Universidad Europea

GRADUATION PROJECT

Degree in Dentistry

SYSTEMATIZED REVIEW OF THE SIDE EFFECTS OF MANDIBULAR ADVANCEMENT DEVICES

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RESUMEN

Introducción: La Apnea Obstructiva del Sueño (AOS) es un trastorno común del sueño caracterizado por la obstrucción de las vías respiratorias superiores, que conduce a un sueño fragmentado y a un aumento de los riesgos para la salud. Los dispositivos de avance mandibular (DAM) se utilizan ampliamente como tratamiento no invasivo de la AOS. Aunque son eficaces, los DAM pueden causar diversos efectos secundarios que pueden afectar al cumplimiento terapéutico y a los resultados a largo plazo. Comprender estos efectos adversos es crucial para optimizar la atención de los pacientes.; **Objetivo:** determinar los efectos secundarios en pacientes mayores de 18 años asociados al uso de DAM en el tratamiento de la AOS.; **Material y Método:** se realizó una revisión sistematizada siguiendo las directrices PRISMA 2020. Se realizaron búsquedas en los bases de datos como Web of Science y Scopus utilizando palabras clave predefinidas relacionadas con los DAM y sus efectos secundarios. La selección de estudios se realizó aplicando criterios de inclusión y exclusión preestablecidos.; **Resultados:** la investigación identificó múltiples efectos secundarios del uso de DAM. Los efectos a corto plazo incluían hipersalivación, xerostomía, dolor dental y molestias en la articulación temporomandibular (ATM). Los efectos a largo plazo incluían cambios oclusales, aumento de la altura facial, alteraciones del plano mandibular y trastornos de la ATM. La gravedad y la persistencia de estos efectos variaron en función del tipo de dispositivo y de la adherencia del paciente.; **Conclusión:** los DAM son una alternativa eficaz al tratamiento con CPAP, pero se debe tener un control exhaustivo de los efectos secundarios que se puedan presentar. Los seguimientos regulares, la selección individualizada del dispositivo y la educación del paciente son esenciales para minimizar los efectos adversos. La investigación futura debe centrarse en estrategias para reducir los cambios dentales y esqueléticos a largo plazo, mejorando la sostenibilidad del tratamiento con DAM.

PALABRAS CLAVE

Odontología, apnea obstructiva del sueño, dispositivos de avance mandibular, efectos secundarios, alteraciones oclusales.

ABSTRACT

Introduction: Obstructive Sleep Apnoea (OSA) is a common sleep disorder characterized by upper airway obstruction, leading to fragmented sleep and increased health risks. Mandibular advancement devices (MADs) are widely used as a non-invasive treatment for OSA. Although effective, MADs can cause a variety of side effects that can affect compliance and long-term outcomes. Understanding these adverse effects is crucial to optimize patient care.; **Objective:** to determine the side effects in patients over 18 years of age associated with the use of DAMs in the treatment of OSA.; **Material and Method:** a systematized review was performed following the PRISMA 2020 guidelines. Databases such as Web of Science and Scopus were searched using predefined keywords related to DAMs and their side effects. Studies were selected using predefined inclusion and exclusion criteria.; **Results:** the research identified multiple side effects of MADs use. Short-term effects included hypersalivation, xerostomia, dental pain and temporomandibular joint (TMJ) discomfort. Long-term effects included occlusal changes, increased facial height, alterations of the mandibular plane and TMJ disorders. The severity and persistence of these effects varied according to the severity and persistence of the effects.; **Conclusions:** MADs are an effective alternative to Continuous Positive Airway pressure (CPAP) therapy, but side effects should be closely monitored. Regular follow-ups, individualized device selection and patient education are essential to minimize adverse effects. Future research should focus on strategies to reduce long-term dental and skeletal changes, improving the sustainability of MAD treatment.

KEYWORDS

Odontology, mandibular advancement device, obstructive sleep apnea, side effects, occlusal changes.

INDICE

1. INTRODUCTION

1.1. History

As early as 5000 BC, the Egyptians built temples to Serapis, the god of dreams, where people would sleep in the hopes of bringing about lucky dreams. In Greek and Indian mythology, sleep and dreams are mentioned. Throughout the decades, civilizations have always been fascinated by sleep (1).

During the 19th century, English author Charles Dickens published a short story entitled *"The Posthumous Papers of the Pickwick Club".* This work depicted the life of an obese man suffering from frequent daytime sleepiness. A few years later, the term "Pickwick syndrome" was coined by Burwell to describe obese patients with hypoventilation problems (2).

In 1923, Pierre Robin initially established the use of a Mandibular Advancement Devices (MADs) to treat sleep apnea (3).

The first medical documentation of patients suffering from "Pickwick syndrome" was established in Germany during 1959, where analysis of the cases revealed carbon dioxide poisoning. It was not until several years later that a neurologist, Kuhl, re-examined this syndrome, concluding that it was not the result of poisoning, but rather of sleep fragmentation (4).

In 1965, three French researchers, Gastaut, Tassinari and Duron, diagnosed repeated episodes of apnea and nocturnal awakening as being caused by upper airway obstruction during sleep. At the same time, Lugaresi validated these findings and identified three categories of apnea: central, mixed and obstructive. During this period, the main treatment for sleep apnea was tracheostomy, first performed by Knohl in 1969, although this permanent procedure was fraught with complications, prompting the search for alternatives (2).

MADs were introduced in 1980, inspired by the osteogenic distraction process described in 1905 by Alessandro Codvilla (3,5).

Cartwright and Samuelson also developed a device able to keep the tongue in a forward position during sleep during 1982. Few years later in 1995, the American Academy of Sleep Medicine (AASM) provided the first practice criteria for using oral appliances to treat OSA and snoring.

1.2. Definition

Nowadays sleep apnea, in particular Obstructive Sleep Apnea (OSA) is emerging as a major health issue, disclosing nocturnal respiratory interruptions usually due to upper airway collapse. OSA highly affects life quality as well as increase mortality and morbidity rate. This pauses in respiratory cycle lead to night-time sleep disruption and consequent diurnal fatigue and drowsiness (6).

There are three main severity grades of obstructive sleep apnea, classified according to the number of respiratory pauses occurring per hour of sleep more commonly known as apnea-hypopnea index (AHI) (7):

- Mild: 5 to 15 pauses per hour
- Moderate: 15 to 30 pauses per hour
- Severe: superior to 30 pauses per hour

1.3. Epidemiology

1.3.1. Prevalence

This disorder concerns a significant proportion of the world's population. Approximately 900 million adults have been diagnosed with an elevated AHI. Moreover in 2022, more than 400 million persons have been identified as having at least a moderate degree of OSA severity. Furthermore, the prevalence of OSA is increasing with age (8).

1.3.2. Risk factors

Today, according to several studies, certain factors have been identified as directly linked to the intensification of cases. Among them gender, age and race are qualified of non-modifiable risk factors while obesity, smoking, medication, coronary diseases and anatomical abnormalities such as a large tongue or retracted lower jaw are modifiable risk factors (9,10).

1.3.3. Co-morbidity

OSA is responsible for many pathologies, due to its systemic effects it leads to an increased risk of cardiovascular disease, hypertension, stroke, as well as type 2 diabetes, long-term cognitive impairment or even dementia (11,13).

1.3.4. Symptoms

Moreover, OSA is associated with clinical symptoms including snoring, which is the most common one, but also pauses in breathing, daytime fatigue, excessive sleepiness and impaired concentration. However, only 20% have been diagnosed, mostly due to a lack of symptoms severe enough to cause concern and so seek for medical advice (8,14). Consequently, identification of OSA often relies on a thorough clinical evaluation combined with specific diagnostic tests.

1.4. Diagnosis

Numerous diagnostic techniques are available to establish an accurate diagnosis of OSA, with their benefits and limitations. These range from initial clinical assessment to more invasive and specialized diagnostic tests.

1.4.1. Berlin questionnaire

In 1996, a questionnaire was developed in Germany, known as the “Berlin Questionnaire” with accurate sensitivity and specificity. This consists of 10 questions divided into three distinct categories, assessing the presence and severity of snoring, the frequency of daytime sleepiness episodes, and the presence of obesity (Body Mass Index (BMI)>30 kg/m2) or hypertension in the patient. Patients identified as being at high risk in two or more categories will be classified as being at high risk of OSA (15).

1.4.2. STOP-Bang questionnaire and Epworth Sleepiness Scale (ESS)

The STOP-Bang questionnaire is an assessment tool designed to evaluate the risk of OSA based on eight criteria, which include snoring, daytime fatigue, occurrences of apnea, hypertension, BMI> 35 kg/m², age over 50, neck circumference exceeding 40 cm, and male gender. Patients respond to each item with a "yes" or "no." Points are assigned such that each "yes" response counts as one point, while "no" responses receive no points. The total score ranges from 0 to 8, with scores between 0 and 2 indicating a low risk and scores between 5 and 8 suggesting a high risk for moderate to severe OSA (16).

The Epworth Sleepiness Scale (ESS) consists of eight questions designed to assess a patient's levels of sleepiness in various daily activities, employing a scoring system ranging from zero to three. A score of zero indicates the absence of sleepiness, while scores of one, two, and three correspond to light, moderate, and severe sleepiness, respectively. The final score will be between 0 and 24 (17).

0-10	Normal
11-14	Mild daytime sleepiness
15-18	Considered moderate daytime sleepiness
19-24	Severe daytime sleepiness

Table 1: Table of ESS classification of OSA risk depending on score

1.4.3. Polysomnography (PSG)

One of the most widely used methods for diagnosing sleep apnea is PSG, considered as the “gold standard”. It records a range of physiological parameters during the night, including oxygen saturation, brain activity (EEG), eye movements (EOG), muscle activity (EMG), thoracic and abdominal breathing and respiratory movements (7). However, PSG is a complex and costly method that requires in-hospital monitoring.

1.4.4. Respiratory polygraphy (RP)

This is why, for some patients, simpler alternatives have been developed, such as RP, which can be performed at home. This test is less invasive and much more accessible, recording mainly parameters such as airflow, oxygen saturation, and thoracic and abdominal breathing (7). However, RP does not measure certain parameters such as brain activity and eye movements, which may limit its use for a comprehensive diagnosis.

1.5. Treatments

To treat OSA there are several treatment options, being invasive or not and surgical or not.

1.5.1. Continuous Positive Airway Pressure (CPAP) and Nasal Expiratory Positive Airway Pressure (EPAP)

CPAP introduced in 1981 is the most common one considered as the “gold standard”, especially in moderate to severe cases with a success rate of 75%. CPAP works by delivering a continuous flow of air through a mask worn over the nose, or nose and mouth

during sleep although not always well tolerated by patients. Air is delivered at a constant pressure, keeping the upper airways open. By preventing collapse of the soft tissues in the throat, this positive pressure prevents apneas and snoring. This treatment has also been shown to be effective in reducing the risk of cardiovascular problems (18). Unlike other treatments, CPAP works in real time, providing immediate support to ensure normal, regular breathing however articles states that to be effective it has to be worn assiduously at least 4 hours every day (19).

One variation of CPAP, known as ENAP, is considered as a non-invasive option for managing OSA. ENAP consists of valves insertion into the nostrils before sleep and are based on a simple mechanism: during inspiration air passes easily through the valves but during exhalation the valves partially close providing restricted exit responsible for backpressure (20). This resistance generates positive pressure in the upper airways, helping to keep them open and prevent obstruction.

Unlike CPAP, EPAP does not require a machine, making this treatment more discreet and portable, and therefore more acceptable to patients. EPAP valves are often recommended for patients with mild to moderate apnea, or for those who cannot tolerate CPAP.

1.5.2. Mandibular Advancement Devices (MADs)

An increasingly popular alternative for the treatment of OSA, snoring, and related symptoms is the use of non-surgical oral appliances. These devices produced a traction force that increased muscle tension in the genioglossus and supra- and infrahyoid areas, expanding the pharyngeal air space. MADs are specifically designed to maintain the lower jaw in a forward position during sleep by encompassing all the teeth. This mechanism facilitates airway opening and effectively reduces both the frequency and duration of apneic episodes by increasing the volume of the oral cavity. These devices provide a reversible, trivial, and affordable treatment alternative to CPAP for those with mild to moderate OSA (21).

1.5.3. Tongue Retainers Devices (TRD)

TRD are another available option to treat OSA. These devices allow the tongue to be kept in a forward position and so preventing its backward movement towards the throat. By preventing the backward movement, the airway obstruction is hindered allowing proper airflow during sleep and a subsequently reduction of respiratory pauses. This appliance has fewer side-effects than others and has the advantage of being able to be

used on completely edentulous patients, unlike MADs, which would suffer from a lack of retention (22).

1.5.4. Rapid Maxillary expansion (RME), Tonsillectomy and Adenoidectomy

Beyond these non-surgical treatments, RME offers a non-invasive alternative especially for children and adolescents. This treatment widens the palate to improve airflow in the upper respiratory tract: a palatal breaker is attached to the upper teeth and exerts progressive pressure to spread the palate bones apart. By enlarging the nasal cavity and palate, RME increases breathing space, reducing obstructions that cause sleep apnea (19).

Tonsillectomy and adenoidectomy are surgical procedures used to treat OSA, particularly in children, by removing enlarged tonsils or adenoids that block the airways and cause apnea episodes. Eliminating these tissues improves breathing and reduces apnea. Although this approach is most common in children, it can also be considered in adults for obstructive apnea tied to enlarged tonsils or adenoids (7).

1.5.5. Others

Many other treatments are also available, some of which are surgical, such as uvulopalatopharyngoplasty, tracheostomy, maxillomandibular advancement surgery…

1.6. Mandibular Advancement Devices

1.6.1. Indications and Contraindications

Indications	**Contraindications**
• Snoring • Mild OSA • Moderate OSA • Severe OSA (alternative to CPAP: patients intolerant, unwilling to use it, or unsuitable for surgery)	• TMJ disorders • Muscle complaints • Less than 8 teeth in mouth • Periodontal disease

Table 2: Table of indications and contraindications for MADs (23)

1.6.2. Custom made vs prefabricated

Custom-made MADs tend to be more expensive but offer superior comfort, effectiveness, and adherence to patient mouth compared to prefabricated appliances. The fabrication of these custom devices necessitates that the dentist obtains dental impressions of both arches, along with measurements of the occlusal relationship, or utilize digital scanning technology. By being adapted to the patient's mouth, the resulting comfort will enhance the patient's compliance and thus the dentist's preferred choice (21,24,25).

Conversely, prefabricated devices, commonly referred to as "boil and bite," are typically constructed from thermoplastic materials. These devices are more economical and do not necessitate laboratory fabrication however they are more likely to fail due to a lack of retention. As implied by their name, they are heated in hot water and then molded directly onto the patient's teeth to conform to their individual anatomy (26,27).

1.6.3. Monoblock vs Bi-Block

Non-titratable devices, also known as “Monoblock” appliances, feature a rigid connection between the upper and lower jaws achieving a maximum mandibular protrusion upon insertion (28). These devices exert an important stress on the temporomandibular joint (TMJ) and surrounding tissues.

In contrast, titratable devices, referred as “Bi-block” models, allow an independent adjustment of the upper and lower components through connectors or screws enabling gradual and continuous advancement of the mandible. The dentist will gradually enhance the protrusion until reaching the optimal level of protrusion. Titratable devices are connected at the lateral or frontal aspects.

This flexibility in design can enhance patient comfort and overall treatment outcomes (28). Several studies indicate that this type of device is more effective in improving oxygen saturation levels and reducing the AHI, thereby making it more advisable than non-titratable alternatives (29).

1.6.4. Side effects

In comparison to other treatment modalities such as CPAP therapy or surgical interventions, mandibular advancement appliances present the advantage of being non-invasive and generally more tolerable for long-term use. Nevertheless, it is important to consider these benefits alongside the potential risks associated with prolonged application.

The common short-term effects often observed are: hypersalivation, dental pain, myofascial pain, headaches and TMJ discomfort (13). Given the extended duration of appliance wear long term side effects are likely to manifest: occlusal contact changes will appear as well as alterations in the inclination of incisors more precisely a retroclination of upper incisors and a proclination of lower incisors (13,30,31).

2. OBJECTIVE

2.1. Objective

To determine the side effects in patient older than 18 years old associated with the use of Mads, in the treatment of obstructive sleep apnea (OSA).

2.2. Formulation of research question

This systematized review was done to address the following research question *: "Do patients over 18 years of age who are treated with mandibular advancement devices (MADs) experience side effects compared to those who do not use them?"*

To formulate our question, we deconstructed it into four key components:
Population (P): Adults with sleep-disordered breathing.
Intervention (I): Use of mandibular advancement appliances.
Comparison (C): Individuals without treatment.
Outcome (O): Side effects associated with the use of MADs.

2.3. Justification and hypothesis

2.3.1 Justification

MADs have gained in popularity for treating OSA and snoring, but uncertainties persist about their long-term side effects. Although adverse outcomes such as occlusal changes, temporomandibular joint (TMJ) discomfort, and tooth movement have been reported, variations in study methods make definitive conclusions difficult. Still, MADs serve as a non-invasive alternative for patients with mild to moderate OSA or those who decline Continuous Positive Airway Pressure (CPAP), improving airway patency and reducing apnea episodes.

A systematized review is crucial to clarify the prevalence, severity, and clinical significance of these side effects, as well as the risk factors and underlying mechanisms. This evidence will guide clinical decision-making, optimize patient outcomes, and shape future research and treatment guidelines.

2.3.2. Hypothesis

Based on current evidence, adults over 18 using MADs typically experience frequent but generally moderate side effects most notably mandibular pain, occlusal changes, and temporomandibular symptoms. These effects tend to be more pronounced at the beginning of treatment but often diminish as patients adapt. Despite these concerns, no significant differences in the clinical impact of side effects have been found when comparing MAD users to those receiving other OSA therapies.

3. MATERIAL AND METHODS

This sistematized review has been developped following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) update of 2020.

3.1. Methodology

3.1.1. Eligibility criteria

Inclusion criteria	
Study Type	Randomized Control Trials, Clinical trials, Prospective studies, Longitudinal studies and Cohort studies investigating the side effects of Mandibular Advancement Devices(MADs).
Languages	Only studies published in English, Spanish, or French.
Target Population	Studies involving adult participants (18 years and older females and males).
Condition	Studies focused on MADs used for the treatment of Obstructive Sleep Apnea(OSA).
Outcome Measures	Reports on side effects of MADs use.

Table 3: Inclusion criteria

Exclusion criteria	
Study Type	Systematic reviews or meta-analyses.
Research Focus	Studies not explicitly examining the side effects of MADs. Studies focusing solely on MAD efficacy without side effect reporting.
Duplicate Publications	Studies published more than once in different journals.
Publication Date	Studies published more than 10 years ago are excluded, except those considered essential for providing background or context in the introduction.

Table 4: Exclusion criteria

3.2.2. Information sources and data search strategy

We conduct a review of two database called Web of Science and Scopus to identify scientific articles. We use MeSH (Medical Subject Headings) vocabulary and Boolean operators as "AND", "NOT" and "OR" for the combination of search terms.

The keywords use for ours advanced researches are the following ones: "mandibular advancement device", "mandibular advancement splints", "side effects", "occlusal change", "temporomandibular pain", "xerostomia", temporomandibular joint disorder", "allergy", "hypersalivation", "tooth pain", "headache", "periodontal disease", gingiva pain".

Scopus advanced research: "mandibular AND advancement AND device OR mandibular AND advancement AND s plints AND side AND effects OR occlusal AND change OR tempormandibular AND pai n OR xerostomia OR temporomandibular AND joint AND disorder OR allergy OR hyper salivation OR tooth AND pain OR headache OR periodontal AND disease OR gingiva AND pain AND (EXCLUDE (EXACTKEYWORD , "Systematic Review") OR EXCLUDE (EXACTKEYWORD , "Meta Analysis") OR LIMIT-TO (EXACTKEYWORD , "Clinical Trial") OR LIMIT-TO (EXACTKEYWORD , "Comparative Study") OR LIMIT-TO (EXACTKEYWORD , "Controlled Study") OR LIMIT-TO (EXACTKEYWORD , "Randomized Controlled Trial") OR LIMIT-TO (EXACTKEYWORD , "Prospective Studies") OR LIMIT-TO (EXACTKEYWORD , "Prospective Study"))

Web of Science advanced research: ((((((((((((ALL=(mandibular advancement device)) OR ALL=(mandibular advancement slpint)) AND ALL=(side effect)) OR ALL=(side effects)) OR ALL=(occlusal change)) OR ALL=(temporomandibular pain)) OR ALL=(xerostomia)) OR ALL=(temporomandibular joint disorder)) OR ALL=(allergy)) OR ALL=(hypersalivation)) OR ALL=(tooth pain)) OR ALL=(headache)) OR ALL=(periodontal disease)) OR ALL=(gingiva pain)and Mandibular Advancement Device (Search within all fields) and Systematic Review (Exclude – Search within all fields) and Meta Analysis (Exclude – Search within all fields) and 2025 or 2024 or 2023 or 2022 or 2021 or 2020 or 2019 or 2018 or 2016 or 2 017 or 2015 or 2014 (Publication Years) and English or French (Languages)

4. RESULTS

4.1. Study selection: Prisma 2020 flow diagram

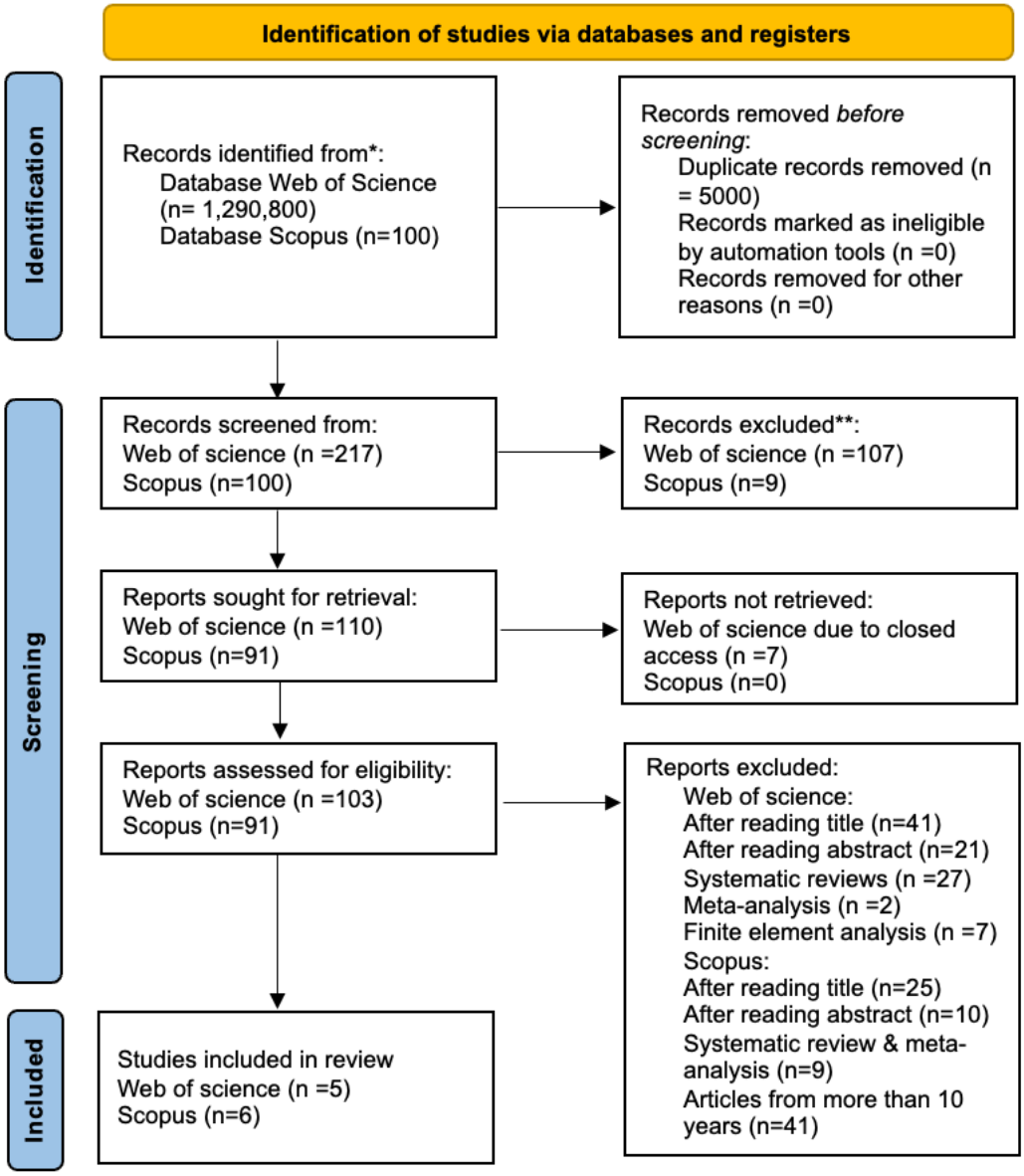

Figure 1: PRISMA 2020 flow diagram

To ensure a thorough review, the research process was carried out in multiple stages following the PRISMA 2020 flow diagram (figure 1). Initially, our search retrieved 1,290,800 records from Web of Science and 100 records from Scopus.

To refine this large dataset, we first applied an automatic duplicate removal process, which identified and excluded 5,000 duplicate articles, leaving us with 1,290,893 unique

records for screening. At this stage, we screened 217 articles from Web of Science after focusing on Mandibular Advancement Devices (MADs) and 100 articles from Scopus. After this preliminary review, we excluded:

- 107 articles from Web of Science and 9 articles from Scopus because they did not specifically focus on MADs and their side effects or because they were not original research, such as conference abstracts or studies on alternative treatment methods.

After this step, 110 articles from Web of Science and 91 from Scopus remained for full-text retrieval.

During the eligibility phase, 7 articles from Web of Science could not be accessed due to restricted availability. This left us with 194 articles for full-text review. At this stage, regarding Web of Science articles we excluded:

- 2 meta-analyses
- 27 systematic reviews
- 7 finite element analysis studies
- 41 based on their title
- 21 based on their abstract

Moreover, regarding Scopus we have excluded 81 articles :

- 41 were older than 10 years
- 25 based on their title
- 10 based on their abstract
- 9 were systematic reviews or meta-analysis

After applying all inclusion and exclusion criteria, we identified 11 trials that met the eligibility requirements, including:

- 4 trials from Web of Science
- 7 trials from Scopus

These studies were included in our final systematized review to analyze the side effects associated with mandibular advancement devices.

4.2. Synthesis of results

Title	Author & Year	Journal	Purpose of the study	Type of study and settings	Data collection methods
Oral appliance therapy vs. nasal Continuous Positive Airway Pressure (CPAP) in Obstructive Sleep Apnea (OSA) : A randomized, placebo-controlled trial on temporoman dibular side-effects (32)	Nikolopo ulou et al., 2020	Clinical and Experimental Dental Research	To assess Temporoman dibular Disorder (TMD) pain and mandibular function impairment between MADs and nasal CPAP	Randomi zed Controlle d Trial, Amsterd am (Netherla nds)	Functional examination, patient questionnair es
The comparison of two different mandibular positions for oral appliance	Makihar a et al., 2022	Clinical and Experimental Dental Research	To compare the effectiveness and side effects of 50% vs. 75% mandibular advancement	Prospecti ve clinical study, Japan	Polysomnog raphy, Epworth Sleepiness Scale, patient reports

therapy in OSA (33)					
Objectively measured adherence may affect side effects of mandibular advancement therapy in subjects with OSA (34)	Pahkala et al., 2024	Sleep and Breathing	To determine the relationship between adherence, dental changes, and TMD symptoms in MAD users	Prospective clinical study, Finland	Objective adherence monitoring, clinical assessments
Effect of long-term oral appliance therapy on obstruction pattern in OSA(35)	Jo et al., 2018	European archives of Oto-Rhino-Laryngology	To assess airway changes and side effects after long-term MAD use	Prospective study, Korea	Drug induced sleep endoscopy, dental assessments
Efficacy and mechanism of MADs for persistent sleep apnea after surgery (36)	Luo et al., 2016	Journal of Otolaryngology - Head and Neck surgery	To evaluate MAD efficacy in patients with persistent OSA after surgery	Prospective clinical study, China	Polysomnography, CT scans, patient reported side effects
The effects of MAD on pressure pain threshold of masticatory muscles : A prospective	Alessandri-Boneti et al., 2016	Journal of Oral & Facial pain and headache	To evaluate changes in muscle pain thresholds in MAD users over 6 months	Prospective controlled cohort study, Italy	Pressure pain threshold (PTT) measurements

controlled cohort study (37)					
Clinical Efficacy of a Position-Responding Mandibular Advancement Device in Patients With OSA (38)	Sung-Woon On et al., 2024	Clinical and Experimental Otorhinolaryngology	To evaluate the efficacy of an auto-titrating MAD in treating OSA and reducing side effects.	Prospective Clinical Trial, Korea	Polysomnography (PSG) before and after 3 months of MAD use, Epworth Sleepiness Scale (ESS), STOP-Bang questionnaire, side effect assessments.
Comparison of Titrable Thermoplastic Versus Custom-Made MAD for the Treatment of OSA (39)	Frédéric Gagnadoux et al., 2017	Respiratory Medicine	To compare the efficacy and side effects of a thermoplastic MAD versus a custom-made MAD for treating OSA.	Prospective Non-Randomized Study, France	Overnight sleep studies, Epworth Sleepiness Scale (ESS), oxygen desaturation index, self-reported side effects and compliance over 6 months.
Clinical Effect of Personalized	Wang W. et al., 2024	British Journal of Hospital Medicine	To assess the clinical effectiveness	Randomized Clinical	Polysomnography, side effect

Adjustable MADs on Obstructive Sleep Apnea(40)			and side effects of a personalized adjustable MAD compared to a traditional MAD.	Trial (RCT), China	questionnaires at 1, 2, and 4 weeks, Cone Beam Computed Tomography (CBCT) for upper airway and TMJ changes.
Dental side effects of long-term OSA therapy: a 10-year follow-up study (41)	Uniken Venema. et al., 2019	Clinical Oral Investigations	To evaluate long-term dental side effects in patients undergoing treatment for OSA with either: MADs and CPAP therapy. To analyze changes in dental occlusion after 2 and 10 years of therapy.	Longitudinal Clinical Study (10-year follow-up study), Netherlands	Evaluation periods: Baseline, 2-year, and 10-year follow-up, dental plaster cast analysis, digital sliding caliper, statistical tests (ANOVA, Chi-square).
Impact of a MAD on Corticomotor Plasticity in Patients with OSA (42)	Costa et al., 2024	Journal of Oral Rehabilitation	To assess the neuroplastic effects of MAD therapy on corticomotor	Randomized, Placebo-Controlled Crossove	Transcranial Magnetic Stimulation (TMS), PSG, ESS, oral health

	excitability in OSA patients.	r Study (RCT), Denmark	questionnaires, TMJ and masseter muscle pain assessments.

Table 5 : Summary of included studies on the side effects of MADs in obstructive sleep apnea management

Title	Sample	Outcomes	Reported side effects
Oral appliance therapy vs. nasal CPAP in OSA : A randomized, placebo-controlled trial on temporomandibular side-effects (32)	N=64	No significant difference in TMD pain between MAD and CPAP users after 6 months.	• Mild TMD pain • Morning jaw stiffness
The comparison of two different mandibular positions for oral appliance therapy in OSA (33)	N=32	Both advancements improved OSA but 75% caused more discomfort.	• Higher TMJ pain and jaw stiffness in 75% advancement group. • Transient sensation of bite misalignment.
Objectively measured adherence may affect side effects of mandibular advancement therapy in subjects with obstructive sleep apnea (34)	N=58		• TMD and jaw symptoms : o TMJ Pain (higher prevalence in females), o Muscle pain (temporarily tripled within 3 months of MAD use but decreased later), o Clicking sounds in the TMJ, jaw stiffness in the morning (common particularly in the early adaptation phase), o Difficulty to open mouth (restricted mouth opening) • Occlusal and dental changes o Overjet reduced by 0.4mm in 12 months and Overbite reduced by 0.25mm in 12 months

			○ Molar occlusion shifts: small changes in molar occlusion observed in some patients (mostly related to prolonged MADs use) ○ Progressive occlusal changes: more pronounced in patients with higher adherence (longer nightly wear). ○ Feeling of occlusal changes: Some patients reported a subjective feeling of bite misalignment. • Soft tissue and oral symptoms ○ Pain in teeth (one of the most common reported side effects) ○ Hypersalivation (most frequent early side effect) ○ Xerostomia ○ Gingival irritation (decrease over time)
Effect of long-term oral appliance therapy on obstruction pattern in OSA (35)	N=79	Significant widening of velum and epiglottis after long-term MAD use.	• Dental and occlusal changes: ○ Significant reduction in overjet and overbite after 2 years of MAD, overjet decreased from 3.19mm to 2.80mm and overbite from 3.30mm to 2.95mm.

			○ Potential long-term occlusal shifts if MAD use continues beyond 2 years. • TMJ and musculoskeletal side effects: ○ Patients with TMD pain in the first 2-3 months were asked to discontinue treatment eliminating patients who might have developed severe TMD later. ○ Jaw discomfort and temporary bite changes were reported in early phases but improved over time
Efficacy and mechanism of MADs for persistent sleep apnea after surgery (36)	N=19	57.9% of patients responded well but mild side effects observed.	• Short term side effects (one week use): ○ Dental soreness ○ Hypersalivation ○ Masseter muscle pain ○ Xerostomia ○ Mucosal ulceration ○ Temporomandibular joint aches ○ Localized tooth pain. ○ Weak occlusion due to a difficulty in bite alignment) • Long-term side effects

			○ Loose of lower incisors ○ TMJ pain ○ All reported symptoms were relieved within one month with proper care and continued MAD use.
The effects of MAD on pressure pain threshold of masticatory muscles : A prospective controlled cohort study (37)	N=27	Increased muscle pain initially, adaptation over 6 months. Some patients dropped out of the study as they did not tolerate MAD therapy.	• Muscle pain and sensitivity: ○ Decrease in pressure pain thresholds (PPTs) of the masseter and temporalis muscles after 15 days of MAD use. ○ Increased sensitivity and muscle in the early weeks • TMJ pain: ○ Morning pain in the cheeks and/or temples ○ Function-related pain (pain triggered by chewing or speaking) • Occlusal and dental changes: ○ Temporary bite misalignment (reported in the morning)
Clinical Efficacy of a Position-Responding Mandibular Advancement Device in Patients With Obstructive Sleep Apnea (38)	N=14	Observed mild side effects with the auto-titrating MAD however no significant long-term adverse effects were reported. The	• Mild to moderate hypersalivation (Mild in 42.9% of the patients and moderate in 21.4%) • Mild tooth pain in 42.9% of the patients • Mild to moderate dry mouth Mild: 28.6%, Moderate: 21.4% • Mild TMJ Discomfort (28.6%)

		reported side effects were manageable, meaning most patients have been able to continue using the MAD without significant interruption.	
Comparison of Titrable Thermoplastic Versus Custom-Made Mandibular Advancement Device for the Treatment of Obstructive Sleep Apnoea (39)	N=158	Thermoplastic MADs lead to a higher incidence of side effects compared to custom-made MADs. Custom-made MADs had fewer side effects however still present. Discomfort and side effects were one of the reasons for discontinuation of therapy in some patients.	• Tooth pain: o Thermoplastic MAD: Higher incidence of tooth pain ($p < 0.0001$) o Custom-Made MAD: Less frequent tooth pain • Self-reported occlusal changes (Bite alterations): o Thermoplastic MAD: More reported occlusal changes ($p = 0.0069$). o Custom-Made MAD: Fewer reported bite alterations. • Jaw pain: o Thermoplastic MAD: Mild cases of jaw pain (not statistically significant). o Custom-Made MAD: Fewer complaints of jaw pain. • Muscle stiffness:

		○ Both MADs: Reported at similar levels • Xerostomia ○ Both MADs: reported at similar levels • Hypersalivation Both MADs: reported at similar levels
Clinical Effect of Personalized Adjustable Mandibular Advancement Device on Obstructive Sleep Apnea (40)	N=40	Personalized adjustable MAD showed fewer side effects compared to traditional ones. Fewer reports of TMJ discomfort, tooth pain, dry mouth, and excessive salivation. No significant side effects were noted in most patients. Side effects were mild and resolved over time. Better patient comfort and compliance were observed with the	• Increased Salivation (reported in both experimental and control groups, but more frequent in the control group) • Xerostomia (persistent side effect, particularly in the control group) • Masticatory muscle aches (more common in the control group, symptoms decreasing over time) • TMJ Discomfort (more experienced in the control group)

		personalized MAD.	
Dental side effects of long-term obstructive sleep apnea therapy: a 10-year follow-up study (41)	N=14 (MADs) N=17 (CPAP)	MADs cause significant and progressive dental changes over time. Changes were more pronounced with MADs compared to CPAP even if CPAP therapy also caused dental changes but to a lesser extent. A long-term follow-up and informed consent are crucial before MAD therapy initiation.	• Dental occlusion changes: o Progressive overjet reduction: ▪ 2-year follow-up: decrease of 1.1 ± 1.8 mm. ▪ 10-year follow-up: decrease of 3.5 ± 1.5 mm. o Progressive overbite reduction: ▪ 2-year follow-up: decrease of 1.1 ± 1.2 mm. ▪ 10-year follow-up: decrease of 2.9 ± 1.5 mm. o Molar occlusion changes: ◦ A shift towards Class III occlusion observed over time. ◦ Significant reduction in posterior occlusal contact points. • TMJ and craniofacial changes:

			○ Temporomandibular dysfunction with reported TMJ pain, joint sounds (clicking), and myofascial pain. ○ Craniofacial alterations: ▪ Increased lower and total anterior facial height. ▪ Downward rotation of the mandible. • Myofacial and dental discomfort: ○ Tooth pain: especially early in treatment. ○ Muscle stiffness: reported jaw muscle discomfort. ○ Xerostomia (leading to discomfort) ○ Hypersalivation ○ Gum Irritation
Impact of a Mandibular Advancement Device on Corticomotor Plasticity in Patients with Obstructive Sleep Apnea (42)	N=28	Minimal side effects, showed improvement in sleep quality and daytime sleepiness.	• TMJ pain: ○ Baseline: 7% of participants reported TMJ pain. ○ After MAD active position use: 3% of participants reported TMJ pain. ○ After MAD placebo position use: No reports of TMJ pain. ○ TMJ pain slightly decreased after using

		MAD in the active position and disappeared in the placebo position. • Masseter muscle pain: o Baseline: 10% of participants reported masseter pain. o After MAD active position use: 10% still reported masseter pain. o After MAD placebo position use: 10% still reported masseter pain. o No significant changes in masseter pain with MAD use. • Discomfort related to jaw protrusion

Table 6: Reported side effects and outcomes of MADs in obstructive sleep apnea treatment

4.2.1. Study Selection and Characteristics

A total of 11 studies summarized in table 5 were included in this systematized review, analyzing the side effects of MADs in the management of OSA. These studies exhibited variations in design, sample size, and data collection methods, incorporating methodologies such as randomized controlled trials (RCTs), prospective cohort studies, and longitudinal follow-ups. The selected research was conducted between 2016 and 2024 across multiple countries, including the Netherlands, Japan, Finland, Korea, China, France, and Italy. The sample sizes ranged from 14 to 158 participants, and data collection techniques included polysomnography (PSG), patient-reported outcomes, clinical assessments, imaging techniques, and pressure pain threshold (PPT) measurements.

4.2.2. Primary Outcomes: Side Effects of MAD Therapy

The primary outcomes of this systematized review focus on the side effects associated with MADs, including TMJ discomfort, dental occlusal changes, soft tissue symptoms, and muscle pain. These findings, derived from the included studies, highlight both short-term and long-term effects of MAD therapy. A detailed breakdown of these outcomes, including specific sample sizes, reported side effects, and study conclusions, is summarized in Table 2.

Several studies focused on the effects of MADs on TMJ function and jaw discomfort. Notably, Nikolopoulou et al. (2020) examined 64 participants and found no significant difference in TMD pain between MAD and CPAP users after six months, although mild TMJ pain and morning jaw stiffness were observed . Similarly, Makihara et al. (2022) conducted a comparative analysis of 50% vs. 75% mandibular advancement in 32 patients, concluding that both advancements effectively improved OSA symptoms, but the 75% advancement group experienced increased TMJ pain and transient bite misalignment . Further evidence from Pahkala et al. (2024) suggested that TMJ pain was more prevalent in females, with muscle pain tripling during the first three months of MAD use before gradually subsiding. Some participants also reported clicking sounds in the TMJ and restricted mouth opening (34). Additionally, Sung-Woon On et al. (2024) evaluated over 14 participants an auto-titrating MAD designed to adjust mandibular advancement based on the patient's response. Their study found that while mild side effects such as hypersalivation, dry mouth, and mild TMJ discomfort were reported (38).

In addition to TMJ-related discomfort, multiple studies identified dental and occlusal modifications associated with MAD therapy. Pahkala et al. (2024) reported a reduction in overjet by 0.4 mm and in overbite by 0.25 mm over 12 months, with more pronounced occlusal changes occurring in patients with higher adherence (34). Likewise, Jo et al. (2018) analyzed 79 patients and documented a significant long-term occlusal shift, where overjet decreased from 3.19 mm to 2.80 mm after two years (35). A more extensive longitudinal analysis by Julia Anne Margarethe Uniken Venema et al. (2019) revealed that MAD users experienced progressive overjet and overbite reduction over a ten year follow-up period, with molar occlusion shifting toward Class III malocclusion (41).

Soft tissue symptoms were also commonly reported among MAD users, with pain in the teeth, hypersalivation, xerostomia, and gingival irritation emerging as frequent concerns. Pahkala et al. (2024) identified hypersalivation as the most common early side effect, which gradually diminished over time (34). Luo et al. (2016), who conducted a study on 19 participants, noted the presence of dental soreness, mucosal ulceration, and localized

tooth pain, though these symptoms resolved within one month (36). Additionally, Costa et al. (2024) described cases of xerostomia and jaw protrusion-related discomfort, but overall, the reported side effects were considered minimal (42). Sung-Woon On et al. (2024) also observed increased salivation and mild TMJ discomfort, but these symptoms were comparable between the experimental and control groups, suggesting that auto-titration may improve patient adaptation.

Muscle pain and sensitivity were evaluated in several studies, with Alessandrini-Bonetti et al. (2016) reporting an initial increase in muscle pain during MAD therapy, followed by adaptation over six months (37). Wang et al. (2024) compared personalized adjustable MADs with traditional ones, finding that the personalized devices resulted in fewer reports of TMJ discomfort, dry mouth, and excessive salivation (40). Additionally, Gagnadoux et al. (2017) observed that thermoplastic MADs led to a higher incidence of occlusal changes, tooth pain, and jaw discomfort than custom-made MADs, which produced fewer, though still present, side effects (39).

The findings of this systematized review revealed that short-term side effects were common among MAD users, with hypersalivation, muscle pain, and TMJ discomfort emerging as the most frequently reported symptoms. These effects typically diminished over time as patients adapted to the device. Additionally, transient occlusal changes and bite misalignment were noted in the first few months of treatment. In contrast, long-term side effects, particularly progressive occlusal changes such as reductions in overjet and overbite, were more prominent in patients with over two years of MAD use. TMJ discomfort tended to be mild to moderate, with a higher incidence among individuals with greater mandibular advancement (>75%).

5. DISCUSSION

5.1. Long-term Mandibular Advancement Device (MAD) use leads to progressive occlusal changes

Reductions in overjet and overbite are a consistent finding in our study during prolonged MAD therapy, aligning with prior research that underscores occlusal alterations as a predictable side effect of long-term appliance use.

Marklund (2006) reported that 14–26% of patients experienced more than a 1mm reduction in overjet within 2 to 3 years, particularly in those presenting with deep bite or nasal congestion (30).

These findings are echoed by Venema et al. (2020), who documented more pronounced changes, approximately 3.5 mm in overjet and 2.9 mm in overbite, after 10 years of therapy, highlighting the cumulative nature of these effects (41).

Furthermore, our observations resonate with Pahkala (2024), who identified that patients with higher adherence, defined by extended nightly use, tend to exhibit more substantial occlusal changes (34).

This supports the notion that the intensity and duration of MAD use are directly proportional to the degree of skeletal and dental modifications observed.

Similarly, Jo et al. (2018) reported mild but clinically meaningful bite changes after two years of consistent use, findings that mirror the occlusal trends noted in our cohort (35).

Notably, Rana et al. (2023) emphasized the directional nature of dental shifts, with continuous MAD use promoting lower incisor proclination and upper incisor retroclination, outcomes that align with the anterior-posterior alterations observed in our cases (13).

The long-term impact of these changes has been further validated by studies such as Jo et al. (2018) and Uniken Venema et al. (2019), both of which advocate for structured and periodic occlusal evaluations during therapy (35,41).

Despite variations in device design, duration of follow-up, and baseline occlusal characteristics across studies, a common conclusion emerges consistent occlusal monitoring is essential to detect, manage, and potentially prevent progressive dental and skeletal changes during MAD therapy which may lead to an orthodontic intervention.

5.2. Craniofacial and muscular alterations may occur over time

Beyond occlusal adaptations, our study shows that MAD treatment results in an increase in broader craniofacial and neuromuscular effects. Craniofacial and muscular changes evolve in discernible phases during prolonged mandibular advancement therapy.

Sutherland & Cistulli (2011) described a mild clockwise rotation of the mandible with lengthening of the lower anterior facial height, a pattern later confirmed in the 10 years cohort of Uniken Venema et al. (2019) (31,41).

Recently Wang et al. (2024) shows that even when the condyle itself remains morphologically intact the soft palate and tongue base expand laterally, suggesting coordinated bone and soft tissue remodeling to accommodate the protruded jaw (40).

Bonetti et al (2016) found that pressure pain thresholds in the masseter and temporalis decrease in the first two weeks, signaling transient hyperactivity, but return to baseline by six months, a timeframe that is consistent with the low prevalence of Temporomandibular Disorder (TMD) with pain reported at six months in the randomized trial by Nikolopoulou et al (2020) (32,37).

Pahkala (2024) demonstrated a dose response relationship, patients wearing the appliance longer each night more clinical TMD signs, underscoring adherence as a key modifier of musculoskeletal load (34).

Taken together, the evidence indicates an initial period of muscle strain and neural up-regulation, followed by longer-term skeletal and soft tissue accommodation. Regular assessments of facial dimensions, masticatory-muscle comfort, and TMJ status are therefore essential to balance respiratory benefit against progressive craniofacial change.

5.3. MADs use affects the soft tissues

Transient mucosal and muscular complaints emerged regularly in our cohort during the initial months of MAD therapy, mirroring a body of evidence that identifies early soft-tissue reactions as the most predictable short-term side effect of appliance wear (36,37,39,40,42).

Wang et al. (2024) found that a fully customized, titratable MAD induced significantly fewer episodes of xerostomia, gingival irritation, and muscular tenderness than a more

traditional fixed device, underscoring how precise fit can protect delicate oral tissues (40).

Gagnadoux et al. (2017) reached a similar conclusion, reporting greater discomfort and dropout with thermo-plastic “boil-and-bite” splints than with laboratory-made appliances, thereby reinforcing the centrality of precision manufacturing (39).

The temporal course of these symptoms was clarified by Bonetti et al. (2016), who noted that soft tissue soreness tends to peak in the first weeks, whereupon a progressive adaptation of mucosa and masticatory muscles (37) .

Our findings also converge with Luo et al. (2016) and Costa et al. (2024), both of whom identified xerostomia and hypersalivation as leading complaints (36,42).

Taken together, the literature indicates that the nature, intensity, and duration of early soft-tissue reactions depend largely on appliance design and individual oral physiology. Precise, adjustable devices, coupled with proactive moisture management and close follow-up, appear key to minimizing discomfort and enhancing patient tolerance during the critical acclimatization phase of MAD therapy.

5.4. Limitations

Although these collective findings are valuable, several limitations should be acknowledged.

First, significant heterogeneity across study designs, follow-up lengths, and patient populations can restrict direct comparisons. Second, there is a shortage of long-term Randomized Controlled Trials (RCTs) investigating definitive links between extended MAD use and permanent occlusal or skeletal alterations.

In addition, some investigations rely on self-reporting of pain or other side effects, which might introduce bias or underestimation of milder complaints. Despite these challenges, the comprehensive overview here affirms that while MADs effectively manage OSA in many patients, they also entail appreciable side effects. Short-term issues, including muscle aches or hypersalivation, usually subside, but progressive occlusal changes warrant long-term professional supervision. These limitations also indicate the need for further analysis of different titration and device designs, along with standardized parameters to enhance the consistency and comparability of reported outcomes.

Although the previously mentioned issues are common during the initial adaptation phase, most patients adapt well, and no major differences in overall clinical impact have been reported when comparing MAD users to non-users or to those treated with other methods like CPAP.

In clinical practice, regular monitoring, personalized device titration, and patient education on the possibility of these changes are vital for ensuring a positive balance between efficacy and comfort.

6. CONCLUSIONS

- The results of this review have shown that adults over 18 undergoing mandibular advancement devices therapy for obstructive sleep apnea commonly experience mild to moderate side effects. These include temporomandibular joint discomfort, occlusal changes, muscle soreness, and soft tissue symptoms such as dry mouth or gingival irritation. While most short-term effects tend to resolve with adaptation, gradual occlusal changes, primarily reductions in overjet and overbite, may develop over time, highlighting the need for regular dental monitoring.

- Further high-quality, long-term clinical trials are necessary to better define the prevalence, progression, and reversibility of these occlusal shifts. Future research should also contribute to the development of standardized clinical protocols that optimize both therapeutic efficacy and long-term oral health.

7. SUSTAINABILITY

For Mandibular Advancement Devices (MADs) to be a sustainable treatment option for Obstructive Sleep Apnea (OSA), they must balance effectiveness, affordability, and environmental impact.

7.1. Environmental Considerations

Most MADs are made of plastics and some metals, which contribute to medical waste. Using biodegradable materials and eco-friendly packaging can help reduce their environmental footprint. Additionally, longer-lasting designs would reduce the frequency of replacements.

7.2. Economic Sustainability

MADs are cheaper than alternative treatments as Continuous Positive Airway Pressure (CPAP) but require regular replacements. Expanding insurance coverage and developing durable, cost-effective designs can make MADs more accessible for patients. Custom MADs improve comfort but remain expensive, so affordable alternatives should be explored.

7.3. Social and Ethical Considerations

Patients must be fully informed about all possible long-term effects, such as bite changes and Temporomandibular Joint (TMJ) discomfort. Especially when it could lead to the need for orthodontic treatment in the future. Equitable access is crucial, especially for low-income patients.

7.4. Future Perspectives

Developing biodegradable MADs, improving insurance policies, and standardized long-term side effects tracking protocols can enhance sustainability. As future dentists, we should advocate for better materials, affordability, and patient education to ensure long-term success.

8. REFERENCES

1. Chokroverty S, Billiard M, editores. Sleep Medicine: A Comprehensive Guide to Its Development, Clinical Milestones, and Advances in Treatment [Internet]. New York, NY: Springer New York; 2015 [citado 2 de noviembre de 2024]. Disponible en: https://link.springer.com/10.1007/978-1-4939-2089-1

2. Chien YH, Guilleminault C. Revue historique sur le syndrome d'apnée obstructive du sommeil chez l'enfant. Arch Pédiatrie. 2017;24:S2-6.

3. Scherr SC, Dort LC, Almeida FR, Bennett KM, Blumenstock NT, Demko BG, et al. Definition of an Effective Oral Appliance for the Treatment of Obstructive Sleep Apnea and Snoring: A Report of the American Academy of Dental Sleep Medicine. J Dent Sleep Med [Internet]. 2014 [citado 16 de octubre de 2024]; Disponible en: https://aadsm.org/docs/JDSM.01.01.pdf

4. Lavie P. Who was the first to use the term Pickwickian in connection with sleepy patients? History of sleep apnoea syndrome. Sleep Med Rev. 2008;12(1):5-17.

5. Li KK, Riley R, Powell N, Hester J. Skeletal expansion by gradual intraoral distraction osteogenesis for the treatment of obstructive sleep apnea. Oper Tech Otolaryngol-Head Neck Surg. 2002;13(2):119-22.

6. Garvey JF, Pengo MF, Drakatos P, Kent BD. Epidemiological aspects of obstructive sleep apnea. 2015;

7. Laratta CR, Ayas NT, Povitz M, Pendharkar SR. Diagnosis and treatment of obstructive sleep apnea in adults. 2017;

8. Fietze I, Penzel T, Alonderis A, Barbe F, Bonsignore MR, Calverly P, et al. Management of obstructive sleep apnea in Europe. Sleep Med. febrero de 2011;12(2):190-7.

9. Dudley KA, Patel SR. Disparities and genetic risk factors in obstructive sleep apnea. Sleep Med. 2016;18:96-102.

10. Al Lawati NM, Patel SR, Ayas NT. Epidemiology, Risk Factors, and Consequences of Obstructive Sleep Apnea and Short Sleep Duration. Prog Cardiovasc Dis. 2009;51(4):285-93.

11. Dunietz GL, Chervin RD, Burke JF, Conceicao AS, Braley TJ. Obstructive sleep apnea treatment and dementia risk in older adults. Sleep. 2021;44(9):zsab076.

12. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev. 2017;34:70-81.

13. Rana A, Raut A, Mathur A. The Occlusal Side Effects of Mandibular Advancement Device Therapy in Adult Sleep Apnea Patients: A Systematic Review. Cureus [Internet]. 2023 [citado 14 de octubre de 2024]; Disponible en: https://www.cureus.com/articles/195268-the-occlusal-side-effects-of-mandibular-advancement-device-therapy-in-adult-sleep-apnea-patients-a-systematic-review

14. Rundo JV. Obstructive sleep apnea basics. Cleve Clin J Med. 2019;86(9 suppl 1):2-9.

15. Tan A, Yin JDC, Tan LWL, Van Dam RM, Cheung YY, Lee CH. Using the Berlin Questionnaire to Predict Obstructive Sleep Apnea in the General Population. J Clin Sleep Med. 2017;13(03):427-32.

16. Zheng Z, Zhang Y, Chen M, Chen X, Li C, Wang C, et al. Application value of joint STOP-Bang questionnaire and Epworth Sleepiness Scale in screening for obstructive sleep apnea. Front Public Health. 29 de septiembre de 2022;10:950585.

17. Sunwoo BY, Kaufmann CN, Murez A, Lee E, Gilbertson D, Bosompra NO, et al. The language of sleepiness in obstructive sleep apnea beyond the Epworth. Sleep Breath. 2023;27(3):1057-65.

18. Batool-Anwar S, Goodwin JL, Kushida CA, Walsh JA, Simon RD, Nichols DA, et al. Impact of continuous positive airway pressure (CPAP) on quality of life in patients with obstructive sleep apnea (OSA). J Sleep Res. 2016;25(6):731-8.

19. Chang H, Chen Y, Du J. Obstructive sleep apnea treatment in adults. Kaohsiung J Med Sci. 2020;36(1):7-12.

20. Sleeper G, Rashidi M, Strohl KP, Najimi N, Chen PL, El Ghoul R, et al. Comparison of expiratory pressures generated by four different EPAP devices in a laboratory bench setting. Sleep Med. 2022;96:87-92.

21. Uniken Venema JAM, Rosenmöller BRAM, De Vries N, De Lange J, Aarab G, Lobbezoo F, et al. Mandibular advancement device design: A systematic review on outcomes in obstructive sleep apnea treatment. Sleep Med Rev. 2021;60:101557.

22. Pimentel MJ, Bacchi A, De Castro GC, Rizzatti-Barbosa CM. Oral Appliance for the Treatment of Severe Obstructive Sleep Apnea in Edentulous Patient. J Indian Prosthodont Soc. 2014;14(S1):255-9.

23. Pokorski M, editor. Medical Science and Research [Internet]. Cham: Springer International Publishing; 2019 [citado 3 de noviembre de 2024]. (Advances in Experimental Medicine and Biology; vol. 1153). Disponible en: http://link.springer.com/10.1007/978-3-030-19059-0

24. Penzel T, Hornero R, editores. Advances in the Diagnosis and Treatment of Sleep Apnea: Filling the Gap Between Physicians and Engineers [Internet]. Cham: Springer International Publishing; 2022 [citado 3 de noviembre de 2024]. (Advances in Experimental Medicine and Biology; vol. 1384). Disponible en: https://link.springer.com/10.1007/978-3-031-06413-5

25. Piskin B, Yılmaz Savaş T, Topal SC, Akbulut K, Ezmek B, Uyar A, et al. Comparison of efficacy and usability of custom mandibular advancement devices fabricated with the conventional method and digital workflow: A pilot clinical study. J Prosthodont. 2024;33(2):123-31.

26. Banhiran W, Kittiphumwong P, Assanasen P, Chongkolwatana C, Metheetrairut C. Adjustable thermoplastic mandibular advancement device for obstructive sleep apnea: Outcomes and practicability. The Laryngoscope. 2014;124(10):2427-32.

27. Soh L, Han HJ, Yue Y, Tay JY, Hao Y, Toh ST. Evaluation of prefabricated adjustable thermoplastic mandibular advancement devices (PAT-MADs) for obstructive sleep apnea: an Asian experience. Sleep Med. 2020;75:96-102.

28. Sivaramakrishnan G, Sridharan K. A systematic review on the effectiveness of titratable over nontitratable mandibular advancement appliances for sleep apnea. J Indian Prosthodont Soc. 2017;17(4):319.

29. Özköylü G, Saraç D, Sasany R, Umurca DG. Comparison of monoblock and twinblock mandibular advancement devices in patiens with obstructive sleep apnea and temporomandibular disorder: effects on airway volume, polysomnography parameters, and sleepiness scale scores. BMC Oral Health. 2024;24(1):1026.

30. Marklund M. Predictors of long-term orthodontic side effects from mandibular advancement devices in patients with snoring and obstructive sleep apnea. Am J Orthod Dentofacial Orthop. 2006;129(2):214-21.

31. Sutherland K, Cistulli P. Mandibular advancement splints for the treatment of sleep apnea syndrome. Swiss Med Wkly [Internet]. 2011 [citado 16 de octubre de 2024]; Disponible en: https://smw.ch/index.php/smw/article/view/1344

32. Nikolopoulou M, Aarab G, Ahlberg J, Hamburger HL, De Lange J, Lobbezoo F. Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnea: A randomized, placebo-controlled trial on temporomandibular side-effects. Clin Exp Dent Res. agosto de 2020;6(4):400-6.

33. Makihara E, Watanabe T, Ogusu H, Masumi S. The comparison of two different mandibular positions for oral appliance therapy in patients with obstructive sleep apnea. Clin Exp Dent Res. 2022;8(6):1567-74.

34. Pahkala R. Objectively measured adherence may affect side effects of mandibular advancement therapy in subjects with obstructive sleep apnea. Sleep Breath. 2024;28(2):813-21.

35. Jo SY, Lee SM, Lee KH, Kim DK. Effect of long-term oral appliance therapy on obstruction pattern in patients with obstructive sleep apnea. Eur Arch Otorhinolaryngol. 2018;275(5):1327-33.

36. Luo H, Tang X, Xiong Y, Meng L, Yi H, Yin S. Efficacy and mechanism of mandibular advancement devices for persistent sleep apnea after surgery: A prospective study. J Otolaryngol - Head Neck Surg. 2016;45(1):56.

37. Alessandri-Bonetti G, Bortolotti F, Bartolucci M, Marini I, D'Antò V, Michelotti A. The Effects of Mandibular Advancement Device on Pressure Pain Threshold of Masticatory Muscles: A Prospective Controlled Cohort Study. J Oral Facial Pain Headache. 2016;30(3):234-40.

38. On SW, Kim DK, Lee MH, Lee JH, Lee KC, Byun SH, et al. Clinical Efficacy of a Position-Responding Mandibular Advancement Device in Patients With Obstructive Sleep Apnea. Clin Exp Otorhinolaryngol. 2024;17(4):302-9.

39. Gagnadoux F, Nguyen XL, Le Vaillant M, Priou P, Meslier N, Eberlein A, et al. Comparison of titrable thermoplastic versus custom-made mandibular advancement device for the treatment of obstructive sleep apnoea. Respir Med. 2017;131:35-42.

40. Wang W, Pang J, Zhang YX, Mo YM, Zhang J, Wei ZH. Clinical Effect of Personalized Adjustable Mandibular Advancement Device on Obstructive Sleep Apnea. Br J Hosp Med. 30 de agosto de 2024;85(8):1-17.

41. Uniken Venema JAM, Doff MHJ, Joffe-Sokolova DS, Wijkstra PJ, Van Der Hoeven JH, Stegenga B, et al. Dental side effects of long-term obstructive sleep apnea therapy: a 10-year follow-up study. Clin Oral Investig. 2020;24(9):3069-76.

42. Costa YM, Hayakawa H, Castrillon EduardoE, Ferreira DMAO, Iida T, Kothari M, et al. Impact of a mandibular advancement device on corticomotor plasticity in patients with obstructive sleep apnea. J Oral Rehabil. 2024;51(12):2600-10.

9. ANNEXES