3] While CPAP has been the treatment of choice, it needs sealed tubing and a power source connected device and use of mask interface. Hence, more often patients develop intolerance. Surgery may have serious side-effects like scarring in soft palate.

Mandibular advancement device (MAD) has been a novel method in the management of snoring and OSA. For mild to moderate sleep apnea, MADs have been a boon. A guideline published by American Academy of sleep Medicine in 1995 stated that MAD was indicated as first-line therapy for mild OSA and a second-line therapy for moderate to severe OSA.

In 1902, Pierre Robin proposed the use of a device (Monobloc), with the purpose of procuring a functional advancement of the jaw, dragging it forward to a more advanced position. Initial publications about oral appliances in the treatment of snoring appeared way back in 1980's. Currently, there are more than 50 types of devices used for treating snoring. There are two versions of MAD's.

- Fixed advancement MAD
- Adjustable advancement MAD.

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The effect of mandibular advancement on upper airway structure in obstructive sleep apnoea

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► Supplementary tables are published online only. To view these files please visit the journal online (<http://thorax.bmj.com>).

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ABSTRACT

Background The mechanisms by which mandibular advancement splints (MAS) improve obstructive sleep apnoea (OSA) are not well understood. This study aimed to evaluate the mechanism of action of MAS by assessing their effect on upper airway structure in patients with OSA.

Methods Patients were recruited from a sleep disorders clinic for treatment with a custom-made MAS. MRI of the upper airway was performed during wakefulness in the supine position, with and without the MAS.

Results Sixty-nine patients with OSA were recruited. Treatment with the MAS reduced the apnoea–hypopnoea index (AHI) from 27.0 ± 14.7 events/h to 12.2 ± 12.5 events/h ($p < 0.001$). There was an increase in the total airway volume with mandibular advancement (16.5 ± 0.7 cm³ vs 18.1 ± 0.8 cm³; $p < 0.01$) that occurred predominantly because of an increase in the volume of the velopharynx (5.7 ± 0.3 cm³ vs 6.5 ± 0.3 cm³; $p < 0.001$). This increase in airway calibre was associated with an increase in the lower anterior facial height (6.8 ± 0.1 cm vs 7.5 ± 0.1 cm; $p < 0.001$), reduction in the distance between the hyoid and posterior nasal spine (7.4 ± 0.1 cm vs 7.2 ± 0.1 cm; $p < 0.001$), lateral displacement of the parapharyngeal fat pads away from the airway (right parapharyngeal fat pad 0.17 ± 0.02 cm; left parapharyngeal fat pad 0.22 ± 0.02 cm) and anterior movement of the tongue base muscles (0.33 ± 0.03 cm). Subanalyses in responders and non-responders to MAS treatment showed that the increase in upper airway calibre with mandibular advancement occurred only in responders.

Conclusion These results suggest that the mechanism of action of MAS is to increase the volume of the upper airway, predominantly by increasing the volume of the velopharynx, and this increased volume is associated with changes in the surrounding bony and soft tissue structures.

INTRODUCTION

Mandibular advancement splints (MAS) are increasingly being used in the treatment of obstructive sleep apnoea (OSA) as an effective alternative to continuous positive airway pressure (CPAP).^{1–5} While CPAP remains the ‘gold standard’ because it is a highly efficacious treatment, there is a need for other treatment options because the clinical effectiveness of CPAP is often limited by poor patient acceptance and tolerance, and suboptimal compliance.^{6–8}

MAS protrude the mandible with the aim of increasing upper airway calibre and thereby

preventing collapse of the upper airway during sleep.⁴ However, the mechanisms by which MAS improve OSA are not well understood. Limited studies have identified an effect of mandibular advancement on aspects of the structure and function of the upper airway.^{9–16} Importantly, these predominantly used cephalometric x-rays which are limited by their two-dimensional nature. However, soft tissue volumes and movements, and the interaction between upper airway structural parameters and treatment response have never been systematically studied in patients using an oral appliance. A better understanding of the biomechanical mechanisms that mediate the efficacy of MAS may have important clinical implications, including the development of more efficacious appliances, and may improve the selection of patients for this treatment modality.

MRI is a powerful, non-invasive research tool and is probably one of the best methods for assessing the three-dimensional structure of the upper airway lumen and the surrounding soft tissue structures.¹⁷ Therefore, this study aimed to evaluate the mechanism of action of MAS in patients with OSA by assessing their effect on upper airway structure during wakefulness using MRI. Preliminary results of this study have been previously reported in the form of abstracts.^{18 19}

METHODS

Subjects

Patients were prospectively recruited from a sleep disorders clinic in a university teaching hospital for treatment of OSA with a custom-made MAS. Inclusion criteria included the presence of at least two symptoms of OSA (such as snoring, witnessed apnoeas, fragmented sleep or daytime sleepiness) and evidence of OSA on nocturnal polysomnography (apnoea–hypopnoea index (AHI) of at least 10 events/h). Patients were excluded if there were contraindications to MAS treatment (such as periodontal disease, insufficient number of teeth or an exaggerated gag reflex). Patients with ferromagnetic prostheses, a contraindication to MRI, were also excluded. The study was approved by the institutional ethics committee and written informed consent was obtained from all patients.

MAS Treatment

A custom-made two-piece MAS was used (SomnoDent MAS; SomnoMed, Crows Nest, Australia), the design features and efficacy of which have previously been published.^{20–25} To permit MRI of the upper airway with the MAS, the

Research Article

Comparison of Titratable Oral Appliance and Mandibular Advancement Splint in the Treatment of Patients with Obstructive Sleep Apnea

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Objective. To compare the effect of two intraoral devices (titratable oral appliance-Klearway (KW) and mandibular advancement splint (MAS)) in mild and moderate obstructive sleep apnea (OSA) patients. **Method and Materials.** The study group was comprised of twenty-four adult volunteer patients with OSA. Twelve subjects were fitted with a titratable oral appliance (group KW) protruding the mandible (85% of maximum protrusion). The other 12 subjects received MAS with 75% protrusion of the mandible (group MAS). Baseline, ("0.PSG"), first week (K1.PSG for KW group and M1.PSG for MAS group), and after the first month (K2.PSG for KW group and M2'. PSG for MAS group). **Results.** Both groups produced similar reduction in apnea-hypopnea index (AHI) from baseline till the end of the first week and first month ($P < .05$). However, the success rate of both groups at the end of the first month was found to be statistically different from the success rate of the first week ($P < .05$). The reduction in mean AHI of group KW-moderate (KW-mo) was significantly different from the mean AHI of group MAS-moderate (MAS-mo) at the end of the first month ($P < .05$). **Conclusion.** This study suggests that Klearway appliance was more effective in treating moderate OSA patients than MAS appliance. It was concluded that an appliance that provides 85% mandibular advancement to open the upper airway was more effective in reducing the number of high apneic events during sleep in comparison to the one which provides 75%.

1. Introduction

Snoring and obstructive sleep apnea syndrome (OSAS) are common disorders related with the narrowing of the upper airway. Many treatment methods have been tried over the years to treat snoring and obstructive sleep apnea (OSA) [1]. Today, three approaches, namely, nasal continuous positive airway pressure (nCPAP), surgical techniques, and use of intraoral appliances (OAs) seem to be the most effective ones [2–5].

Intra-OAs are indicated in patients with primary snoring or having mild OSA who do not respond to or are not appropriate candidates for treatment with behavioral measures such as weight loss or change of sleep position. On the other hand, OAs have been advised for patients with moderate to severe OSA who cannot tolerate or refuse treatment with nCPAP or subjects who are not suitable surgical candidates

[6, 7]. Intra-OAs are worn in the mouth during sleep to prevent the oropharyngeal tissues and the base of the tongue from collapsing and obstructing the airway [8–11].

Mandibular advancement splint (MAS) is a nonadjustable, one-piece appliance (monoblock) and functions to repose and maintain the mandible in a protruded position and vertical opening between 5 and 7 mm during sleep [2, 8, 11–13]. **Titratable OA is an adjustable, two-piece appliance.** Among these devices, Klearway appliance is the most thoroughly researched OA for treatment of snoring and OSAS [12–16]. Both appliances are mandibular repositioners (MRs) that advance the mandible and tongue base, increasing the space between the base of the tongue and the posterior pharyngeal wall.

Lawton et al. [15] compared the Twin Block and Herbst mandibular advancement splint in the treatment of patients with obstructive sleep apnea. They found that both

Efficacy of custom made oral appliance for treatment of obstructive sleep apnea

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Abstract

Introduction: oral appliance for the treatment of OSA is considered as an effective, low-risk alternative to CPAP. Demand for oral appliance increases as an alternative for those who cannot tolerate CPAP and refuse surgery. Oral appliances uses the traditional methods to advance the mandible thus modify the posture and their by enlarge the airway or otherwise reduce the collapsibility. **Aims and Objectives:** The main objective of this study was to evaluate the efficacy of custom made oral appliance on sleep characteristics of OSA patients. **Materials and Methods:** Polysomnography was done on 15 patients of 24-60 years of age before (T1), and after the delivery of the custom made oral appliance (T2). **Statistical Analysis:** Paired t tests were performed to determine the significance of change in the polysomnographic and cephalometric variables. $P < 0.05$ was considered as significant. **Results:** All patients with oral appliance showed an improvement in sleep parameters with an increase in sleep efficiency, and desaturation index with the use of oral appliance. ESS and cephalometric findings showed improvement in the sleep apnea in concordance with the sleep parameters. **Conclusions:** Custom made oral appliance is a useful treatment option for improving quality of sleep and can be considered as an alternative treatment modality.

Keywords: Continuous positive airway pressure, obstructive sleep apnea, obstructive sleep apnea appliance

Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive episodes of partial or complete obstruction of the upper airway during sleep, often resulting in arterial oxygen desaturation and arousals.^[1] This is associated with many symptoms and comorbidities, which include excessive daytime sleepiness, cognitive problems, obesity, type 2 diabetes mellitus, hypertension, exacerbation of chronic obstructive pulmonary disease reduced quality of life, and significant increase in risk of industrial and traffic accidents. It is also considered as an independent risk factor for cardiovascular disease and ischemic stroke.^[2]

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Clinically, the patient history reveals loud snoring, experiences apneas, nocturnal awakening, gasping or choking episodes during sleep, unrefreshing sleep, morning headaches, excessive daytime sleepiness, etc., the diagnosis of OSA is established using polysomnography (PSG).

The various imaging techniques such as lateral cephalometry, computed tomography (CT), cone-beam computed tomography, magnetic resonance imaging are used for the evaluation of upper airway. Even though lateral cephalogram provides only a two-dimensional image, it is most widely used technique in clinical practice.

The ideal treatment for OSA should be capable of normalizing breathing during sleep, consequently eliminating excessive daytime sleepiness, and neuropsychiatric and cardiovascular changes.^[3]

Continuous positive airway pressure (CPAP) is the primary noninvasive treatment of choice for OSA since its introduction in the early 1980s. It is associated with various problems which makes it noncomplaint to the patient such as nasal congestion, discomfort secondary to pressure sensation and air leak, mask intolerance due to skin inflammation, claustrophobia, and issues pertaining to chronic use in younger and less severe patients.^[4]

Other alternatives include behavioral and surgical weight-loss therapies, positional therapy, pharmacologic therapies, pharyngeal and maxillomandibular surgeries, and oral appliances (OA). Among these modalities except for the OA, clinical results with nonsurgical OSA therapies have been largely unsatisfactory.

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Les orthèses d'avancée mandibulaire dans le traitement du SAOS de l'adulte

Mandibular advancement device as a therapy in obstructive sleep apnea

I. Prime*

Les orthèses d'avancée mandibulaire (OAM) sont, dans l'ensemble, une application à la médecine du sommeil des appareils orthopédiques utilisés chez les enfants pour stimuler le potentiel de croissance de la mandibule et, ainsi, donner notamment du volume à la "boîte à langue".

Les OAM ont investi le domaine du syndrome d'apnées-hypopnées obstructives du sommeil (SAOS) dans les années 1980.

En 1999, l'Agence nationale d'accréditation et d'évaluation en santé (ANAES), puis, en 2006, la Haute Autorité de santé (HAS), ont produit des documents sur l'évaluation de la chirurgie dans le SAOS (1) et sur la pose d'un appareillage en propulsion mandibulaire (2). Le premier inclut dans ses recommandations "les orthèses d'avancement mandibulaire, qui semblent efficaces chez certains patients mais pour lesquelles le recul est encore limité" pour le traitement du SAOS et du syndrome de haute résistance des voies aériennes supérieures. La ventilation par pression positive continue (PPC) est le traitement de référence. Le deuxième, considérant le service attendu suffisant, rend cette fois un avis positif pour l'inscription de l'appareillage en propulsion mandibulaire à la liste des actes prévus à l'article L. 162-1-7 et le place dans la stratégie thérapeutique, avec les indications "en première intention pour les SAOS légers voire modérés sans somnolence diurne", et "en deuxième intention pour les SAOS sévères et modérés symptomatiques quand le patient ne supporte pas la PPC (encombrement, bruit, claustrophobie, voyages,

raisons sociales)". Une actualisation du Service d'évaluation des actes professionnels de la HAS a été publiée en décembre 2009 (3). Deux orthèses y figurent, avec les références des études spécifiques s'y rapportant. La Commission d'évaluation des produits et des prestations recommande que le renouvellement des conditions d'inscription de ces orthèses soit conditionné non seulement à leur efficacité confirmée sur la pathologie (symptômes, qualité de vie et paramètres polygraphiques) et à leur tolérance, mais aussi à l'observance à long terme. Les arrêtés du Journal Officiel (4-6) autorisent l'inscription à la Nomenclature des produits et des prestations remboursables des orthèses ORM® des laboratoires Narval puis Resmed (figure 1) et l'AMO® (OrthoSom) [figure 2]. La prise en charge est assurée pour le traitement du SAOS sévère, en deuxième intention, après refus ou intolérance d'un traitement par PPC. Une polygraphie ventilatoire ou une polysomnographie devra confirmer l'efficacité de l'orthèse. Un suivi rigoureux (pathologie et appareil manducateur) est requis. Le renouvellement ne sera autorisé que si l'OAM est efficace et si le suivi odontologique est assuré. À l'heure actuelle, une troisième orthèse est susceptible d'être remboursée pour les mêmes indications (7) : l'OAM Tali SAS (Tali). D'autres orthèses rejoindront ces trois-là, après acceptation de la HAS sur la base d'études. Elles seront remboursables, mais sans doute encore dans l'indication précitée, et dans cette seule indication.

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Clinical guidelines for oral appliance therapy in the treatment of snoring and obstructive sleep apnoea

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ABSTRACT

The purpose of this review is to provide guidelines for the use of oral appliances (OAs) for the treatment of snoring and obstructive sleep apnoea (OSA) in Australia. A review of the scientific literature up to June 2012 regarding the clinical use of OAs in the treatment of snoring and OSA was undertaken by a dental and medical sleep specialists team consisting of respiratory sleep physicians, an otolaryngologist, orthodontist, oral and maxillofacial surgeon and an oral medicine specialist. The recommendations are based on the most recent evidence from studies obtained from peer reviewed literature. Oral appliances can be an effective therapeutic option for the treatment of snoring and OSA across a broad range of disease severity. However, the response to therapy is variable. While a significant proportion of subjects have a near complete control of the apnoea and snoring when using an OA, a significant proportion do not respond, and others show a partial response. Measurements of baseline and treatment success should ideally be undertaken. A coordinated team approach between medical practitioner and dentist should be fostered to enhance treatment outcomes. Ongoing patient follow-up to monitor treatment efficacy, OA comfort and side effects are cardinal to long-term treatment success and OA compliance.

Keywords: Mandibular advancement splint, obstructive sleep apnoea, oral appliance, review, snoring.

Abbreviations and acronyms: AASM = American Academy of Sleep Medicine; ADA = Australian Dental Association; AHI = apnoea–hypopnoea index; ASA = Australasian Sleep Association; BMI = body mass index; CBCT = cone beam computed tomography; CT = computed tomography; ESS = Epworth Sleepiness Scale; MAS = mandibular advancement splints; OA = oral appliances; OSA = obstructive sleep apnoea; PSG = polysomnogram; SDB = sleep disordered breathing; TMD = temporomandibular disorder; TMJ = temporomandibular joint; TRD = tongue retaining device; TSD = tongue stabilizing device; UARS = upper airway resistance syndrome; UPPP = uvulopalatopharyngoplasty.

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INTRODUCTION

Obstructive sleep apnoea (OSA) is a breathing disorder during sleep that is characterized by snoring and recurrent collapse of the pharyngeal airway during sleep, resulting in a partial reduction (hypopnoea) or complete cessation (apnoea) of airflow despite ongoing breathing effort.¹ OSA is at one end of a spectrum of disorders encompassed in the term 'sleep disordered breathing' (SDB). There is a continuum from mild intermittent snoring at one end of the spectrum, through heavy obstructed snoring and high upper airway resistance, heavy snoring and runs of partial and complete obstruction, through to repetitive obstructive apnoea occurring throughout the entirety

of sleep. Chronic snoring occurs in up to 30% of adult subjects, and some degree of obstructive apnoea and hypopnoea occurs in 9% of males and around 5% of females. More strictly defined OSA (which is the combination of confirmed apnoea on sleep study and symptoms) has been found to affect 2% to 4% in males and approximately half that in females.^{2,3} While the current accepted measure of severity is based on the apnoea–hypopnoea index (AHI), or the respiratory disturbance index (RDI), and or the number and severity of oxyhaemoglobin desaturations per hour of sleep, none of these indices have a clear relationship to symptoms. As an approximate guide, an AHI between 5 and 15 per hour is mild SDB, between 15 and 30 per hour is 'moderate' and above



Mandibular Advancement Devices for OSA: An Alternative to CPAP?

Claire E. Francis · Tim Quinnell 

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ABSTRACT

Obstructive sleep apnea (OSA) is a prevalent condition causing unrefreshing sleep and excessive daytime sleepiness. It has individual socioeconomic impacts and, through association with increased risk of road traffic accidents, diabetes, and cardiovascular disease, OSA is a public health issue. Continuous positive airway pressure (CPAP) is the first-line treatment for moderate-to-severe OSA. It is effective in improving excessive daytime sleepiness and quality of life. There is also evidence that CPAP therapy has cardiovascular benefits although nature and extent remain uncertain. Despite its benefits, a significant proportion of patients are unable to tolerate CPAP. There are also patients with mild but symptomatic disease, for whom CPAP is usually not available or appropriate, so there is a need for other treatment options. Mandibular advancement devices (MADs) offer an effective alternative to CPAP and can improve daytime symptoms and quality of life.

There are many devices available, representing a range of complexity and cost. It is challenging to properly evaluate the effectiveness of this ever-evolving range. The more basic MADs are cheaper and more accessible but are less well tolerated. More complex devices are better tolerated and may be more effective. However, they are more expensive and often require dental expertise, so access is more limited. Efforts continue to try to improve accessibility to effective MAD therapy. Alongside increasing awareness, this may be facilitated by developing and refining devices that could be fitted by non-dental clinicians, and potentially by patients themselves. Research efforts need to focus on determining how to efficiently identify patients who are likely to respond to MAD therapy, so as to improve clinical and cost-effectiveness of OSA therapy overall.

Keywords: CPAP alternatives; Mandibular advancement device; Obstructive sleep apnea

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An update on mandibular advancement devices for the treatment of obstructive sleep apnoea hypopnoea syndrome

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Contributions: (I) Conception and design: T Quinnell, S Basyuni; (II) Administrative support: T Quinnell; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Continuous positive airway pressure (CPAP) remains the gold standard treatment for obstructive sleep apnoea hypopnoea syndrome (OSAHS). However, the high efficacy of CPAP is offset by intolerance and poor compliance, which can undermine effectiveness. This means that alternatives to CPAP are also necessary. In recent years, oral appliances have emerged as the leading alternative to CPAP. There is now a strong body of evidence supporting their use in OSAHS and clinical guidelines now recommend their use in mild OSAHS and in more severe cases when CPAP fails. These devices are by no means a homogenous group as they differ greatly in both design and action. The most commonly used appliances are mandibular advancement devices (MAD) that increase airway diameter with soft tissue displacement achieved by mandibular protrusion. Despite the growing evidence, there are still barriers to MAD provision. Their effectiveness can be difficult to predict and there is debate about the required level of design sophistication. These uncertainties prevent more widespread inclusion of MAD within clinical sleep services. This review will focus on the efficacy, effectiveness, design features, side-effects of and patient selection for MAD therapy. Comparison will also be made between MAD and CPAP therapy.

Keywords: Obstructive sleep apnoea; sleep apnoea; mandibular advancement devices (MAD); oral appliances

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Introduction

Obstructive sleep apnoea hypopnoea syndrome (OSAHS) is a common sleep disorder characterised by intermittent upper airway collapse resulting in oxygen desaturation and sleep fragmentation. Excessive daytime sleepiness (EDS) is associated with cognitive impairment, mood disturbance and decreased quality of life (QoL). OSAHS is also linked with increased risk of road traffic accidents, cardiovascular disease and all-cause mortality (1,2). It affects 2–7% of adults (3) and an estimated 1% of UK men have severe OSAHS (4). Many cases go untreated due to not being diagnosed or intolerance of treatment. The consequences are estimated to cost the NHS around £432 million each year (2,5).

The pathogenesis of OSAHS is a complex interaction of multiple factors including pharyngeal anatomy, dilator muscle dysfunction and reduced lung volume (6). Whilst the relative contributions of these mechanisms vary between patients, the common result is sleep related upper airway collapse. The gold standard treatment remains continuous positive airway pressure (CPAP) therapy (7). It pressurises the upper airway to prevent collapse, reducing the frequency of apnoeas and hypopnoeas. However, CPAP effectiveness is limited by intolerance and poor compliance, with failure rates of 46–83% (8). There is a pressing need for alternatives to CPAP.

In recent years, oral appliances have emerged as the leading alternative to CPAP. These devices are by no means a homogenous group as they differ greatly in both design

Place de l'Orthèse d'Avancée Mandibulaire (OAM)
dans la prise en charge du
Syndrome d'Apnées Hypopnées Obstructives du Sommeil (SAHOS)

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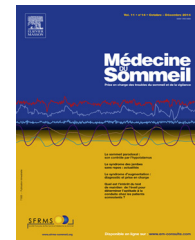


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FICHE PRATIQUE

Les orthèses d'avancée mandibulaire (OAM)



The mandibular advancement device

G. Besnainou

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Disponible sur Internet le 12 août 2016

MOTS CLÉS

Orthèse d'avancée mandibulaire ;
Mode d'action ;
Complications ;
Critères d'une bonne orthèse

Résumé L'orthèse d'avancée mandibulaire est un dispositif issu de la philosophie et des techniques orthodontiques (activateur de classe II). Elle est utilisée avec succès dans le traitement du ronflement et du SAS modéré. Ses indications sont aujourd'hui bien codifiées et ses limites sont aujourd'hui repoussées du fait des améliorations techniques. Le but de cet article est de définir les critères communs et spécifiques des OAM (mode d'action, type de gouttière, rigidité, complète), de proposer 10 critères sur lesquels pourrait reposer le choix de la bonne orthèse pour un patient donné afin d'optimiser la réussite du traitement et enfin de recenser les effets secondaires rencontrés.

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KEYWORDS

Mandibular advancement device;
Way of working;
Criteria;
Side effects

Summary The mandibular advancement device is an oral appliance derived from the orthodontic philosophy and techniques (Class II activator). It is used successfully in the treatment of snoring and moderate SAS since 1990. The indications to its usage are now well codified and the limitations are now partially eliminated due to technical improvements. The purpose of this article is to identify the common and specific criteria of MAD (mode of action, type of gutter, rigid, full), to set 10 criteria to help the choice of the correct oral appliance for a singular patient to optimize the success of the treatment and to define the side effects encountered in my experience.

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Gouttières occlusales
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Protège-dents



Jean-Philippe Ré

Préface de
Jean-Daniel Orthlieb

Editions CdP

Sleep duration and health status self-assessment (SF-36) in the elderly: a population-based study (ISA-Camp 2008)

Duração do sono e estado de saúde autorreferido (SF-36) em idosos: estudo de base populacional (ISA-Camp 2008)

Margareth Guimarães Lima ¹
Marilisa Berti de Azevedo Barros ¹
Maria Cecília Goi Porto Alves ²

Abstract

The aim of this study was to determine the association between sleep duration and health status among the elderly. A population-based study was carried out with 1,418 elderly individuals using data from the health survey of Campinas, São Paulo State, Brazil (ISA-Camp 2008). Linear regression models were used to determine associations between the physical and mental components and subscales of the SF-36 and sleep duration. Elderly male individuals who slept ≤ 6 hours obtained lower mean SF-36 scores for the vitality and mental health scales and the mental component summary than those who slept for seven to eight hours. All scales were negatively associated with sleep duration ≥ 10 hours, except bodily pain. Scores for the mental health, vitality and role-emotional subscales were lower among women who slept for less than five hours. Mental health was negatively associated with ≥ 10 hours of sleep. Sleep deprivation and excessive sleep were associated with poorer health status, with differences between genders, principally in the long duration sleep categories.

Quality of Life; Sleep; Health of the Elderly; Health Status

Introduction

Health status and health-related quality of life can be self-assessed using the 36-item Short-Form Health Survey (SF-36). This instrument assesses different dimensions of health in individuals or populations such as the physical, emotional and social aspects of quality of life, bodily pain, mental health, vitality and general health ¹. A number of studies report a strong correlation between the health dimensions addressed by the SF-36 and the presence of health conditions and clinical symptoms ^{2,3} and also suggest that self-assessment may serve to predict mortality ⁴. The measurement of health status dimensions provides useful indicators of health conditions and wellbeing that may complement evaluations of illness and mortality indicators ^{1,5}.

An association has been reported between sleep duration under 7 to 8 hours (considered the medium sleep duration pattern of sleep) and an increase in mortality from all causes ^{6,7}, in addition to a greater prevalence of diseases such as diabetes ⁸, hypertension ⁹, depression ¹⁰, rheumatic disease, osteoporosis ¹¹ and obesity ^{12,13}. Literature also suggests that good quality sleep provides for daily recovery from physical and mental stresses, improves mood, concentration and memory and reduces the risk of accidents ^{8,14,15}.

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Ready-made versus custom-made mandibular advancement appliances in obstructive sleep apnea: A systematic review and meta-analysis

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Summary

Mandibular advancement appliances (MAAs) are an increasingly accepted treatment choice in obstructive sleep apnea management. The ready-made MAAs has questioned the need for a customised MAAs, given the former is more accessible and considerably cheaper. We conducted a systematic review and meta-analysis to evaluate both objective and patient-centred outcomes in relation to ready-made and custom-made MAAs. Biomedical electronic databases, clinical trials registers and Grey literature were searched to January 2017, for randomised controlled trials. Meta-analyses of clinical trials were conducted for a range of objective (apnea-hypopnea index, treatment response) and subjective scales (daytime sleepiness; quality of life; patient preference and adherence). The review included three randomised controlled trials, which revealed low risk of bias. Custom-made MAAs achieved a significant mean difference in the apnea-hypopnea index (-3.2 ; 95% confidence interval -5.18 , -1.22 ; $p = .004$), daytime sleepiness (-0.98 ; 95% confidence interval -1.97 , 0.01 ; $p = .05$), observed mean difference in Functional Outcomes of Sleep Questionnaire scores (0.76 ; 95% confidence interval 0.14 , 1.38 ; $p = .02$), self-reported adherence (6.4–7 nights per week and 5–6.3 hr per night) and expressed preference ($p \leq .001$) when compared with the ready-made MAAs. Custom-made MAAs offer clear definable advantages, demonstrating significant clinical effectiveness, patient preference and adherence.

KEYWORDS

oral appliances, OSA, comparison

1 | INTRODUCTION

Obstructive sleep apnea (OSA) remains a prevalent public health issue, characterised by repeated collapse of the pharyngeal airway, with resultant excessive daytime sleepiness, reduced cognitive functioning and quality of life (QoL), and reported as an independent risk factor for cardiovascular disease (Malhotra & White, 2002; Marin, Carrizo, Vicente, & Agusti, 2005; Pepin et al., 2014; Somers et al., 2008). The National Institute for Health and Care Excellence recommends the use of continuous positive airway pressure (CPAP) as clinically and cost-effective first-line therapy

for moderate and severe OSA. However, the greatest challenge remains CPAP intolerance, with wide variance in their reported adherence, ranging to as low as 46% (Weaver et al., 2012). In this context, mandibular advancement appliances (MAAs) are now regarded as an effective alternative to CPAP therapy from both a tolerance and therapeutic perspective (Johal, Fleming, Manek, & Marinho, 2015; Lim, Lasserson, Fleetham, & Wright, 2006; Ramar et al., 2015).

Mandibular advancement appliances are intra-oral devices, worn overnight to posture the mandible in a forward and downward direction, and are regarded as relatively non-invasive with a

SCIENTIFIC INVESTIGATIONS

Reliability and Validity of the Functional Outcomes of Sleep Questionnaire – Spanish Short Version (FOSQ-10SV) in Peruvian Patients With Obstructive Sleep Apnea

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Study Objectives: The aim of this study was to verify the reliability and validity of the Spanish short version of the Functional Outcomes of Sleep Questionnaire (FOSQ-10SV) in Peruvian patients with obstructive sleep apnea (OSA).

Methods: Participants underwent physical examinations, completed the FOSQ-10SV, and polysomnography tests were carried out.

Results: A total of 672 patients were analyzed, 75 females (11%), mean age 50.5 ± 13.8 years. A total of 563 patients (84%) had OSA. The mean FOSQ-10SV score was 15.96 ± 3.23 . The FOSQ-10SV Cronbach alpha was 0.84 and two significant factors were extracted in the factor analysis—both factors explained a variance of 43% and 14%. A significant correlation was found between the FOSQ-10SV score and the apnea-hypopnea index. Patients with more severe disease have a lower FOSQ-10SV score ($P = .003$). Ninety-nine patients with OSA who started continuous positive airway pressure treatment were followed, and we observed an improvement in the FOSQ-10SV score from pretreatment to posttreatment ($P < .001$).

Conclusions: The FOSQ-10SV has internal consistency, construct validity, and the sensitivity to change in Peruvian patients with OSA who undergo treatment.

Keywords: Functional Outcomes of Sleep Questionnaire, FOSQ-10, quality of life, reliability, sleep apnea, validity

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea (OSA) is a chronic disease that affects quality of life (QOL). Thus, we evaluated the reliability and validity of a Spanish short version of the Functional Outcomes of Sleep Questionnaire (FOSQ-10SV) in a clinical population of Peruvian patients suspected to have OSA.

Study Impact: The FOSQ-10SV has an internal validity and construct validity in patients with OSA. The FOSQ-10SV has the sensitivity to change in patients with OSA who started continuous positive airway pressure treatment.

INTRODUCTION

The classification of sleep-related respiratory disorders proposed by the American Academy of Sleep Medicine (AASM) includes obstructive sleep apnea (OSA), central apnea syndrome, and related hypoventilation disorders.^{1,2} The prevalence of OSA in the general middle-aged population is 2% to 6% and in the population between age 70 to 100 years 15% to 26%.^{3–6} OSA is caused by a partial or complete obstruction of the upper airway during sleep, leading to an intermittent oxygen desaturation, electroencephalographic microarousals, sleep fragmentation, daytime sleepiness, neurocognitive changes, and poor quality of life (QOL).⁷ The most frequent symptoms are intense snoring, respiratory pauses with choking during sleep, and daytime sleepiness. Medical information has consistently documented that OSA is a risk factor for high blood pressure, cerebrovascular and heart disease, traffic accidents

while driving due to sleepiness, and death due to myocardial infarction or stroke.^{8–13}

Researchers have designed instruments to evaluate the effect of sleep disorders on the multidimensional concept of QOL from the patient's perspective.¹⁴ The tools provide complementary information from that obtained by conventional clinical practice methods. Among QOL questionnaires, the best known is the SF-36 or Short Form-36.^{15,16} Those specifically oriented toward OSA include the Calgary Sleep Apnea Quality of Life Instrument (SAQLI),¹⁷ Obstructive Sleep Disorders-6 Survey (OSD-6),¹⁸ Functional Outcomes of Sleep Questionnaire (FOSQ),¹⁹ and Pediatric Obstructive Sleep Apnea Instrument (OSA-18), used in the pediatric population.²⁰ The purpose of this study was to establish the reliability and validity of a Spanish short version of the Functional Outcomes of Sleep Questionnaire (FOSQ-10SV) in a clinical population of Peruvian patients suspected to have OSA.

Mandibular advancement splints for the treatment of sleep apnoea syndrome

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Summary

Oral devices, in particular Mandibular Advancement Splints (MAS), which hold the mandible in a protruded position during sleep, are increasingly used for the treatment of Obstructive Sleep Apnoea (OSA). These devices can be effective in treating OSA across a range of severity. Complete resolution of OSA (Apnoea-Hypopnoea Index [AHI] reduced $<5/\text{hr}$) with use of an MAS occurs in around 40% of patients. Overall two thirds of patients experience some clinical benefit ($\geq 50\%$ AHI reduction AHI) however others will not objectively respond to this form of treatment, despite improvement in symptoms. Although MAS are less efficacious in reducing polysomnographic indices of OSA than the standard treatment, Continuous Positive Airway Pressure (CPAP), improvements in health outcomes appear to be comparable. Therefore, the superiority of CPAP in improving oxygen desaturations and reducing AHI may be extenuated by its low compliance, resulting in both treatments having similar effectiveness in clinical practice. MAS are now recommended as a first line treatment for mild to moderate OSA, as well as in more severe patients who are unable to tolerate or refuse CPAP. Success with MAS treatment has been associated with factors such as female gender, younger age, supine-dependent OSA, lower BMI, smaller neck circumference and craniofacial factors, however a reliable, validated method for prediction in the clinical setting has yet to be established. MAS are well tolerated, however short-term side effects are common although generally minor and transient. Long-term dental changes are for the most part subclinical, but can be problematic for a minority of patients. MAS are a dental-based treatment for a medical sleep disorder and, as such, an interdisciplinary care model is considered important for the attainment of optimal patient outcomes.

Key words: dental devices; mandibular advancement; obstructive sleep apnoea; oral appliances; upper airway

Introduction

Obstructive Sleep Apnoea (OSA) is a disorder characterised by repetitive closure of the upper airway during sleep, resulting in sleep fragmentation and nocturnal oxygen de-

saturation, leading to daytime sleepiness and neurocognitive impairment. Long-term consequences of OSA include increased risk of cardiovascular morbidity and all cause mortality [1]. Thus with the estimated prevalence of OSA at 4% of men and 2% of women in the middle-aged population [2] and the associated symptoms and increased risk of adverse long-term consequences, OSA is a significant public health problem. Therefore implementation and sustentation of effective treatment is vital. The current gold standard treatment, Continuous Positive Airway Pressure (CPAP), involves delivering positive pressure generated by a machine to the upper airway via tubing and a facial/nasal mask interface to pneumatically splint open the airway at night. Although CPAP is highly efficacious in preventing upper airway collapse, its obtrusive nature makes adherence to treatment suboptimal [3–4]. Over the last decade or so, oral devices have emerged as a viable alternative to CPAP therapy for the treatment of OSA. Oral devices are worn during sleep to alter the upper airway configuration thereby reducing the propensity to collapse. Some



Figure 1

Mandibular Advancement Splint (MAS). Example of a customised two-piece device with plates that attach to the upper and lower dental arches (SomnoMed MASTM). With this device the level of mandibular advancement is adjusted via the lateral screws on the upper plate. The acrylic extensions on the lower plate provide the coupling to the upper plate to maintain the jaw in the protruded position.

A randomised titrated crossover study comparing two oral appliances in the treatment for mild to moderate obstructive sleep apnoea/hypopnoea syndrome

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SUMMARY The objective of this study was to compare the efficiency of two oral appliances in patients with mild to moderate obstructive sleep apnoea/hypopnoea syndrome (OSAHS) by the analysis of objective and subjective evaluations and measurement of upper airway parameter. A randomised crossover design trial was carried out on 16 patients with OSAHS. Two different types of oral appliances were tested in each patient, a one-piece monoblock and the SILENT NITE® (GlideWell Laboratories, Newport Beach, CA, USA), a two-piece appliance. Each oral appliance needed to be worn for two 3-month periods separated by a 2-week wash-out period in between. The objective and subjective efficiency and upper airway parameters associated with the oral appliances were assessed. One-way analysis of variance (ANOVA) test was performed to compare the changes in upper airway morphology and the treatment efficiency between the appliances. The monoblock and SILENT NITE® (GlideWell Laboratories) appliances reduced Apnoea Hypopnoea Index (AHI) from 26.38 ± 4.13 to 7.58 ± 2.28 ($P < 0.001$) and 8.87 ± 2.88 ($P < 0.001$), respectively. The monoblock

appliance was statistically more efficient in reducing AHI and Apnoea Index (AI) than the SILENT NITE® (GlideWell Laboratories) ($P < 0.05$). The scores on Epworth's Sleepiness Scale (ESS) and Snoring Scale (SS) were improved significantly by both appliances. The upper airway spaces showed considerable enlargement by both mandibular advancement appliances (MAAs) ($P < 0.05$), while no significant differences were found between the two appliances ($P > 0.05$). Both MAAs showed good efficacy in the treatment for mild to moderate OSAHS. Use of the monoblock appliance should be considered when patients with OSAHS choose MAA treatment, as it was more efficient in reducing the AHI and AI compared to the two-piece appliance and was preferred by most patients. Long-term efficiency should be evaluated in future prospective studies.

KEYWORDS: obstructive sleep apnoea/hypopnoea syndrome, mandible advancement appliance, oral appliance, sleep-disordered breathing

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Introduction

Obstructive sleep apnoea/hypopnoea syndrome (OSAHS) is characterised by multiple episodes of apnoea or hypopnoea. These periods of apnoea/hypopnoea are caused by intermittent collapse of the upper airway. It is evidenced that OSAHS is associated with increased risk of hypertension, cardiovascular disease, stroke, daytime sleepiness,

motor vehicle accidents and diminished quality of life (1, 2).

Continuous positive airway pressure (CPAP) has already been proven by several randomised controlled studies to be an effective treatment for OSAHS and has become the standard treatment for patients with moderate to severe OSAHS (3–5). However, the low compliance, which is caused by mask discomfort, nasal dryness and difficulty in adapting to the



Review

The Efficacy of Device Designs (Mono-block or Bi-block) in Oral Appliance Therapy for Obstructive Sleep Apnea Patients: A Systematic Review and Meta-Analysis

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Abstract: Oral appliance (OA_m) therapy has demonstrated efficacy in treating obstructive sleep apnea (OSA). The aim of this systematic review was to clarify the efficacy of device designs (Mono-block or Bi-block) in OA_m therapy for OSA patients. We performed a meta-analysis using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system. Two studies (Mono-block OA_m versus Bi-block OA_m) remained eligible after applying the exclusion criteria. When comparing Mono-block OA_m and Bi-block OA_m, Mono-block OA_m significantly reduced the apnea–hypopnea index (2.92; 95% confidence interval (95%CI), 1.26 to 4.58; $p = 0.0006$), and patient preference for Mono-block OA_m was significantly higher (2.06; 95%CI, 1.44 to 2.06; $p < 0.0001$). Lowest SpO₂, arousal index, non-REM stage 3, sleep efficiency, Epworth Sleepiness Scale (ESS), Snoring Scale, and side effects were not significantly different between the two groups (lowest SpO₂: −11.18; 95%CI, −26.90 to 4.54; $p = 0.16$, arousal index: 4.40; 95%CI, −6.00 to 14.80; $p = 0.41$, non-REM stage 3: −2.00; 95%CI, −6.00 to 14.80; $p = 0.41$, sleep efficiency: −1.42, 95%CI, −4.71 to 1.86; $p = 0.40$, ESS: 0.12; 95%CI, −1.55 to 1.79; $p = 0.89$, Snoring Scale: 0.55; 95%CI, −0.73 to 1.83, $p = 0.55$, side effects: 1.00, 95%CI, 0.62 to 1.61, $p = 1.00$). In this systematic review, the use of Mono-block OA_m was more effective than Bi-block OA_m for OSA patients.

Keywords: obstructive sleep apnea; oral appliance; systematic review; mono-block; bi-block

Randomized Controlled Trial

Use of bibloc and monobloc oral appliances in obstructive sleep apnoea: a multicentre, randomized, blinded, parallel-group equivalence trial

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Summary

Background: The clinical benefit of bibloc over monobloc appliances in treating obstructive sleep apnoea (OSA) has not been evaluated in randomized trials. We hypothesized that the two types of appliances are equally effective in treating OSA.

Objective: To compare the efficacy of monobloc versus bibloc appliances in a short-term perspective.

Patients and methods: In this multicentre, randomized, blinded, controlled, parallel-group equivalence trial, patients with OSA were randomly assigned to use either a bibloc or a monobloc appliance. One-night respiratory polygraphy without respiratory support was performed at baseline, and participants were re-examined with the appliance in place at short-term follow-up. The primary outcome was the change in the apnoea–hypopnea index (AHI). An independent person prepared a randomization list and sealed envelopes. Evaluating dentist and the biomedical analysts who evaluated the polygraphy were blinded to the choice of therapy.

Results: Of 302 patients, 146 were randomly assigned to use the bibloc and 156 the monobloc device; 123 and 139 patients, respectively, were analysed as per protocol. The mean changes in AHI were –13.8 (95% confidence interval –16.1 to –11.5) in the bibloc group and –12.5 (–14.8 to –10.3) in the monobloc group. The difference of –1.3 (–4.5 to 1.9) was significant within the equivalence interval ($P = 0.011$; the greater of the two P values) and was confirmed by the intention-to-treat analysis ($P = 0.001$). The adverse events were of mild character and were experienced by similar percentages of patients in both groups (39 and 40 per cent for the bibloc and monobloc group, respectively).

Limitations: The study shows short-term results with a median time from commencing treatment to the evaluation visit of 56 days and long-term data on efficacy and harm are needed to be fully conclusive.

Comparison between mono-bloc and bi-bloc mandibular advancement devices for obstructive sleep apnea

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Abstract Although mandibular advancement device (MAD) is widely used, there are a few papers comparing the efficacy and compliance at the same time according to the type of MAD. The aim of this study is to compare the efficacy and compliance between mono-bloc and bi-bloc MAD in the treatment of obstructive sleep apnea (OSA). Ninety-three patients who treated with mono-bloc MAD and 60 patients with bi-bloc MAD from January 2007 through September 2011 were retrospectively enrolled. All the patients underwent full-night polysomnography (PSG) before and 3 months after MAD was applied. The response rate was significantly higher in the patients using mono-bloc than those using bi-bloc MAD (77.4 vs. 58.3 %; $P = 0.012$). In contrast, the compliance rate of MAD use was significantly higher in the patients using bi-bloc than those using mono-bloc MAD (68.8 vs. 83.3 %; $P = 0.044$) at 1 year. According to the severity of OSA, the response

rate was significantly higher in severe OSA than in mild to moderate OSA ($P = 0.033$ for mono-bloc MAD and $P = 0.048$ for bi-bloc MAD). However, there was no difference in the compliance between mild to moderate OSA and severe OSA. Our study showed that mono-bloc MAD was superior to bi-bloc MAD in efficacy while bi-bloc MAD is superior to mono-bloc MAD in compliance. We propose that both the efficacy and compliance should be considered in using MAD for treatment of OSA.

Keywords Obstructive sleep apnea ·
Mandibular advancement device · Efficacy ·
Compliance

Introduction

Obstructive sleep apnea (OSA) is a prevalent disease characterized by recurrent episodes of partial or complete obstruction of the upper airways during sleep [1]. Population-based epidemiology studies have showed that OSA is associated with hypertension, type II diabetes, cardiovascular disease and stroke [2, 3]. Because the first description in the medical literature, many treatment methods, such as weight loss, oral appliances and surgery of the upper airway have been proposed for OSA, but it has been thought that the most efficacious treatment is nasal continuous positive airway pressure (CPAP) therapy [4]. CPAP therapy requires the use of a mask interface, which have made many OSA patients discontinue CPAP treatment because of its discomfort. Surgery of the upper airway also has limitations of morbidity associated with surgery and variable surgical success rate [5].

MAD is one of oral appliance and has emerged over the last decades as an alternative therapy for OSA [4] because MAD can also effectively reduce the collapsibility of the

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Comparison of Adjustable and Fixed Oral Appliances for the Treatment of Obstructive Sleep Apnea

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Study Objectives: To compare the efficacy of adjustable and fixed oral appliances for the treatment of OSA.

Methods: Retrospective review of consecutive patients with OSA treated with either adjustable or fixed oral appliances. Polysomnography was conducted before and during therapy. Effective treatment was defined as an apnea-hypopnea index (AHI) < 5 events/h or < 10 events/h with resolution of sleepiness (Epworth < 10). We compared efficacy rates between fixed and adjustable appliances and sought to identify factors associated with greater success.

Results: We included 805 patients, 602 (74.8%) treated with an adjustable and 203 (25.2%) a fixed oral appliances. Among the cohort, 86.4% were men; mean age was 41.3 ± 9.2 years. Mean AHI was 30.7 ± 25.6, with 34.1% having mild (AHI 5-14.9), 29.2% moderate (AHI 15-29.9), and 36.8% severe (AHI ≥ 30) OSA. Successful therapy was significantly more common with adjustable appliances. Obstructive events were reduced to < 5/h in 56.8% with adjustable compared to

47.0% with fixed appliances (p = 0.02). Similarly, a reduction of events to < 10 with resolution of sleepiness occurred in 66.4% with adjustable appliances versus 44.9% with fixed appliances (p < 0.001). For both devices, success was more common in younger patients, with lower BMI and less severe disease.

Conclusions: Adjustable devices produced greater reductions in obstructive events and were more likely to provide successful therapy, especially in moderate-severe OSA. Fixed appliances were effective in mild disease, but were less successful in those with higher AHIs. Given these findings, the baseline AHI should be considered when selecting the type of oral appliance.

Keywords: Oral appliance, mandibular advancement device, obstructive sleep apnea, efficacy

Citation: Lettieri CJ; Paolino N; Eliasson AH; Shah AA; Holley AB. Comparison of adjustable and fixed oral appliances for the treatment of obstructive sleep apnea. *J Clin Sleep Med* 2011;7(5):439-445.

While continuous positive airway pressure (CPAP) therapy remains the treatment of choice for most patients with obstructive sleep apnea (OSA), its efficacy is often limited by intolerance and poor adherence.¹⁻³ The need for a reliable source of electricity and inconvenience with travel further limit its use.

A commentary on this article appears in this issue on page 447.

Mandibular advancement devices, or oral appliances (OAs), are an approved, frequently effective alternative to CPAP for the treatment of OSA.⁴⁻⁷ Numerous studies have established the ability of OAs to ablate obstructive apneas and hypopneas.⁸⁻¹³ Existing research demonstrates that OA therapy is superior to commonly offered surgical procedures,^{8,9} and may be comparable to CPAP when adherence is included in the definition of successful treatment.¹²⁻²¹ In 2006, the American Academy of Sleep Medicine (AASM) published updated OSA treatment guidelines which state that OAs are a reasonable alternative to CPAP in patients with mild to moderate OSA who prefer these devices or do not tolerate CPAP.⁵

Mandibular advancement devices provide a therapeutic effect by protruding the mandible relative to the maxilla, simultaneously advancing the tongue and reducing the propensity for airway collapse during sleep. Mandibular advancement devices are either fixed (i.e., the degree of mandibular advancement cannot

BRIEF SUMMARY

Current Knowledge/Study Rationale: Oral appliances are an approved, frequently effective alternative to CPAP for the treatment of OSA. Both fixed and adjustable devices are available. However, the ability of fixed devices to provide adequate therapy has not been established. The purpose of this study was to compare the efficacy of fixed and adjustable oral appliances in the treatment of OSA.

Study Impact: Among a large cohort of patients with a wide range of OSA severity, we found adjustable appliances provided greater reductions in the AHI and were more likely to provide successful therapy compared with fixed devices, particularly in those with moderate-severe disease. Similar to previous reports, we found that successful therapy was more common in patients who were younger, had lower BMIs and less severe disease.

be changed) or adjustable (i.e., mandibular advancement can be increased or decreased). The degree of mandibular advancement sought is a balance between tolerance, side effects, and efficacy.¹⁰

Both fixed and adjustable oral appliances are custom molded and individually fabricated from models made by impressions of the patient's dentition to fit the upper and lower teeth. Fixed OAs are typically set to advance the mandible between 50% and 80% of its maximal protrusion and fabricated in a permanent position for therapeutic use. Adjustable OAs, on the other hand, can be further titrated (i.e., using a screw-type or similar advancing mechanism) to optimize therapeutic efficacy. Upon

Oral Appliance Treatment for Obstructive Sleep Apnea: An Update

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Oral appliances (OA) have emerged as an alternative to continuous positive airway pressure (CPAP) for obstructive sleep apnea (OSA) treatment. 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. 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. 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.

Keywords: Obstructive sleep apnea, oral appliance, mandibular advancement, adherence, effectiveness

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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 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}

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.⁴ 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 (OA_m). 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 OA_m enlarges the upper airway space, most notably in the lateral dimension of the velopharyngeal region.⁵ 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.⁶ Various amounts of anterior tongue movement also occur with mandibular advancement.⁶ Alternative OA designs which protrude the tongue instead of the mandible (tongue-retaining device [TRD]) are also available.⁷⁻⁹ 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

RESEARCH ARTICLE

Open Access



Antero-posterior mandibular position at different vertical levels for mandibular advancing device design

P. Mayoral¹, M. O. Lagravère^{2*}, M. Míguez-Contreras³ and M. García⁴

Abstract

Introduction: Mandibular Advancement Devices (MAD) have been reported to be an alternative treatment to CPAP in moderate to severe obstructive sleep apnea (OSA) cases. The design of MAD has a major influence on its success rate on the patient, and design features that have an influence on efficacy, tolerance, and compliance. The aim of this study was to determine the range of mandibular protrusion at different vertical points; 2, 5, 8 and 11 mm in a young adult population.

Methods: Fifty two students aged 19 to 23 years (mean 21.3 ± 1.7 ; 29 females and 23 males), with full permanent dentition participated in the study. The absolute range of maximal mandibular protrusion and retrusion was measured (mm) with the use of the George Gauge. Descriptive statistics, ANOVA and paired t-test using SPSS were used.

Results: Range of mandibular advancement was possible to be determined for the 4 levels of vertical opening with the gauges: 2 mm fork mean mandibular advance $13.10 \text{ mm} \pm 0.604$; 5 mm mean $11.98 \text{ mm} \pm 1.075$; 8 mm mean $11.20 \text{ mm} \pm 1.369$; 11 mm mean $9.87 \text{ mm} \pm 1.886$. No significant differences were found between class I, II, and III.

Conclusions: There is an impact of increased inter-incisal distance of effective mandibular protrusion when constructing a MAD. As vertical dimension increases the mandible rotates posteriorly and places itself in a more retrusive location, and the range of mandibular advancement reduces (**0.3 mm for every 1 mm of vertical increase**).

Keywords: Obstructive sleep apnea. Mandibular advancement device. Oral appliance design. Mandibular position, Vertical opening. Mandibular protrusion

Introduction

One of the symptoms of Obstructive sleep apnea (OSA) is the presence of recurrent episodes of partial/complete collapse of the upper airway [1]. This may lead to a fragmentation of the sleep pattern, a decrease in oxygen saturation and a partial pressure rise of CO₂ in the blood [2]. The arousals and the nocturnal hypoxemia can cause excessive daytime sleepiness, loss of concentration, hypertension and atherosclerosis [3]. In more severe cases, OSA may lead to stroke and heart failure, resulting in an increased prevalence of cardiovascular morbidity and mortality [4].

A type of treatment for OSA consists of the use of mandibular advancement devices (MAD) [1, 5]. These appliances keep the mandible in a forward/protruded position during sleep increasing the width of the airway and reducing its collapsibility [6]. Even though there are conflicting reports on the success rate of these appliances [1, 7], MAD have been reported to be an alternative treatment to Continuous Positive Airway Pressure (CPAP) in moderate to severe OSA cases [6, 8].

It should be noted that the range of success of MAD is limited and can present a high variability between individuals [9]. Clinical evidence over the success rate of MAD are not conclusive thus more research is needed to be able to determine its predictability [10, 11].

The design of the MAD has a major influence on its success rate on the patient [12], and the design features

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Effects of varying mandibular protrusion and degrees of vertical opening on upper airway dimensions in apneic dentate subjects

Einfluss verschieden starker Unterkieferverlagerungen und Bissanhebungen durch Protrusionsschienen auf die sagittale Atemwegsfläche von bezahnten Apnoepatienten

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Abstract

Introduction. Despite numerous studies investigating the dimensional and therapeutic effects of mandibular advancement splints (MASs), data regarding the effects of differently designed individual and non-adjustable MASs on the upper airway in fully dentate apneic subjects in the sagittal plane including comparison of these effects with a placebo device are sparse. The present study aimed to determine the dimensional changes in the sagittal plane created by differently designed MASs in the upper airway in fully dentate apneic subjects and to compare these changes with the effects of a placebo device.

Materials and methods. Magnetic resonance (MR) images of 9 dentate apneic subjects with 5 differently designed MASs and without a MAS were obtained. We measured the area of the entire pharynx (velopharynx, oropharynx, hypopharynx) on these MR images and compared the dimensional changes.

Results. The dimensional changes triggered by two specific MASs (75% of the maximum mandibular protrusion with 5 mm vertical opening, and 75% of the maximum mandibular protrusion with 10 mm of vertical opening) in the entire pharynx in the sagittal plane were statistically significant compared to the other

Zusammenfassung

Einleitung. Trotz zahlreicher Untersuchungen zu dimensional und therapeutischen Effekten von Protrusionsschienen gibt es bislang kaum Vergleichsdaten zum Einfluss verschiedener individueller, nicht einstellbarer Schienenkonstruktionen (bzw. Placeboschienen) auf die oberen Luftwege in der Sagittalebene. Die Studie an vollständig bezahnten Apnoepatienten sollte entsprechende Messwerte liefern.

Methode. Auf je 6 median-sagittalen MRT(Magnetresonanztomographie)-Aufnahmen von 9 Patienten, die auf 5 dieser Bilder unterschiedlich ausgeführte Schienen (4 Protrusionsschienen, 1 Placeboschiene) und auf einem Bild keine Schiene trugen, vermaßen wir jeweils die Querschnittsflächen des gesamten Rachenraums sowie seiner Teilabschnitte (Velo-, Oro-, Hypopharynx) und verglichen die jeweiligen Dimensionsänderungen.

Resultate. Bezogen auf die sagittale Gesamtfläche des Rachenraums bewirkten 2 der Protrusionsschienen (5 bzw. 10 mm Bissanhebung und Vorverlagerung um jeweils 75% der maximalen Unterkieferauslenkung) signifikante Dimensionsänderungen gegenüber den anderen Protrusionsschienen ($p < 0,05$). Bezogen auf die einzelnen Rachenabschnitte bewirkte lediglich die 10-mm-/75%-Schiene eine signifikante Ausdehnung des Velopharynx ($p \leq 0,003$).

Schlussfolgerung. Bei bezahnten Apnoepatienten beeinflusst die relative Strecke der Unterkieferverlagerung durch Protrusionsschienen die Dimension der oberen Luftwege in der Sagittalebene. Demgegenüber nimmt das Ausmaß der Bissanhebung durch solche Schienen keinen signifikanten Einfluss. Im Velopharynx sind diese Effekte der Unterkieferverlagerung größer als in den anderen Rachenabschnitten.

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Health Outcomes of Continuous Positive Airway Pressure versus Oral Appliance Treatment for Obstructive Sleep Apnea

A Randomized Controlled Trial

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Rationale: Continuous positive airway pressure (CPAP) and mandibular advancement device (MAD) therapy are commonly used to treat obstructive sleep apnea (OSA). Differences in efficacy and compliance of these treatments are likely to influence improvements in health outcomes.

Objectives: To compare health effects after 1 month of optimal CPAP and MAD therapy in OSA.

Methods: In this randomized crossover trial, we compared the effects of 1 month each of CPAP and MAD treatment on cardiovascular and neurobehavioral outcomes.

Measurements and Main Results: Cardiovascular (24-h blood pressure, arterial stiffness), neurobehavioral (subjective sleepiness, driving simulator performance), and quality of life (Functional Outcomes of Sleep Questionnaire, Short Form-36) were compared between treatments. Our primary outcome was 24-hour mean arterial pressure. A total of 126 patients with moderate-severe OSA (apnea hypopnea index [AHI], 25.6 [SD 12.3]) were randomly assigned to a treatment order and 108 completed the trial with both devices. CPAP was more efficacious than MAD in reducing AHI (CPAP AHI, 4.5 ± 6.6/h; MAD AHI, 11.1 ± 12.1/h; $P < 0.01$) but reported compliance was higher on MAD (MAD, 6.50 ± 1.3 h per night vs. CPAP, 5.20 ± 2 h per night; $P < 0.00001$). The 24-hour mean arterial pressure was not inferior on treatment with MAD compared with CPAP (CPAP-MAD difference, 0.2 mm Hg [95% confidence interval, -0.7 to 1.1]); however, overall, neither treatment improved blood pressure. In contrast, sleepiness, driving simulator performance, and disease-specific quality of life

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Author Contributions: P.A.C., R.R.G., M.A.D., G.B.M., and C.L.P. were responsible for the concept and design of the study. A.S.M., V.K.S., M.A.D., and C.L.P. were responsible for data acquisition. C.L.P., P.A.C., G.B.M., R.R.G., and A.S.M. performed the analysis and interpretation of data. C.L.P., P.A.C., and G.B.M. drafted the manuscript. All authors were responsible for revising of the manuscript for important intellectual content. C.L.P. and G.B.M. performed all statistical analyses. P.A.C., R.R.G., and M.A.D. obtained funding for the study. P.A.C., C.L.P., B.J.Y., and A.S.M. provided administrative, technical, and material support for the study. C.L.P. and P.A.C. supervised the study. C.L.P. is the guarantor.

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AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Continuous positive airway pressure (CPAP) is considered to be the treatment of choice for obstructive sleep apnea (OSA). Oral appliance (OA) therapy, such as the mandibular advancement device (MAD), is a viable alternative with growing use, particularly in patients with milder OSA. Comparative effectiveness studies that examine multiple important health outcomes with these treatment modalities in patients with the full spectrum of OSA severity are lacking.

What This Study Adds to the Field

In the short term, health outcomes in patients with moderate to severe OSA were similar after treatment with CPAP and MAD. This was likely explained by the greater efficacy of CPAP being offset by inferior compliance relative to MAD. These findings strongly challenge current practice parameters recommending MAD treatment be considered only in patients with mild to moderate OSA. Long-term comparative effectiveness studies between CPAP and MAD that include objectively measured treatment compliance are needed to better define treatment strategies for patients with OSA.

improved on both treatments by similar amounts, although MAD was superior to CPAP for improving four general quality-of-life domains.

Conclusions: Important health outcomes were similar after 1 month of optimal MAD and CPAP treatment in patients with moderate-severe OSA. The results may be explained by greater efficacy of CPAP being offset by inferior compliance relative to MAD, resulting in similar effectiveness.

Clinical trial registered with <https://www.anzctr.org.au> (ACTRN 12607000289415).

Keywords: obstructive sleep apnea; continuous positive airway pressure; mandibular advancement device; health outcomes; efficacy and compliance

Obstructive sleep apnea (OSA) affects up to 17% of adults in the United States. The prevalence is similar in other western and eastern populations (1). OSA is characterized by disordered breathing during sleep, resulting in sleep fragmentation and intermittent hypoxemia. Patients often suffer excessive daytime

Effects of CPAP and mandibular advancement device treatment in obstructive sleep apnea patients: a systematic review and meta-analysis

Martha Schwartz¹ · Luis Acosta¹ · Yuan-Lung Hung¹ · Mariela Padilla² · Reyes Enciso³ 

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Abstract The purpose of this review is to conduct a systematic review and meta-analysis comparing the effects of continuous positive airway pressure (CPAP) with a mandibular advancement device (MAD) in improving the quality of life (sleepiness, cognitive, and functional outcomes) in patients diagnosed with obstructive sleep apnea (OSA). Authors identified randomized, placebo-controlled studies from MEDLINE through PubMed, Web of Science, and the Cochrane Library. Studies were assessed for inclusion and exclusion criteria, as well as risk of bias. Initial search yielded 240 unduplicated references, which the authors reduced to 12 relevant studies. Patients with CPAP therapy showed no statistically significant difference in the post-treatment quality of life measured with the SF-36 mental health component ($p = .994$), or the SF-36 physical functioning component ($p = .827$). There was no significant improvement in neither Functional Outcomes of Sleep Questionnaire ($p = .788$) nor cognitive performance ($p = .395$) compared to

patients treated with oral appliances. However, the meta-analyses' overall results showed a significant improvement in the post-treatment apnea–hypopnea index (AHI) in favor of CPAP therapy as compared with the oral appliance group ($p < .001$). Meta-analyses showed unclear results for sleepiness with no significant differences in average post-treatment Epworth Sleepiness Scale [ESS] ($p = .203$), but significant differences in change in ESS from baseline favorable to CPAP treatment ($p = .047$). Further studies are needed. Compliance with treatment was 1.1 h per night significantly lower with CPAP than MAD ($p = .004$), which could explain why though efficacy (AHI) is better with CPAP, no significant results are shown for quality of life, cognitive, and functional outcomes. **Though CPAP is significantly more efficient in reducing AHI (moderate quality of evidence), it has a significantly lower compliance resulting in no differences with MAD in quality of life, cognitive, or functional outcomes.** Sleep medicine professionals

Never presented at a conference.

No clinical trial, Systematic review.

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Oral Appliance Versus Continuous Positive Airway Pressure in Obstructive Sleep Apnea Syndrome: A 2-Year Follow-up

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Study Objectives: Oral appliance therapy has emerged as an important alternative to continuous positive airway pressure (CPAP) in treating patients with obstructive sleep apnea syndrome (OSAS). In this study we report about the subjective and objective treatment outcome of oral appliance therapy and CPAP in patients with OSAS.

Design: Cohort study of a previously conducted randomized clinical trial.

Setting: University Medical Center, Groningen, The Netherlands.

Patients or Participants: One hundred three patients with OSAS.

Interventions: CPAP and oral appliance therapy (Thornton Adjustable Positioner type-1, Airway Management, Inc., Dallas, TX, USA)

Measurements and Results: Objective (polysomnography) and subjective (Epworth Sleepiness Scale, Functional Outcomes of Sleep Questionnaire, Medical Outcomes Study 36-item Short Form Health Survey [SF-36]) parameters were assessed after 1 and 2 years of treatment. Treatment was considered successful when the apnea-hypopnea index (AHI) was < 5 or showed substantial reduction, defined as reduction in the index of at least 50% from the baseline value to a value of < 20 in a patient without OSAS symptoms while undergoing therapy.

Regarding the proportions of successful treatments, no significant difference was found between oral appliance therapy and CPAP in treating mild to severe OSAS in a 2-year follow-up. More patients (not significant) dropped out under oral appliance therapy (47%) compared with CPAP (33%). Both therapies showed substantial improvements in polysomnographic and neurobehavioral outcomes. However, CPAP was more effective in lowering the AHI and showed higher oxyhemoglobin saturation levels compared to oral appliance therapy ($P < 0.05$).

Conclusions: Oral appliance therapy should be considered as a viable treatment alternative to continuous positive airway pressure (CPAP) in patients with mild to moderate obstructive sleep apnea syndrome (OSAS). In patients with severe OSAS, CPAP remains the treatment of first choice.

Clinical Trial Information: The original randomized clinical trial, of which this study is a 2-year follow-up, is registered at [ISRCTN.org](http://www.isrctn.org); identifier: [ISRCTN18174167](http://www.isrctn.org/ISRCTN18174167); trial name: Management of the obstructive sleep apnea-hypopnea syndrome: oral appliance versus continuous positive airway pressure therapy; URL: <http://www.controlled-trials.com/ISRCTN18174167>.

Keywords: Continuous positive airway pressure, obstructive sleep apnea syndrome, oral appliances, treatment outcome

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a sleep related breathing disorder characterized by snoring and repetitive pharyngeal collapse.¹ It is associated with excessive daytime sleepiness, a decreased quality of life, increased cardiovascular morbidity, and a higher risk of traffic accidents.^{2,3} The standard treatment, i.e., continuous positive airway pressure (CPAP), reduces upper airway obstructions and improves quality of life.⁴ However, because of the cumbersome nature of CPAP, patients often have difficulty adhering to or may even abandon treatment. Oral appliance therapy has been shown to be superior to CPAP regarding treatment success in patients with mild to moderate OSAS in

the short term.⁵ Furthermore, many patients prefer oral appliance therapy to CPAP.⁶ Long-term outcomes of oral appliance therapy have been described in a few studies.⁷⁻¹¹ In four studies, respiratory parameters deteriorated in some patients during the follow-up period, even in patients who were treated successfully at short-term follow-up.^{7,8,10,11} Some studies have been restricted to those patients with mild and moderate OSAS or included patients who had already undergone surgical treatment of OSAS. To our knowledge, no published parallel study has evaluated the 2-y outcome of oral appliance versus CPAP therapy in previously untreated patients with mild to severe OSAS.

The primary aim of this parallel cohort study was to evaluate the 2-y objective and subjective outcome of oral appliance and CPAP therapy in patients with OSAS, representing the entire spectrum of the disorder and to gain more insight into the specific indications for both treatments. In this study we report on the 2-y follow-up of a cohort of a previously conducted randomized controlled trial (RCT).⁵

METHODS

Patients and Study Protocol

After assessing 228 patients with OSAS, 103 participants were recruited (between September 2002 and August 2005) for the

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Titrated mandibular advancement *versus* positive airway pressure for sleep apnoea

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ABSTRACT: The aim of this study was to compare mandibular advancement device (MAd) therapy and continuous positive airway pressure (CPAP) for obstructive sleep apnoea/hypopnoea syndrome (OSAHS) after one-night polysomnographic (PSG) titration of both treatments.

59 OSAHS patients (apnoea/hypopnoea index (AHI): 34 ± 13 events·h⁻¹; Epworth scale: 10.6 ± 4.5) were included in a crossover trial of 8 weeks of MAd and 8 weeks of CPAP after effective titration. Outcome measurements included home sleep study, sleepiness, health-related quality of life (HRQoL), cognitive tests, side-effects, compliance and preference.

The median (interquartile range) AHI was 2 (1–8) events·h⁻¹ with CPAP and 6 (3–14) events·h⁻¹ with MAd ($p < 0.001$). Positive and negative predictive values of MAd titration PSG for treatment success were 85% and 45%, respectively. Both treatments significantly improved subjective and objective sleepiness, cognitive tests and HRQoL. The reported compliance was higher for MAd ($p < 0.001$) with >70% of patients preferring this treatment.

These results support titrated MAd as an effective therapy in moderately sleepy and overweight OSAHS patients. Although less effective than CPAP, successfully titrated MAd was very effective at reducing the AHI and was associated with a higher reported compliance. Both treatments improved functional outcomes to a similar degree. One-night titration of MAd had a low negative predictive value for treatment success.

KEYWORDS: Continuous positive airway pressure, mandibular advancement, obstructive sleep apnoea, titration, treatment

Obstructive sleep apnoea/hypopnoea syndrome (OSAHS) is a highly prevalent disease [1] characterised by recurrent episodes of partial or complete obstruction of the upper airways during sleep. Nasal continuous positive airway pressure (CPAP) is the primary treatment of OSAHS, but many patients are unable or unwilling to comply with this treatment. Of OSAHS patients in whom CPAP is recommended, 5–50% reject this treatment and 12–25% of the remaining patients can be expected to discontinue CPAP, especially if they have mild OSAHS and/or if they are not “subjectively sleepy” [2, 3]. Mandibular advancement device (MAd) therapy has emerged over the last decade as an alternative therapy for OSAHS [4]. Randomised control trials have demonstrated a reduction of the apnoea/hypopnoea index (AHI) and an improvement of daytime sleepiness with MAd therapy [5, 6]. In most randomised studies evaluating MAd therapy in OSAHS, the degree of mandibular advancement (MA) was arbitrarily set without any titration procedure, for example at 80% of the maximal comfortable MA [5, 7].

A dose-dependent effect of MA on the AHI, nocturnal oxygen desaturations and pharyngeal collapsibility has been previously demonstrated [8–10], suggesting the potential benefit of an individual MA titration in patients with OSAHS. Comparative studies of MAd and CPAP should therefore include a titration procedure for both treatments. In a pilot study [11], it was demonstrated that it is possible to mobilise the mandible during polysomnography without waking the patient during the advancement manoeuvres. The simple propulsion system that was used in this study allowed one-night titration of the effective MA away from the patient's bedside and prediction of the capacity of MAd to reduce AHI. To the best of our knowledge, no published randomised study has evaluated MAd therapy in OSAHS after polysomnographic (PSG) titration of the effective MA.

The aim of this multi-site, randomised crossover study was to compare 8 weeks of MAd therapy and 8 weeks of CPAP in a mixed-severity group of patients with OSAHS in terms of efficacy, reported side-effects, compliance and preference.

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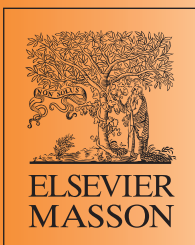
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Références

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Original Investigation

CPAP vs Mandibular Advancement Devices and Blood Pressure in Patients With Obstructive Sleep Apnea

A Systematic Review and Meta-analysis

Daniel J. Bratton, PhD; Thomas Gaisl, MD; Annette M. Wons, MD; Malcolm Kohler, MD

 Supplemental content at jama.com

IMPORTANCE Obstructive sleep apnea is associated with higher levels of blood pressure (BP), which can lead to increased cardiovascular risk.

OBJECTIVE To compare the association of continuous positive airway pressure (CPAP), mandibular advancement devices (MADs), and inactive control groups (placebo or no treatment) with changes in systolic BP (SBP) and diastolic BP (DBP) in patients with obstructive sleep apnea.

DATA SOURCES The databases of MEDLINE, EMBASE, and the Cochrane Library were searched up to the end of August 2015 and study bibliographies were reviewed.

STUDY SELECTION Randomized clinical trials comparing the effect of CPAP or MADs (vs each other or an inactive control) on BP in patients with obstructive sleep apnea were selected by consensus. Of 872 studies initially identified, 51 were selected for analysis.

DATA EXTRACTION AND SYNTHESIS Data were extracted by one reviewer and checked by another reviewer. A network meta-analysis using multivariate random-effects meta-regression was used to estimate pooled differences between each intervention. Meta-regression was used to assess the association between trial characteristics and the reported effects of CPAP vs inactive control.

MAIN OUTCOMES AND MEASURES Absolute change in SBP and DBP from baseline to follow-up.

RESULTS Of the 51 studies included in the analysis (4888 patients), 44 compared CPAP with an inactive control, 3 compared MADs with an inactive control, 1 compared CPAP with an MAD, and 3 compared CPAP, MADs, and an inactive control. Compared with an inactive control, CPAP was associated with a reduction in SBP of 2.5 mm Hg (95% CI, 1.5 to 3.5 mm Hg; $P < .001$) and in DBP of 2.0 mm Hg (95% CI, 1.3 to 2.7 mm Hg; $P < .001$). A 1-hour-per-night increase in mean CPAP use was associated with an additional reduction in SBP of 1.5 mm Hg (95% CI, 0.8 to 2.3 mm Hg; $P < .001$) and an additional reduction in DBP of 0.9 mm Hg (95% CI, 0.3 to 1.4 mm Hg; $P = .001$). Compared with an inactive control, MADs were associated with a reduction in SBP of 2.1 mm Hg (95% CI, 0.8 to 3.4 mm Hg; $P = .002$) and in DBP of 1.9 mm Hg (95% CI, 0.5 to 3.2 mm Hg; $P = .008$). There was no significant difference between CPAP and MADs in their association with change in SBP (-0.5 mm Hg [95% CI, -2.0 to 1.0 mm Hg]; $P = .55$) or in DBP (-0.2 mm Hg [95% CI, -1.6 to 1.3 mm Hg]; $P = .82$).

CONCLUSIONS AND RELEVANCE Among patients with obstructive sleep apnea, both CPAP and MADs were associated with reductions in BP. Network meta-analysis did not identify a statistically significant difference between the BP outcomes associated with these therapies.

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Conclusion Il s'agit des premiers résultats permettant d'évoquer les facteurs conditionnant le comportement de la pression au cours du traitement par PPC pouvant orienter le choix thérapeutique dans la prise en charge du SAHOS.

Déclaration de liens d'intérêts Les auteurs déclarent ne pas avoir de liens d'intérêts.

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Bénéfices cliniques d'une orthèse d'avancée mandibulaire (OAM) sur mesure CAD/CAM sur la pression artérielle dans le syndrome d'apnées hypopnées obstructives du sommeil (SAHOS)



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(J.C. Meurice)

Introduction ORCADES est une étude prospective multicentrique française évaluant à long terme les bénéfices cliniques d'une OAM sur mesure dans le traitement du SAHOS après refus ou échec de PPC [1]. Les résultats à 3–6 mois sur l'évolution de la pression artérielle sous traitement sont présentés dans la Figure 1.

Méthodes Au total, 299 pts SAHOS éligibles traités avec une OAM sur mesure CAD/CAM (Narval, ResMed) ont bénéficié d'une évaluation au repos de la pression artérielle avant traitement par orthèse puis lors de la visite de suivi. Le patient était considéré hypertendu à l'inclusion lorsque la pression artérielle systolique (PAS) était ≥ 140 mmHg et/ou la pression artérielle diastolique (PAD) était ≥ 90 mmHg.

Résultats Notre population concernait 77 (26 %) patients hypertendus (HTN, PAS 140 ± 8 mmHg, PAD 89 ± 8 mmHg) et 222 (74 %) patients non hypertendus (non HTN, PAS 122 ± 9 mmHg, PAD 74 ± 8 mmHg) : 75 % d'hommes, âge 53 ± 11 ans, IAH 29 ± 15 /h. Dans le groupe HTN, l'IMC était plus élevé et la SpO₂ minimale plus basse. À 3–6 mois, l'efficacité du traitement par orthèse (réduction de l'IAH initial ≥ 50 %) était supérieure dans le groupe non HTN vs HTN (84 % vs 66 %, $p = 0,0012$). L'amélioration de la saturation en oxygène, des symptômes et de la qualité de vie était similaire dans les deux groupes, sans variation de poids. Dans le groupe HTN, la PAS et la PAD étaient diminuées sous traitement par orthèse de respectivement $-7,6 \pm 12,7$ et $-6,8 \pm 10,2$ mmHg ($p < 0,0001$ vs inclusion et $p < 0,0001$ vs groupe non HTN) ; la pression artérielle était normalisée chez 59 % des patients. Il n'y avait aucune modification de la PAS ou de la PAD dans le groupe non HTN. La baisse de PAS était corrélée avec l'amélioration de la SpO₂ moyenne ($\rho = -0,30$, $p = 0,022$). Huit pour cent des patients ont arrêté prématurément le traitement pour effets indésirables. L'observance moyenne était de 6,7 h/nuit et de 6,7 jours/semaine.

Conclusion Une OAM CAD/CAM sur mesure est efficace dans le traitement du SAHOS léger à sévère avec des bénéfices additionnels sur la pression artérielle.

Groupe	PA	Inclusion	3 mois suivi	Δ	P
HTN	PAS, mmHg	140.3 \pm 7.8	133.3 \pm 12.0	-7.6 \pm 12.7 *	<0.0001
NON HTN	PAS, mmHg	122.3 \pm 9.0	123.5 \pm 13.2	1.5 \pm 12.8	NS
HTN	PAD, mmHg	88.6 \pm 8.0	81.8 \pm 9.1	-6.8 \pm 10.2 *	<0.0001
NON HTN	PAD, mmHg	74.1 \pm 7.6	75.4 \pm 9.7	1.5 \pm 10.4	NS

Fig. 1 Évolution de la pression artérielle sous traitement par OAM. HTN : hypertendu ; non HTN : non hypertendu ; PAD : pression artérielle diastolique ; PAS : pression artérielle systolique. * $p < 0,000$, vs non HTN.

Déclaration de liens d'intérêts J.C. Meurice déclare les liens d'intérêts : ResMed : Investigateur et membre du Comité Scientifique de l'étude ORCADES.

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ORIGINAL ARTICLE

Cardiovascular mortality in obstructive sleep apnoea treated with continuous positive airway pressure or oral appliance: An observational study

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ABSTRACT

Background and objective: The objective of this study was to evaluate the **long-term cardiovascular mortality in patients with severe obstructive sleep apnoea (OSA)** treated with either continuous positive airway pressure (CPAP) or mandibular advancing device (MAD).

Methods: A non-concurrent cohort study of 570 subjects with severe OSA (apnoea/hypopnoea index (AHI) ≥ 30 /h) and a control group of 269 subjects (AHI < 5 /h) were followed up for a median of 79 months (interquartile range 76–88 months). All patients received CPAP initially. MAD was offered for those who were non-adherent to CPAP. The endpoint was cardiovascular death.

Results: Two hundred and eight control subjects, 177 patients treated with CPAP, 72 with MAD and 212 who declined treatment were analysed. Forty-two patients had a fatal cardiovascular event during the course of the study. The non-apnoeic group had the lowest cardiovascular death rate (0.28 per 100 person-years (95% confidence interval (CI): 0.08–0.71)) followed by the CPAP-treated (0.56 per 100 person-years (95% CI: 0.20–1.23)) and the MAD-treated OSA group (0.61 per 100 person-years (95% CI: 0.13–1.78)), with the highest cardiovascular mortality rate observed in the untreated OSA group (2.1 per 100 person-years (95% CI: 1.37–2.92)). Although residual AHI for MAD-treated patients was significantly higher than CPAP-treated patients (16.3 ± 5.1 /h vs. 4.5 ± 2.3 /h; $P < 0.001$), there was no difference in cardiovascular death rate between the two groups (hazard ratio 1.08 (95% CI: 0.55–1.74); $P = 0.71$).

Conclusions: Both CPAP and MAD may be equally effective therapy in reducing the risk of fatal cardiovascular events in patients with severe OSA.

SUMMARY AT A GLANCE

This study suggests for the first time that oral appliances may confer reduction in cardiovascular mortality for patients with severe obstructive sleep apnoea intolerant to continuous positive airway pressure.

Key words: cardiovascular mortality, continuous positive airway pressure, obstructive sleep apnoea, oral appliance, outcome.

Abbreviations: CI, confidence interval; CPAP, continuous positive airway pressure; MAD, mandibular advancing device; OSA, obstructive sleep apnoea.

INTRODUCTION

Continuous positive airway pressure (CPAP) is the gold standard treatment for severe obstructive sleep apnoea (OSA). Randomized trials have shown CPAP benefits in daytime sleepiness, blood pressure, quality of life and endothelial dysfunction.^{1–3} Large-scale studies have demonstrated that CPAP reduces also the risk of fatal and non-fatal cardiovascular events in severe OSA.^{4,5} However, the clinical effectiveness of CPAP is often limited by poor patient and partner acceptance and suboptimal compliance.⁶ Mandibular advancing device (MAD) therapy has emerged as a non-invasive alternative to CPAP for the treatment of snoring and mild to moderate OSA.^{7,8} Although less efficacious than CPAP in ameliorating polysomnographic indices, oral appliances are generally more preferred by patients than CPAP.⁹ Prospective studies have shown efficacy of MAD in reducing respiratory disturbance index, blood pressure, and improved sleepiness, sleep quality, and subject's and bed partner's satisfaction.^{10–14} A major drawback of these clinical investigations is the limited

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OPEN ACCESS

ORIGINAL ARTICLE

Objective measurement of compliance during oral appliance therapy for sleep-disordered breathing

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► Additional data are published online only. To view these files please visit the journal online (<http://dx.doi.org/10.1136/thoraxjnl-2012-201900>)

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ABSTRACT

Background Oral appliance (OA) therapy is increasingly prescribed as a non-continuous positive airway pressure treatment modality for sleep-disordered breathing (SDB). Although OA therapy is reported to be efficacious for the treatment of SDB, data on compliance remain limited to self-report.

Methods In this 3-month prospective clinical trial, the main outcome was to assess the safety and feasibility of an objective measurement of compliance during OA therapy using an embedded microsensor thermometer with on-chip integrated readout electronics in 51 consecutive patients with an established diagnosis of SDB (AHI 18.0±11.9/h; age 47±10 y; BMI 26.6±4.0 kg/m²; men/women: 31/20). Patients were unaware of the purpose of the study.

Results No microsensor-related adverse events were recorded. In addition, no problems were encountered during the readout of the compliance data. Out of 51 microsensors, one had a technical defect and was lost to follow-up. In this study, the overall objective mean rate of OA use was 6.6±1.3 h per day with a regular OA users' rate of 82% at the 3-month follow-up. Statistical analysis revealed no significant differences between objective and self-reported OA compliance data in this study.

Measurement of the objective OA compliance allowed us to calculate the mean disease alleviation (MDA) as the product of objective compliance and therapeutic efficacy. MDA serves as a measure of the overall therapeutic effectiveness, and turned out to be 51.1%.

Conclusions The results illustrate the safety and feasibility of objective measurement of OA compliance. The objective measurement of OA compliance allows for calculation of the MDA.

INTRODUCTION

The prevalence of sleep-disordered breathing (SDB) is remarkably high among middle-aged adults, with estimates reaching 9% for women and 24% for men.¹ SDB in adults spans a wide pathophysiological continuum of severity, from snoring over obstructive sleep apnoea (OSA) to obesity hypoventilation syndrome.² Epidemiological studies provide clear evidence that SDB is a strong and independent risk factor for hypertension with consequent cerebro- and cardiovascular morbidity and high mortality.^{3–5} As a result, SDB has major socio-economic consequences.⁶

OSA is characterised by repetitive pharyngeal collapse (apnoea) or upper airway narrowing

Key messages

What is the key question?

- To assess the safety and feasibility of the objective measurement of compliance during oral appliance (OA) therapy for sleep-disordered breathing (SDB) using a microsensor thermometer embedded in the OA.

What is the bottom line?

- Although OA therapy is reported to be efficacious for the treatment of SDB, data on compliance remain limited to self-report.

Why read on?

- The objective measurement of OA compliance allows for the calculation of the mean disease alleviation, defined as a combined function of efficacy and compliance, being a measure of the overall therapeutic effectiveness, and will become imperative in the evaluation of OA therapy success rates in the treatment of SDB.

(hypopnoea) during sleep, leading to hypoxaemia and hypercapnia, and causing sleep fragmentation that in turn leads to daytime sleepiness and increased risk of motor vehicle and occupational accidents.^{7–9} OSA is defined as the occurrence of more than five apnoeas and hypopnoeas per hour of sleep, expressed as the apnoea/hypopnoea index, or apnoea/hypopnoea index (AHI). The American Academy of Sleep Medicine (AASM) considers an AHI of between five and 15 to be mild OSA, between 15 and 30 to be moderate OSA, and >30 to be severe OSA.¹⁰

The gold standard for the treatment of OSA is continuous positive airway pressure (CPAP).^{11–12} CPAP improves systemic hypertension, and it has been demonstrated that successful CPAP treatment prolongs survival.⁵ Because of the high efficacy of CPAP, the therapeutic effectiveness of CPAP is potentially high. Its clinical effectiveness, however, is often limited by low patient acceptance, poor tolerance and a suboptimal CPAP compliance.^{13–14} Therefore, CPAP could result in a less favourable effectiveness than required.¹³ Accordingly, non-CPAP alternatives for the treatment of SDB have gained growing interest.^{13–16} Oral appliance (OA) therapy is increasingly prescribed as a non-invasive first-line alternative to CPAP.¹⁵ Mandibular

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SCIENTIFIC INVESTIGATIONS

Long-Term Objective Adherence to Mandibular Advancement Device Therapy Versus Continuous Positive Airway Pressure in Patients With Moderate Obstructive Sleep Apnea

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Study Objectives: Comparable health effects of mandibular advancement device (MAD) and continuous positive airway pressure (CPAP) therapy have been attributed to higher adherence with MAD compared with CPAP therapy. The objective of this study was to make a direct comparison of the objective adherence between MAD and CPAP in patients with moderate obstructive sleep apnea (OSA).

Methods: Adherence was monitored for 12 months in 59 patients with moderate OSA (apnea-hypopnea index 15–30 events/h) as part of a randomized controlled trial. Objective adherence with MAD was assessed using the TheraMon microsensor. Objective adherence with CPAP was assessed using the built-in registration software with readout on SD card. Self-reported adherence with both therapies was assessed using a questionnaire.

Results: Forty patients (68%) completed the study with the therapy to which they were randomly assigned. Median (interquartile range) objective adherence (h/night) in the 3rd month was 7.4 (5.2–8.2) for MAD and 6.8 (5.7–7.6) for CPAP ($P = .41$), compared to 6.9 (3.5–7.9) with MAD and 6.8 (5.2–7.6) with CPAP ($P = .85$) in the 12th month. There were no significant changes between the 3rd and 12th month for both MAD ($P = .21$) and CPAP ($P = .46$). Changes in adherence were not significantly different between MAD and CPAP ($P = .51$). Self-reported adherence was significantly higher with MAD than CPAP at all follow-ups. Self-reported adherence with CPAP was lower than objective CPAP adherence at the 6th and 12th month ($P = .02$).

Conclusions: Objective adherence with MAD and CPAP is comparable and consistent over time. Self-reported adherence is higher with MAD than with CPAP giving rise to interesting discrepancy between objective and self-reported adherence with CPAP.

Clinical Trial Registration: Registry: [ClinicalTrials.gov](https://clinicaltrials.gov); Identifier: NCT01588275

Keywords: sleep apnea, patient adherence, randomized controlled trial

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Although current evidence suggests higher adherence with a mandibular advancement device (MAD) than with continuous positive airway pressure (CPAP) therapy, a direct comparison between the objective adherence profiles of both treatment modalities has not yet been performed in patients with moderate obstructive sleep apnea (OSA).

Study Impact: This study shows that objective adherence with MAD and CPAP therapy is comparable and consistent over time. Self-reported adherence is higher with MAD than with CPAP therapy, and objective adherence with CPAP is higher than self-reported adherence with CPAP. This study enhances the knowledge about adherence rates of two regularly used treatment modalities in moderate OSA. The results do not support the general idea that adherence with MAD is higher compared with CPAP therapy.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder¹ characterized by repeated upper airway collapse during sleep resulting in a complete cessation or a substantial reduction in airflow. The repetitive airflow limitation

causes intermittent hypoxia, which in turn sets off a chain of events, including activation of the sympathetic nervous system, brief awakenings from sleep (arousals) and sleep fragmentation. Other consequences may include excessive daytime sleepiness, impaired quality of life, an increased risk to become involved in occupational^{2,3} and traffic accidents,^{4,5}

Review

Oral Appliances in Obstructive Sleep Apnea

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Abstract: Oral appliance therapy is increasingly prescribed as a non-invasive treatment option for patients diagnosed with obstructive sleep apnea. The custom-made titratable mandibular advancement devices (MAD) are the recommended type of oral appliances. Mandibular advancement devices are efficacious in reducing the severity of obstructive sleep apnea, however, only to a lesser extent than standard therapy using continuous positive airway pressure (CPAP). Although oral appliance therapy is known to reduce the severity of obstructive sleep apnea in most of the patients, one out of three patients still show negligible improvement under MAD therapy. Therefore, the selection of the appropriate candidates for this therapy is imperative and several upfront prediction tools are described. Overall, the health outcome of mandibular advancement device therapy is similar to that of CPAP, probably due to the inferior compliance of CPAP compared to MAD therapy, resulting in similar clinical effectiveness.

Keywords: mandibular advancement therapy; treatment; sleep-disordered breathing

1. Introduction

Obstructive sleep apnea (OSA) is an increasingly common disorder, affecting approximately 17% of adult women and 34% of men [1]. The main pathophysiological feature of OSA is repetitive narrowing (hypopnea) or closure (apnea) of the upper airway (UA) during sleep, causing intermittent hypoxia, intrathoracic pressure swings, sympathetic surges, and sleep fragmentation [2]. Due to these perturbations, OSA is linked to a range of harmful sequelae: excessive daytime sleepiness, fatigue, an impaired cognitive performance, a reduced quality of life, an increased risk of occupational and traffic accidents [3], metabolic disturbances [4], hypertension [5], cardio- and cerebrovascular morbidity, and OSA-related mortality [6].

Due to the high prevalence, as well as the individual and socioeconomic healthcare issues related to OSA, the effective management of this chronic disorder is imperative. The standard treatment for patients with moderate to severe OSA is continuous positive airway pressure (CPAP), applying pressurized air throughout the respiratory cycle to keep the upper airway patent [7]. Although CPAP is highly efficacious in reducing the severity of OSA, the clinical effectiveness is often compromised by low patient acceptance and suboptimal adherence [8].

Oral appliance therapy is increasingly prescribed as a non-invasive treatment option for patients with OSA. Oral appliances are indicated for use in patients with mild to moderate OSA who prefer oral appliance therapy to CPAP, who do not respond to CPAP, are not appropriate candidates for CPAP, or who fail treatment attempts with CPAP [9].



Dental side effects of long-term obstructive sleep apnea therapy: a 10-year follow-up study

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Abstract

Objectives Patients with obstructive sleep apnea (OSA) are usually treated with either mandibular advancement device (MAD) or continuous positive airway pressure (CPAP) therapy. The objective of this study is to evaluate changes in dental occlusion associated with long-term MAD and CPAP therapy.

Materials and methods Data from 14 OSA patients using MAD and 17 OSA patients using CPAP therapy were evaluated at baseline, 2-year and 10-year follow-up. Changes in dental occlusion were analyzed from dental plaster casts with a digital sliding caliper.

Results At 2-year follow-up, MAD therapy resulted in significant dental changes when compared with baseline values. In MAD therapy, overjet and overbite decreased with 1.1 ± 1.8 mm and 1.1 ± 1.2 mm respectively. With CPAP therapy overjet and overbite decreased significantly with 0.2 ± 0.5 mm and 0.3 ± 0.5 mm, respectively. Both groups also showed significant changes in molar occlusion. After a 10-year follow-up, significant and more pronounced changes were seen in overjet and overbite. In MAD therapy, overjet and overbite decreased with 3.5 ± 1.5 mm and 2.9 ± 1.5 mm respectively when compared with baseline values. In CPAP therapy, overjet and overbite decreased with 0.7 ± 1.5 mm and 0.8 ± 1.4 mm respectively when compared with baseline values.

Conclusions This study demonstrates that MAD and CPAP therapy result in significant changes in dental occlusion. These changes appear progressive and more pronounced with MAD compared to CPAP therapy.

Clinical relevance Long-term OSA treatment results in significant dental side effects that may progress over time. Informed consent is fundamental before starting MAD treatment and individualized long-term follow-up is of eminent importance.

Keywords Obstructive sleep apnea · Mandibular advancement device · Continuous positive airway pressure · Treatment outcome · Dental side effects

Boudewijn Stegenga deceased.

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00784-019-03175-6>) contains supplementary material, which is available to authorized users.

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Étude d'une orthèse d'avancée mandibulaire dans le traitement du syndrome d'apnées obstructives du sommeil

RÉSUMÉ



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Introduction

Le but de cette étude était d'évaluer l'efficacité et la tolérance d'une orthèse mandibulaire en traction de type optimisation de la retenue mandibulaire (orthèse type ORM) dans le traitement des syndromes d'apnées obstructives du sommeil (SAOS) modérés à sévères avec une prise en charge ambulatoire simple n'imposant pas de protocole de titration de l'avancée.

Matériel et méthodes

40 patients, 10 présentant un SAOS sévère en échec ou refus de PPC avec un indice d'apnée-hypopnée (IAH) ≥ 30 , et 30 un SAOS modéré ($15 \leq \text{IAH} < 30$) ont été inclus dans 4 centres. Une polygraphie respiratoire nocturne, des questionnaires de qualité de vie et de qualité du sommeil ont été utilisés pour évaluer l'effet du traitement après 45 jours.

Résultats

35 patients ont terminé l'étude. La fréquence des événements respiratoires, la somnolence diurne, la qualité du sommeil évaluée par le patient, le questionnaire SF-36 de qualité de vie, et l'index de qualité du sommeil du questionnaire de Pittsburgh (PSQI) ont été significativement améliorés avec l'orthèse. 60 % des patients étaient répondeurs au traitement avec une diminution de l'IAH d'au moins 50 %. L'observance du traitement était élevée (80 % des patients ont porté leur orthèse toutes les nuits). Les effets indésirables ont été mineurs et transitoires.

Discussion

L'efficacité sur les paramètres respiratoires et la somnolence de cette orthèse mandibulaire en retenue a été validée avec un taux de réponse similaire à celui publié dans la littérature. Cette étude montre une amélioration constante des paramètres de qualité de vie et de qualité du sommeil sous orthèse. Le traitement par l'orthèse type ORM dans le cadre d'une prise en charge ambulatoire simple sans titration systématique avec contrôle rapide par polygraphie ventilatoire est approprié pour la prise en charge des patients porteurs d'un SAOS, particulièrement si ce SAOS est modéré.

Mots clés

- apnées obstructives du sommeil
- qualité de vie
- traitement

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Effect of long-term oral appliance therapy on obstruction pattern in patients with obstructive sleep apnea

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Abstract

Purpose Oral appliance therapy is an alternative treatment modality for obstructive sleep apnea (OSA). However, there have been no studies to determine whether changes in the obstructive pattern occur following long-term use of oral devices. Therefore, we examined whether the obstructive pattern changes in patients with OSA who undergo long-term oral appliance therapy using drug-induced sleep endoscopy (DISE).

Methods We investigated 156 consecutive patients diagnosed with OSA. Seventy-nine of these patients were found to be eligible for inclusion in this study. All enrolled patients underwent two DISE examinations: before and after oral appliance use. We compared the DISE findings for each patient in terms of degree and configuration of airway obstruction at the levels of the velum, oropharynx, tongue base, and epiglottis.

Results We found that dental problems, as assessed using the average values of overjet and overbite, were significantly decreased after 2 years of oral appliance use. Comparisons of the DISE findings revealed that there was significant widening of the upper airway structures following long-term oral appliance therapy, especially in the velum ($P=0.022$) and epiglottis ($P=0.001$). However, changes in the configuration of upper airway obstruction were not observed in any of the structures of the upper airway.

Conclusions We found evidence possibly indicating decreased obstruction at the levels of the velum and epiglottis after long-term use of oral appliances. We suggest further cohort studies to confirm these findings.

Keywords Obstructive sleep apnea · Drug-induced sleep endoscopy · Nasendoscopy · Oral appliance

Introduction

Obstructive sleep apnea (OSA) is characterized by episodes of partial or complete obstruction of the upper airway during sleep, and leads to sleep fragmentation and oxygen desaturation [1]. OSA is clinically associated with excessive daytime sleepiness, sexual dysfunction, loud snoring, or witnessed breathing interruptions during sleep [2]. OSA is also related to neurocognitive deficits and higher rates of cardio-cerebrovascular morbidity and mortality [3, 4]. In addition, OSA

contributes to the increased incidence of negligent accidents and vehicle collisions [5].

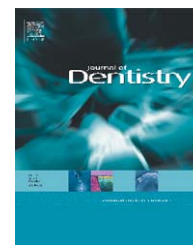
Of the various treatment options for OSA, continuous positive airway pressure (CPAP) therapy has generally been considered the “gold standard” [6]. Even though CPAP is highly efficacious for patients with OSA, poor adherence to the treatment limits its overall effectiveness [7]. Oral appliance therapy is a viable alternative treatment for patients with mild-to-moderate OSA, especially those unwilling or unable to tolerate CPAP [8]. In general, the aim of oral appliance use is the prevention of upper airway collapse during sleep by holding the mandible in a forward and downward position [9].

To date, mandibular advancement devices (MADs) have been the most widely used oral appliances because of their simplicity, safety, and cost-effectiveness. Recent studies have also shown evidence for the high efficacy of MADs in patients with OSA [10, 11]. Several studies have shown that dental changes, such as decreased overjet and overbite,

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Long-term oral-appliance therapy in obstructive sleep apnea: A cephalometric study of craniofacial changes[☆]

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ABSTRACT

Objectives: The aim of this randomized controlled study was to cephalometrically assess possible changes in craniofacial morphology associated with long-term use of an adjustable oral-appliance compared with continuous positive airway pressure (CPAP) in patients with the obstructive sleep apnea/hypopnea syndrome (OSAHS). In addition, we wanted to study the relationship between these possible changes and the degree of mandibular protrusion associated with oral-appliance therapy.

Methods: Fifty-one patients were randomized to oral-appliance therapy and 52 patients to CPAP therapy. At baseline and after follow-up (2.3 ± 0.2 years), a lateral cephalogram of all patients was made in maximum intercuspation to determine relevant cephalometric variables. Both baseline and follow-up cephalograms were traced digitally whereupon cephalometric variables were compared. Changes in craniofacial morphology between the oral-appliance- and CPAP group were evaluated with a linear regression analysis.

Results: Compared with CPAP, long-term use of an oral-appliance resulted in small but significant (dental) changes. Overbite and overjet decreased, 1.0 (±1.5) mm and 1.7 (±1.6) mm, respectively. Furthermore we found a retroclination (−2.0 (±2.8)°) of the upper incisors and a proclination (3.7 (±5.4)°) of the lower incisors. Moreover, the lower- and total anterior facial height increased significantly, 0.8 (±1.5) mm and 0.9 (±1.4) mm, respectively. No changes in skeletal variables were found. Linear regression analysis revealed that the decrease in overbite was associated with the mean mandibular protrusion during follow-up ($B = -0.029$, $SE = 0.014$, $p < 0.05$).

Conclusions: Oral-appliance therapy should be considered as a life long treatment, and there is a risk of craniofacial changes to occur. Therefore, patients treated with an oral-appliance, need a thorough follow-up by a dentist or dental-specialist experienced in the field of dental sleep medicine.

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1. Introduction

The obstructive sleep apnea/hypopnea syndrome (OSAHS) is a sleep-related breathing disorder, characterized by disruptive

snoring and repetitive partial or complete obstructions of the upper-airway (i.e. hypopneas and apneas, respectively).¹ The severity of the disorder is usually expressed by the apnea-hypopnea index (AHI), i.e. the mean number of apneas and

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Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on dental side effects

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Abstract

Objectives This study aimed to assess possible dental side effects associated with long-term use of an adjustable oral appliance compared with continuous positive airway pressure (CPAP) in patients with the obstructive sleep apnea syndrome and to study the relationship between these possible side effects and the degree of mandibular protrusion associated with oral appliance therapy.

Materials and methods As part of a previously conducted RCT, 51 patients were randomized to oral appliance therapy and 52 patients to CPAP therapy. At baseline and after a 2-year follow-up, dental plaster study models in full occlusion were obtained which were thereupon analyzed with respect to relevant variables.

Results Long-term use of an oral appliance resulted in small but significant dental changes compared with CPAP. In the oral appliance group, overbite and overjet decreased 1.2

(± 1.1) mm and 1.5 (± 1.5) mm, respectively. Furthermore, we found a significantly larger anterior–posterior change in the occlusion (-1.3 ± 1.5 mm) in the oral appliance group compared to the CPAP group (-0.1 ± 0.6 mm). Moreover, both groups showed a significant decrease in number of occlusal contact points in the (pre)molar region. Linear regression analysis revealed that the decrease in overbite was associated with the mean mandibular protrusion during follow-up [regression coefficient (β)= -0.02 , 95 % confidence interval (-0.04 to -0.00)].

Conclusions Oral appliance therapy should be considered as a lifelong treatment, and there is a risk of dental side effects to occur.

Clinical relevance Patients treated with the oral appliance need a thorough follow-up by a dentist or dental-specialist experienced in the field of dental sleep medicine.

Keywords CPAP · Obstructive sleep apnea syndrome · Oral appliance · Side effects · Study models · Therapy

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Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive episodes of pharyngeal collapse with increased airflow resistance during sleep [1] and is often accompanied by extensive snoring. OSAS is associated with excessive daytime sleepiness, (sexual) dysfunction, neurocognitive deficits, and higher rates of cardiovascular and cerebrovascular morbidity and mortality [2–5]. In the North American population, OSAS affects approximately 4 % of the male and 2 % of the female adults [4]. The severity of the disorder is usually expressed by the apnea–hypopnea index (AHI), i.e., the mean number of apneas and hypopneas per hour of sleep and is classified as mild (AHI 5–15), moderate (AHI



Original Article

Long-term side effects of sleep apnea treatment with oral appliances: nature, magnitude and predictors of long-term changes



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ABSTRACT

Objectives: Oral appliances for the treatment of obstructive sleep apnea (OSA) reduce upper airway collapse by advancing the mandible (OAm) and associated soft tissues. OAm are well tolerated but have side effects, mainly dental movement. It is not yet clear whether there are irreversible skeletal changes associated with treatment. As oral appliance treatment for OSA is a life-long therapy, careful and extended follow-up of patients is required. The objectives of this study were to evaluate the magnitude and progression of the dental and skeletal changes associated with long-term treatment, in addition to determining the predictors of the changes.

Methods: Lateral cephalograms of adults treated for primary snoring or mild to severe OSA with a custom-made titratable OAm for a minimum of eight years were retrospectively studied. The magnitude and rate of progression of any changes over time was determined and initial patient and dental characteristics were investigated as possible predictors of the observed side effects.

Results: Records of 62 patients with an average treatment time of 12.6 years (range:8–21 years) were included. Cephalometric analysis revealed significant ($p < 0.001$) maxillary incisor retroclination (mean of $\approx 6^\circ$) and mandibular incisor proclination (mean of $\approx 8^\circ$) over the observation period. Maxillary incisors demonstrated a constant rate of retroclination $-0.5^\circ/\text{year}$, the rate of mandibular incisors proclination was variable. The number of treatment years was significantly associated with these variables ($p < 0.001$). A greater body mass index (BMI) and Subspinale, Nasion, Supramentale angle (ANB) were associated with more maxillary and mandibular incisor proclination respectively. Although statistically significant ($p < 0.001$) skeletal changes were noted over this extended observation period, the difference in the Sella, Nasion, Supramentale point B (SNB) and mandibular plane angles were approximately 1° and were deemed not clinically significant.

Conclusions: This study represents the longest observation period to date examining OAm side effects with up to 21 years of follow up for some patients. It confirms that there are significant and progressive dental changes with prolonged OAm use. Conversely, over the same time period skeletal or postural changes were negligible. Additionally, treatment duration was the predictor consistently associated with the magnitude of the observed side effects.

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1. Introduction

Obstructive sleep apnea (OSA) is a chronic condition in adults which, at present, has no permanent cure and all currently available treatment options require life-long adherence. An increasingly common treatment option are oral appliances, which protrude the mandible (OAm), improves the upper airway patency and decrease

its collapsibility [1]. The short-term side-effects of OAm treatment have been shown to be mild and transient [2,3].

Tooth movement leading to changes in occlusion is a common side effect of long-term OAm use. Dental cast analysis and cephalometric analysis have been used to assess the dentoalveolar changes and studies have shown decreased overbite and overjet [4–12], maxillary incisor retroclination and mandibular incisor proclination [4,7,13,14] mesialization of the mandibular molars and distalization of the maxillary molars [7,15,16] as well as changes in dental arch crowding [8,15]. These dental changes develop as a result of the forces exerted on the upper and lower dental arches by the oral

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Dental Side Effects of Long-Term Obstructive Sleep Apnea Therapy: A Comparison of Three Therapeutic Modalities

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STUDY OBJECTIVES: Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by repetitive obstruction of the upper airway during sleep. Patients are often treated with either continuous positive airway pressure (CPAP) or a mandibular advancement device (MAD). The objective of this study was to evaluate changes in dental occlusion, associated with long-term MAD and CPAP therapy.

METHODS: Patients with OSA who used a bilateral thrust MAD (n = 31) were matched with a patient group from a previous randomized trial evaluating the dental side effects of an anterior traction MAD and CPAP therapy. Changes in dental occlusion were analyzed from dental plaster casts taken at baseline and after 2 years of treatment.

RESULTS: The number of occlusal contact points in the (pre)molar region significantly decreased in all treatment groups (MAD groups; $P < .01$) (CPAP group; $P = .03$). The changes in overbite and anterior-posterior movement was significantly different between the anterior traction MAD and CPAP group ($P < .01$) and between both MAD groups (overbite; $P = .01$, anterior-posterior movement; $P < .01$). The anterior traction MAD group was associated with more pronounced occlusal changes when compared with the bilateral thrust MAD group.

CONCLUSIONS: Significant changes in dental occlusion are seen following 2 years with both MAD and CPAP therapy. Specific features in oral appliance design may affect the extent of changes in dental occlusion.

KEYWORDS: continuous positive airway pressure, mandibular advancement devices, obstructive sleep apnea, side effects

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INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by repetitive obstructions of the upper airway during sleep.^{1–3} During sleep the muscle tone of the upper airway decreases and the airway trembles or collapses. OSA can be diagnosed when patients have five or more partial obstructions (hypopneas) and/or complete obstructions (apneas) of the upper airway per hour of sleep. The number of apneas and hypopneas per hour of sleep are quantified by the apnea-hypopnea index (AHI).^{3–6} OSA is a sleep-related breathing disorder associated with excessive daytime sleepiness and an increased risk of cardiovascular disease that usually requires a lifelong treatment.^{7–10}

The precise treatment of OSA depends on the severity of symptoms and disease, and the patient's anatomical characteristics and health status.¹¹ There are several treatment options for OSA, including lifestyle changes, continuous positive airway pressure (CPAP), a mandibular advancement device (MAD), and upper airway surgery.¹²

CPAP is generally applied through a nasal mask. As a result of this positive pressure, the upper airway is pneumatically splinted and obstructed breathing events are prevented.^{13–15}

CPAP is usually very effective in reducing the number of apneas, but may be complicated by suboptimal acceptance and adherence in a relatively high proportion of patients.^{8,16–18}

A MAD is possibly a more patient friendly alternative to CPAP, especially in patients with mild to moderate disease. In order to prevent upper airway obstructions, a MAD is designed to advance the mandible in a more forward position. A MAD improves upper airway patency by pulling the tongue base, epiglottis and soft palate forward. In addition, MAD therapy has been shown to stimulate the musculature of the palate, tongue base and pharynx, resulting in a decreased upper airway resistance.^{19,20} Acceptance of and therapeutic outcome with a MAD is favorable in many patients, especially in the treatment of mild to moderate OSA.^{6,8,21–23} However, mild and transient side effects have been reported in the initial period of therapy. These may include tooth pain, myofascial pain, temporomandibular joint pain, excessive salivation or a dry mouth, and gum irritation.^{21,24–28} Long-term MAD use is associated with changes in craniofacial morphology^{26,27} as well as changes in dental occlusion, including a reduction in overjet, overbite, and the number of occlusal contact points.^{20,21,25,27,29,30} The amount of mandibular protrusion with the MAD has been

Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on temporomandibular side effects

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Abstract The objective of this study was to assess variations in the occurrence of temporomandibular disorders (TMDs) and the risk of developing pain and function impairment of the temporomandibular complex in obstructive sleep apnea syndrome (OSAS) patients treated with either an oral appliance (mandibular advancement device) or continuous positive airway pressure (CPAP) in a 2-year follow-up study. In addition, we assessed the relationship between the mean mandibular protrusion and the frequency of wearing the appliance during follow-up with the occurrence of pain and function impairment of the temporomandibular complex. Fifty-one patients were randomized to oral appliance therapy and 52 patients to CPAP therapy. TMDs (diagnosed according to the Axis I Research Diagnostic Criteria for TMD), pain intensity and disability and mandibular function impairment were recorded at baseline, after 2 months, 1 year and 2 years of therapy. Only in the initial period of treatment the occurrence of pain-related TMDs was considerably higher (24%) in the oral appliance group compared to CPAP (6%). Oral appliance therapy furthermore resulted in more temporomandibular pain compared to CPAP (odds ratio 2.33, 95% confidence interval (1.22–4.43)). However, there were no limitations in mandibular function in

both groups during the (entire) follow-up period. Although generally not serious and of transient nature, oral appliance therapy results in more pain-related TMDs in the initial period of use compared with CPAP therapy. Oral appliance therapy is associated with increased pain in the temporomandibular complex in the initial period of use. Because of the transient nature, this pain is not a reason to contra-indicate an oral appliance in OSAS patients. Moreover, TMDs and the risk of developing pain and function impairment of the temporomandibular complex appear limited with long-term oral appliance use.

Keywords Obstructive sleep apnea syndrome · Oral appliance · CPAP · Side effects · Temporomandibular dysfunction · Research diagnostic criteria

Introduction

Obstructive sleep apnea syndrome (OSAS) is a highly prevalent sleep-related breathing disorder affecting approximately 4% of the male and 2% of the female adults in the North American population [1]. The disorder is characterized by disruptive snoring and repetitive partial or complete obstructions of the upper airway (i.e. hypopneas and apneas, respectively) during sleep [2]. This disrupted sleep may result in various (serious) neurobehavioral and cardiovascular sequelae, ultimately depriving the patient's quality of life and life expectancy [3, 4]. Standard treatment with continuous positive airway pressure (CPAP) is very effective in reducing symptoms [5, 6]; however, because of the obtrusive nature of CPAP, patients may abandon or adhere poorly to this therapy [7]. Oral appliance therapy has been demonstrated an effective alternative in treating

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