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Prevalence of Preexisting or Development of Temporomandibular Disorders In Obstructive Sleep Apnea Patients Prior to and During Therapy With Intra-oral Mandibular Advancement Appliance

A thesis submitted in partial satisfaction

of the requirements for the degree

Master of Science in Oral Biology

by

Sogol Seghatoleslami

2020

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ABSTRACT OF THE THESIS

Prevalence of Preexisting or Development of Temporomandibular Disorders

In Obstructive Sleep Apnea Patients Prior to and During Therapy

With Intra-oral Mandibular Advancement Appliance

by

Sogol Seghatoleslami

Master of Science in Oral Biology

University of California, Los Angeles, 2020

Professor Renate Lux, Chair

Introduction: Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder that affects more than 12 % of the US population. It is considered to be a serious problem associated with multiple physiological processes that affect normal body function including stroke, cardiovascular disease, hypertension, and type 2 diabetes. Risk factors for OSA include BMI higher than 35 kg/m^2, male gender, neck circumference, and high blood pressure. The STOP-BANG questionnaire is a reliable screening tool for OSA; nevertheless, the gold standard for diagnosis of OSA is the overnight polysomnography (PSG) test. If the physician diagnoses a patient with OSA, different treatment modalities can be provided based on individual patient needs and preferences. OSA treatment modalities include positive airway pressure (PAP) therapy, surgery, and mandibular advancement devices (MADs). Even though PAP therapy is the

gold standard treatment method for obstructive sleep apnea in adults, a large number of patients cannot tolerate it; therefore, for many of those patients, MADs are a valuable treatment alternative. MADs reduce the upper airway collapse by advancing the mandible and associated soft tissue; as a result, there is generally an increase in the upper airway volume at the oropharynges level and improvement in pharyngeal patency. Occasionally, treatment of sleep apnea with MADs may be associated with the development of symptoms of Temporomandibular Disorder (TMD) and posterior open bite (POB). The definition of TMD includes clusters of signs and symptoms affecting the masticatory musculature, temporomandibular joints (TMJ), and associated structures. Pain is one of the most common symptoms of TMD. TMD disorders have a high prevalence in the general population, which increases the probability that OSA patients who are referred for MAD therapy could already present with TMD, or possibly could develop it during MAD therapy. Another side effect of MAD is POB, defined as no occlusal contact between the maxillary and mandibular posterior teeth when the patients try to hold their jaws in a maximum intercuspation position. This study aims to evaluate the incidence and prevalence of TMD in OSA patients prior to receiving MAD, and to determine the overall prevalence of TMD problems and POB during MAD therapy. This study also aims to evaluate the effectiveness of daily physical medicine exercise instructions on management of TMD and POB development during usage of MAD.

Materials and Methods: This was a retrospective study for which medical records of UCLA patients were reviewed. In order to determine prevalence of TMD in OSA patients prior to receiving MAD, the charts of 195 patients who were referred to the UCLA Orofacial Pain Clinic between June 2016 to June 2019 for MAD therapy were screened as the study group. One hundred and fifty-five patients met the study group criteria. Additionally, we screened the data of

400 new patients in the UCLA School of Dentistry's general dental clinic from June 2016 to June 2019 as control group. A total of 188 patients were included in the control group.

One hundred and four subjects of the study group met the criteria to investigate the prevalence of TMD problems and POB during MAD therapy. One hundred and one of the 104 patients whose data contained records of physical exercise compliance were included to explore the effectiveness of physical exercise protocols to manage and prevent TMD and POB during MAD therapy. The follow-up PSG data with oral appliance in place were available for 16 patients. These were reviewed to evaluate the efficacy of MAD in reduction of AHI (Apnea–Hypopnea Index). Successful management of OSA with MAD therapy was considered as at least 50% reduction of AHI compared to the respective baseline AHI.

Results: At baseline, TMD prevalence was 94% among the OSA patients and 28% in the control group, which was significantly different ($p<0.05$). Sixty-six percent of OSA patients who received MAD did not experience painful TMD, 24% had myalgia and only 8% had both myalgia and arthralgia during MAD therapy. The number of patients with painful TMD was significantly reduced from 98 patients at baseline to 34 patients after receiving MAD ($p<0.05$). Physical exercise protocols effectively and significantly reduced painful TMD during MAD therapy ($p < 0.05$). Incidence of POB was 11.5%, but daily jaw repositioning physical exercises reduced the prevalence and incidence of POB during MAD therapy. MAD therapy had successful outcome in 75% of the patients.

Conclusion: The prevalence of TMD in OSA patients is significantly higher compared to the control group. Therefore, it is crucial for dentists who provide MAD for OSA patients to have appropriate training and background to assess, diagnose, and document preexisting TMD, and to

be able to manage signs and symptoms of TMD before MAD therapy. Physical exercise protocols are effective and valuable tools to manage and prevent possible side effects of MAD usage including TMD and POB. Therefore, physical exercise instructions should be given at the MAD-delivery visit and be emphasized during follow-up visits.

The thesis of Sogol Seghatoleslami is approved.

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2020

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TABLE OF CONTENT

1. Introduction

1-1. Background

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder affecting approximately 12 % of the population of the USA.[1] During the sleep cycle, an OSA patient may experience episodes of diminished airflow (termed “hypopnea”) or no airflow (termed “apnea”) to the lungs, despite continuing respiratory efforts. Intermittent obstruction of the airway by the tongue or by excessive collapsibility of a small airway during sleep may cause airflow restriction. These repetitive lapses in respiration may result in hypoxia, which is associated with an increase in morbidity and mortality. Numerous medical problems including stroke,[2] cardiovascular disease,[2,3] hypertension,[4] and type 2 diabetes[5] can develop in OSA patients.

The comprehensive in-laboratory polysomnography (PSG) test is the gold standard for diagnosing sleep-disordered breathing. The main outcome used to define OSA severity is the apnea-hypopnea index (AHI). This index represents the number of breathing stoppages (apneas) and reduced airflow (hypopneas) lasting greater than 10 seconds that result in reduced oxygenation and brief awakening (arousal) per hour of sleep. While severity cutoffs vary, typically mild sleep apnea is defined as 5–15 events per hour, moderate as 15–30 events, and severe as more than 30 respiratory events per hour of sleep.[6]

The gold standard for treatment of OSA is positive airway pressure (PAP) which is reported to have a successful outcome for over 95 % of users.[7] However, as many as 50 % of patients cannot tolerate the use of PAP[8] or will only wear it less than half of the night. Mandibular advancement devices (MADs) are valuable treatment alternatives for many of those patients. MADs work by mechanically protruding the mandible, thereby moving the tongue off

the posterior pharyngeal wall. This is similar to the effect of the head tilt–chin lift maneuver used in cardiopulmonary resuscitation (CPR) and results in an increased airway space with reduced airflow resistance. Studies have shown that MAD therapy can be a valuable treatment option for patients with all degrees of OSA.[9] However, it is most predictably effective in mild to moderate OSA.[10,11,12] MADs are not as effective as PAP in reducing AHI.[13,14,15] However, patients tend to favor the use of MADs over PAP for a variety of reasons. [8] In addition, MADs can improve sleep quality as evidenced by decreased subjective complaints of sleepiness and snoring the following day.[16] They also provide improvement in blood pressure similar to PAP.[17,18,19,20]

MADs protrude and maintain the mandible in a non-habitual position during sleep, potentially negatively impacting the stomatognathic system with the possible development of signs and symptoms of temporomandibular disorder (TMD). TMDs are defined as clusters of signs and symptoms affecting the masticatory musculature, temporomandibular joints (TMJ), and associated structures.[21] One of the most common symptoms associated with TMDs is pain. TMD disorders are quite common in the general population, and in fact, after dental pains, the next most common pain complaints reported by patients in the dental office are TMDs.[22,23] In the case of OSA patients treated with MADs, the clinician needs to determine whether the problem was caused by the MAD or if the TMD problem was an undiagnosed pre-existing condition. It is critical that the dentist who is providing MAD for OSA performs a thorough physical and neurologic assessment of the temporomandibular joint (TMJ) and associated structures before providing such a device, so that preexisting TMD problems are identified and discussed with the patient.[24] There are few studies that investigated the incidence/prevalence of TMD-associated OSA, and TMD during MAD therapy; therefore, additional data are needed.[25]

1-2. Obstructive Sleep Apnea

Obstructive sleep apnea occurs as a function of increased blockage or collapsibility of the upper airway. The pharyngeal critical closing pressure (Pcrit) is the pressure at which the upper airway collapses. This collapsibility is influenced further by impaired neuromuscular tone. Respiratory effort increases to maintain airflow through the constricted airway, accompanied by a relative increase in serum carbon dioxide (hypercarbia) and decrease in serum oxygen (hypoxemia). The increased work of breathing results in a cortical arousal from sleep, which in turn raises sympathetic neural activity leading to increased heart rate and blood pressure that may result in cardiac arrhythmia. With the cortical arousal from sleep comes an increase in airway patency and resumption of normal ventilation, followed by a subsequent return to sleep and recurrence of sleep related upper airway collapsibility. This disruption in breathing may occur multiple times per hour during the total sleep time of the patient.[26]

1-2-1. Consequences of Obstructive Sleep Apnea Syndrome

Untreated OSA can cause serious clinical consequences including excessive daytime sleepiness that increases the risk of motor vehicle accidents and may adversely affect quality-of-life. Neurocognitive disfunction leads to decreased academic and professional performance. Chronic intermittent hypoxemia and heightened sympathetic neural tone, endothelial damage and heightened inflammation are related to metabolic dysfunction and damage to major organs. Untreated obstructive sleep apnea increases risk of insulin resistant diabetes, coronary artery disease, congestive heart failure, hypertension, myocardial infarction, stroke, cardiac arrhythmia, and sudden cardiac death.[26]

1-2-2. Risk Factors

Individuals with certain characteristics appear to be predisposed to OSA. Conditions that have been identified as risk factors for the development of OSA in adults include obesity as measured by body-mass index (BMI) higher than 35 kg/m^2, male gender, neck circumference, increased age, menopause, craniofacial abnormalities, and lifestyle.[26]

1-2-3. Obesity and Airway

Among all risk factors, it appears that obesity, specifically weight gain, is the most important.[27] Data from the prospective Wisconsin Cohort Study over a 4-year interval shows that a 10% weight gain predicted a 32% increase in the AHI; while, a 10% weight loss predicted a 26% decrease in the AHI.[28] A 10% increase in weight predicted a 6-fold increase in the odds of developing moderate-severe OSA.[28] It is estimated that 58% of moderate or worse OSA (AHI $\geq$ 15) adult cases are attributable to excess weight.[29] Neck circumference has been shown to be one of the most significant risk factors for OSA.[30,31]

1-2-4. Age and Gender

Community-based data from the Sleep Heart Health Study (n=5615) shows that OSA prevalence increases with age and reaches a plateau after 60 years of age.[32] The highest prevalence is among 40-60 year-old men.[32] Among women, prevalence is highest in the post-menopausal age group.[27] This apparent gender disparity in prevalence of OSA could be in part due to OSA being clinically under-recognized in women since they tend not to report symptoms of loud snoring. Another reason may be the gender-related differences in the anatomical properties of the upper airway between men and women.[33]

1-2-5. OSA Screening Tools

The Epworth Sleepiness Scale may be used to gauge or track symptomatic impairment (or response to treatment). However, it is not a screening tool for OSA, as it detects abnormalities in levels of daytime sleepiness regardless of the cause of sleepiness.[26] In adults, a validated tool for OSA risk assessment is the STOP-Bang questionnaire, which asks yes or no questions based on its acronym: Snoring (S), Tiredness (T), Observed pauses in breathing (O), high blood pressure (P), BMI higher than 35 kg/m^2 (B), Age older than 50 years (A), Neck circumference of 17 inches or larger in males, or 16 inches or larger in females (N), and if the patient's Gender is male (G). A patient is considered to be at low risk for OSA if the questionnaire has 2 or fewer "yes" answers, at intermediate risk if there are 3 to 4 "yes" answers, and at high risk if there are more than 5 "yes" answers.[26]

1-2-6. OSA Diagnosis

Obstructive sleep apnea and other sleep-related breathing disorders can only be diagnosed by a physician boarded in sleep medicine. It is not within the scope of the dentist to diagnose obstructive sleep apnea or any other sleep-related breathing disorder.[26]
Diagnostic confirmation of obstructive sleep apnea is performed by a boarded sleep medicine specialist using the gold standard in-center overnight sleep study, polysomnography (PSG) or out of center sleep testing (OCST) for appropriately selected patients. Home sleep apnea testing (HSAT) is a type of OCST. Attended PSG includes at least seven channels of recording, including electroencephalography (EEG), monitoring of sleep, airflow through the nose and mouth, pulse oximetry, respiratory effort, electrocardiography, and leg movement. HSAT

includes four to seven channels. It is important to note that HSAT typically does not include EEG monitoring of sleep so cannot determine stages of sleep.[26]

1-2-7. Treatment Planning and Modalities in Adult OSA Patients

If the patient is diagnosed with OSA, the physician will prescribe the appropriate course of treatment.[26] Management of OSA includes PAP therapy, surgery, and oral appliances.[34] The OSA treatment plan should be based on careful consideration of the patient's individual needs and treatment goals. If the treatment plan involves a dentist, a plan for treatment, monitoring, and long-term follow up care should be developed by all practitioners involved.[26] The dentist who is providing the MAD should consider working in a collaborative way with the physician, providing related treatment when necessary, as long as it does not interfere with the medical treatment.

1-2-7-1. Positive airway pressure (PAP)

Positive airway pressure (PAP) therapy is the gold standard treatment method for obstructive sleep apnea in adults.[34] PAP acts as a pneumatic splint that maintains patency of the upper airway. PAP is delivered through a mask interface as either continuous positive airway pressure (CPAP), bi-level positive airway pressure (BPAP) or auto-titrating positive airway pressure (APAP). CPAP use can decrease OSA-related cognitive impairment along with improving objective and subjective measures of sleepiness, particularly in patients with severe OSA (AHI $\geq$ 30/hour).[26,35] While definitions of PAP non-adherence vary across studies, a common definition is mean use of less than 4 hours per night.[36,37] Early adherence to PAP use predicts longer-term PAP use; a study of 100 patients started on CPAP showed that CPAP use for at least four hours per night three days after starting therapy was predictive of CPAP

adherence 30 days after treatment initiation.[38] Factors that affect PAP adherence include OSA severity, ability to tolerate the prescribed pressure setting, mask fit, spousal support, and other psychological and social influences.[36]

Other treatment options include positional therapy (avoidance of back-sleeping), elevating the head of the bed, and long-term weight reduction as indicated. Nasal congestion and allergic rhinitis may be managed with nasal steroids and other oral medications as indicated. For some patients, nasal surgery may be performed as adjunctive therapy to decrease intranasal resistance and facilitate better adherence to PAP therapy. For selected patients, multilevel surgery including nasal and/or palatal surgery with or without mandibular surgery, genioglossus advancement, and hyoid suspension may be considered. Other soft tissue surgeries might be indicated that involve the tonsils, adenoids, frena, and tongue. Hypoglossal nerve stimulation addresses the impaired neuromuscular tone in obstructive sleep apnea and may be considered in certain patients with OSA.[26]

1-2-7-2. Oral Appliance Therapy

Oral appliances (OA), which include both mandibular advancing oral appliances (MADs) and tongue retaining devices, are usually effective options for OSA management in appropriately selected patients. MADs are intended to hold the mandible and/or the associated soft tissues forward, resulting in an increased caliber of the upper airway at the oropharyngeal level. A substantial body of research supports the use of oral appliances for patients with OSA. Specifically, MADs may be used for treatment of mild to moderate OSA and for treatment of patients with severe OSA who are unwilling or unable to use PAP therapy. Published guidelines

(American Academy of Sleep Medicine/American Academy of Dental Sleep Medicine) describe how oral appliances fit into the OSA management paradigm.[39,40]

Functional appliances and MADs are considered the first line of treatment for patients with OSA that prefer MADs over PAP and for those patients that do not respond to PAP therapy. While typically well tolerated, it should also be noted that not all patients with OSA will respond to treatment with MADs. This form of therapy is reported to be completely effective in 36% to 70% of OSA cases[26], however, definitions of MAD treatment success vary. Treatment success is mainly defined by a reduction in AHI with or without requirement for symptomatic improvement. Some studies defined treatment success in terms of AHI reduction. Those studies considered MAD therapy efficacy as a percentage reduction in AHI, typically more than 50% AHI reduction, from baseline which is considered to be clinically significant.[41]

Many types of oral appliances are used in the treatment of OSA in adults. The appliances vary based on the coupling design, mode of fabrication and activation, titration capability, degree of vertical opening, lateral jaw movement, and whether they are custom made or prefabricated. Proper indications for each design should be considered.[26]

1-3. Temporomandibular Disorder (TMD)

Occasionally, treatment of sleep apnea with MADs may be associated with the development of symptoms of TMD.[24] It is crucial for the clinician to determine if the TMD was caused by the oral appliance or if it was a preexisting problem prior to using MAD. The use of the MAD may cause transient TMD symptoms when the device is first worn, but usually these symptoms resolve within a few days. If those TMD problems become persistent, the dentist should start treatment of the TMD symptoms.[24]

1-3-1. Classification of TMD

TMDs are broken down into three general categories: masticatory muscle disorders, TMJ articular disorders, and inflammatory disorders. The status of the TMJs and musculature must be determined before treatment of OSA with an MAD.[24]

1-3-1-1. Masticatory Muscle Disorders

There are many factors that can affect masticatory muscles and cause different conditions such as: myalgia, myofascial pain, muscle trismus, and myositis. Myalgia is described as a dull, aching, and continuous pain associated with muscle function.[24] This condition can be caused by trauma, injuries, overuse, and tension.[24] Myofascial pain is defined as muscle pain associated with active or latent trigger points that radiate pain to remote sites such as adjacent muscle groups or non-muscle structures such as the TMJs, sinuses, or teeth.[24] Muscle trismus or splinting is a protective mechanism that occurs when the muscle fibers shorten and become painful as a protective mechanism limiting movement, or a response to trauma.[42] Myositis is an inflammatory disorder of the muscles caused by infection or trauma within the muscle tissue or by a noninfectious process induced by systemic disease such as polymyositis.[43]

1-3-2. TMJ Articular Disorders

Disc derangements are common in the general population, with prevalence estimates ranging from 40% to 75% of the population.[44] The temporomandibular disc becomes displaced due to different conditions including major trauma (such as fight, fall, sports injury, oral surgery, or motor vehicle accident), or excessive parafunctional activity (such as gum chewing, bruxism, bracing, or clenching).[45] Generalized disc ligament laxity may lead to early manifestation of changes seen in a developing systemic arthritic disease process, altering the condylar form and

allowing disc slippage.[45] The presence of joint noises such as clicking or crepitus should also have been determined, diagnosed, and noted in the chart before MAD therapy. Clicking sounds may indicate anterior disc displacement with reduction, whereas crepitus indicates degenerative changes of the condyles.[24]

The TMD mechanical problems are subcategorized as follows:

1. Disc displacement with reduction: the joint clicks
2. Disc displacement without reduction (close lock): the joint used to click but is now silent
3. Open dislocation
4. Open lock
5. Posterior disc displacement
6. Ankylosis.

1-3-2-1. Disc Displacement with Reduction: The Joint Clicks

It is not fully understood why disc slippage occurs but condylar remodeling or stress-induced alterations of the fibrocartilage lining of the joint may predispose the disc to slip forward and occasionally cause pain. In addition, clicks in the joint may not indicate displacement but can be caused by tearing or injury to the disc. Joint noises may also be caused by a stick-slip phenomenon, in which the articular surface of the joint is inadequately lubricated, causing the disc to briefly stick to the anterior surface of the eminence.[24]

1-3-2-2. Disc Displacement without Reduction with Limited Opening

Disc displacement without reduction and limited opening is an intracapsular biomechanical disorder involving the condyle-disc complex. In the closed mouth position, the

disc is in an anterior position relative to the condyle, and the disc does not reduce to its normal condylar position with opening of the mouth. Typically, there is no clicking sound associated with disc displacement without reduction, but it restricts the maximum assisted jaw opening including vertical incisal overlap to less than 40 mm.[22]

1-3-3. Inflammatory Joint Disorders

1-3-3-1. Arthralgia/Capsulitis

Inflammatory conditions of the TMJs are categorized as localized arthralgia (capsulitis), localized arthritis, and polyarthritis involving the TMJs. This is pain of joint origin or tenderness that is called arthralgia or capsulitis. The diagnosis of capsulitis is confirmed after tenderness and pain has been located with palpation of TMJ lateral pole. Arthralgia is used to describe palpable joint pain with no evidence of crepitus or osseous changes on the radiographs.[24] The most important cause of arthralgia is trauma, either from external injury or traumatic parafunction.[24]

1-3-3-2. Osteoarthritis

Osteoarthritis is defined as degenerative condition of the joint. TMJ osteoarthritis is one of the joint problems reported to occur in the population being treated for OSA. The prevalence of osteoarthritis increases with age, and this is the same age group in which the prevalence of OSA is more likely to occur.[46]

In order to diagnose osteoarthritis, all following criteria should be positive: (1) palpable joint pain, (2) crepitus, and (3) radiological evidence of joint degeneration. Most arthritic TMJs have crepitant noises with joint movement. The presence of osteoarthritis needs to be diagnosed and documented in the initial examination. Moreover, degenerative changes and crepitus may be present without pain. Detecting degenerative changes are important in the treatment of OSA with

MAD because these conditions could make the TMJ more susceptible to abnormal stresses with the use of a MAD.[24]

1-3-3-3. Rheumatoid Arthritis

Rheumatoid arthritis is an autoimmune disorder that causes joint inflammation resulting in pain or destruction of the patient's own tissues. It starts as a generalized inflammatory soft tissue disease. In the early stages of the disease, it may not demonstrate any evidence of bony degeneration by imaging. This condition may present in various forms from no swelling and symptoms to only pain to only swelling.[24]

1-4. Adverse Effects of MAD

1-4-1. Muscle and Joint Tenderness

OSA therapy with MADs may be associated with myalgia or artheralgia.[24] The most common complaint after patients start using MADs is jaw tenderness. It is important to document preexisting muscle or joint tenderness prior to delivery of the device. Pain problems including a headache history should be explored in the face-to-face history. The physical examination should include a neurologic examination, evaluation of jaw function, and a palpation examination of the TMJs and cervical and masticatory muscles. Usually, OSA patients who receive the MAD complain about morning headache. However, muscle pain and most particularly myofascial pain (MFP) are also frequently associated with or cause headache. A thorough palpation examination, performed as part of the initial examination, is crucial in order to document preexisting myalgia/MFP and/or associated headache.[24]

TMJ tenderness can occur with use of MADs. When a MAD appliance holds the jaw in a protrusive position during the night, the TMJ may become inflamed and tender to palpation. The

general term for this condition is capsulitis. Preexisting capsulitis should have been identified before delivery of the appliance, and a definitive diagnosis made at baseline.[47]

1-4-2. Bite Changes

Some articles reported the association of bite changes with using MADs.[48,49] Commonly, transitional occlusal changes are observed in the morning when the device is removed, and in order to manage this side effect, patients are required to perform instructed physical exercises to bring the lower jaw to its regular habitual position and reestablish the occlusal contacts. However, evidence is mounting that long-term use of MADs may cause permanent changes in the occlusal relationship. Although patients are given instructions regarding the necessity of performing exercises to bring the posterior teeth back into the contact, noncompliance with those exercises by some patients may lead to permanent bite changes.[50,51] Furthermore, changes in the relationship of the maxilla to the mandible have also been reported.[52] These changes represent a substantial shift in the jaw relationship, especially if the patient had an initial class II malocclusions due to excessive overjet, or a camouflaged class III malocclusions in which the anterior incisors are in an edge-to-edge relationship with no maxillary teeth interference during protrusion beyond the edge-to-edge relationship. Although dentofacial and occlusal changes can be attributed to use of a MAD, a recent study reported that long-term use of the PAP (positive airway pressure) mask without an MAD could also lead to dentofacial changes, due to pressure exerted on the teeth and jaw by the mask.[53]

1-5. Epidemiology of TMD Symptoms and Bite Changes Associated with MAD use

Some studies report that TMD prevalence is not generally increased with use of MADs in the treatment of OSA.[54,55] However, others have reported that between 10% to 13% of patients using MAD therapy could not use their appliance due to development of TMD symptoms.[56,57]

1-6. TMD Examination and Diagnosis

There are several components of the physical examination done to assess patient with sleep apnea.[24] The overall examination has five parts as following: (1) the chief complaint and history of present illness, (2) the cranial nerve examination, (3) the stomatognathic examination, (4) the palpation examination, and (5) other warranted examinations and tests, for example, radiological assessment of the joints.[24]

1-7. Treating TMD Problems During MAD Therapy for OSA

Treatment of TMD is provided based on the type of problem that the patient developed during MAD therapy. In addition to joint pain, myalgia and myofascial pain are the most common side effects of TMDs associated with MAD. As discussed earlier, it is important to distinguish between the two disorders in the examination by looking for referral pain and radiation of tenderness by systematically palpating for tender areas in the muscles.

In addition, changes in occlusion that may occur during the MAD therapy need to be managed early in the MAD treatment because changes that have been ignored or unevaluated for weeks to months may become irreversible and cannot be managed with simple exercises. Therefore, more advanced dental treatments including dental restorative procedures or orthodontics may be needed to resolve the problem.[58,59]

1-7-1. Anterior Disc Displacement with Reduction (The Clicking Joint)

The presence of a click should have been determined and documented before treatment with an MAD. TMJ clicks may occur with anterior disc displacement. Clicks do not usually happen or incidence increase with the use of an MAD because the mandibular advancement generally reduces the incidence of the disc displacement anteriorly and is considered a treatment option for TMJ clicking if it is due to anterior disc displacement.[25] Moreover, mandibular advancement and irritation of the appliance may exacerbate bruxism during the night with consequent development of clicking due to increased working of the joints.[24]

1-7-2. Anterior Disc Displacement Without Reduction (The Locked Joint)

Clinicians should document the patient's passive opening before delivery of MAD and on each follow-up visit because limited passive opening less than 40 mm could be a sign of anterior disc displacement without reduction or muscle pain. Patients who have developed a closed lock condition should be seen by an orofacial pain specialist or an oral surgeon who has training to manage this situation.[24]

1-7-3. Myogenous Pain

Masticatory and cervical muscle tenderness is a very common problem observed with TMD. Research shows that it can be managed effectively by daily physical exercises, physical medicine techniques, and possibly medication management to optimize the treatment. If the patient develops muscle tenderness during MAD therapy, the clinician should instruct the patient to perform stretching of the masticatory muscles during the day.[24]

In addition, specific physical exercises are needed to reestablish the patient's jaw relationship and bring back the posterior teeth to contact if that is part of the problem. Patients

should perform these exercises after removal of the MAD in the morning and continue these exercises until posterior tooth-to-tooth contacts are reestablished. The patient should be instructed to stretch the jaw by placing the tongue on the palate behind the upper front teeth and stretching open as far as they can stretch without pulling the tongue off of the palate. The stretch should be held for six seconds, repeated six times and the process is repeated six times per day. This exercise stretches the masseter, medial pterygoid, and temporalis muscles. If the muscles are severely tender, the patient should use moist heat for five minutes before the stretching exercises and then ice to cool down the muscles for five minutes after the stretching.[24]

The patient should also be instructed to keep the jaw in a relaxed resting position during the day. This practice helps to decrease daytime clenching that can cause pain in muscles and TMJ. The patient is instructed to place the tongue on the palate similar to the jaw position instructed for the stretch, but the lips are brought together and the teeth kept slightly apart. The patient is also instructed to breathe through the nose in this position. This rest position relaxes and decreases masseter, medial pterygoid, and temporalis muscle activity.[24]

1-8. Physical Exercises Protocol for Patients Receiving MAD

Perez et al.[25] instructed their patients to perform a jaw repositioning exercise in the morning following removal of the MAD. The exercise included placing of a plastic two millimeters thick bite wafer between the maxillary and mandibular incisors. The patient was then instructed to protrude the mandible as far as possible, then to retrude the mandible as far as possible, and while in the maximally retruded position, the patient should try to clench his/her back teeth for five seconds. This cycle is to be repeated six times. These instructions should be reinforced and reviewed at each follow-up appointment as needed.

Cunali et al.[60] instructed their patients to exercise twice a day, in three sets of five repetitions of each movement, prior to and after removal of the MAD. These mandibular exercises, have proven to be efficient and effective in the treatment of TMD. The exercise protocol developed by Cunali et al.[60] was maintaining the tongue in contact with the palate, followed by a sequence of lateral left–right movement of the mandible against light-hand resistance. This type of movement was used with the intent to exercise the lateral pterygoid muscles and the TMJ.

In addition, Cunali et al.[60] instructed their patients to open the mouth against light resistance of the hand, followed by a maximum opening of the mouth assisted by the fingers, with the intent of stretching the temporal and masseter muscles. They reported that mandibular exercises help OSA patients with TMD to manage their TMD symptoms; exercises were also found to be effective in increasing MAD compliance and producing a significant improvement in the quality of life and quality of sleep.[60]

The isometric and passive jaw stretching exercises reported by Sheats et al.[61] consisted of instructing patients to move the mandible against resistance both vertically and laterally, and to stretch the mandibular range of motion assisted by the fingers, in order to decrease the level of discomfort of the masticatory muscles and consequently improve adherence to MAD usage.[61]

1-9. Study Significance

Even though some studies have reported the side effects of MADs for the treatment of OSA, few have reported the prevalence of TMD in OSA patients at baseline and development or

aggravation of TMD during OSA treatment by MAD. There are a very few articles that investigated the effectiveness of physical exercises on TMD during MAD therapy.

1-10. Hypothesis

TMD prevalence is significantly higher in OSA patients. Patients receiving MAD would not develop TMD and/or posterior open bite if they were compliant with the daily physical exercise instructions.

1-11. Null Hypothesis

OSA patients do not have statistically higher incidence of TMD. Patients who use MAD may develop TMD and posterior open bite regardless of adherence to daily physical exercises.

1-12. Study Aims

The purpose of this retroactive study was to determine the prevalence of pain associated with temporomandibular disorders (TMD) in obstructive sleep apnea (OSA) patients referred to the UCLA Orofacial pain clinic for oral sleep appliance therapy between June 2016 to June 2019. Additionally, patients who were treated with a MAD were assessed to determine variations in the occurrence of temporomandibular disorders (TMDs) and development or recurrence of pain associated with the temporomandibular joit and masticatory muscles. This was accomplished by reviewing existing UCLA School of Dentistry patients' electronic records.

Aim 1: To determine the proportion of OSA patients having TMD symptoms prior to receiving an oral appliance.

Aim 2: To determine the overall prevalence of TMD problems during MAD therapy. To explore prevalence of pain in TMJ and/or masticatory muscle during MAD therapy.

Aim 3: To determine the proportion of patients developing de novo TMD after receiving the oral appliance, in order to explore the effects of MAD on TMD. To determine the effectiveness of instructed daily physical exercise in management of painful TMD during MAD therapy.

Aim 4: To evaluate the incidence and prevalence of posterior open bite associated with the MAD, and the effectiveness of daily physical exercise instructions to prevent posterior open bite.

2. Materials and Methods

This is a retrospective study evaluating the prevalence of TMD and painful TMD in OSA patients prior to and during therapy with an intra-oral mandibular advancement appliance from the UCLA Orofacial Pain Center. This study also investigates the effectiveness of daily physical medicine exercises on management of painful TMD and POB during MAD therapy. Additionally, efficacy of MAD on AHI reduction was evaluated. This study was approved by the UCLA Institutional Review Board (UCLA IRB#19-001388).

2-1. Evaluation of Comorbidity of TMD and OSA

2-1-1. Subject Selection:

A retrospective analysis of data from 195 patients with a diagnosis of OSA was obtained from the UCLA Orofacial Pain Center for the time period June 2016 to June 2019. The study group inclusion criteria for this study group were as follows: subjects over the age of 20 years who presented with an initial $5 \leq AHI < 30$ as determined by polysomnographic studies (PSGs). Standard PSGs were performed as requested by the referring physician. The PSGs evaluated

sleep stages through electroencephalogram, electrooculogram, and submental electromyogram. Patients were required to have at least eight healthy teeth on each jaw and no major periodontal problem. Exclusion criteria were edentulism (in one or both jaws), trauma to the face and/or head within six months, arthritic disease of the TM joint, neuropathy, epilepsy, intraoral lesions, or severe OSA (AHI ≥ 30 events/h of sleep).

One hundred and fifty-five patients of the 195 screened patients met these criteria, while 40 OSA patients were excluded from the study group because their initial sleep study test was missing or they presented with AHI ≥30 (severe OSA). The remaining 155 patients with mild to moderate OSA who were included in the study group were 59±14 years of age (range 21-87). The study group contained 81 male subjects and 74 female subjects (male: 53%, Female: 47%) with a BMI of 27.7±6.3 kg/m^2.

As a control group, the data of 400 new patients at the UCLA School of Dentistry's general dental clinic were obtained for the time period June 2016 to June 2019. Control group inclusion criteria were as follows: a minimum age of 20 years, at least eight healthy teeth on each jaw. Exclusion criteria for the control group were as follows: edentulism (in one or both jaws), trauma to the face and/or head within six months, arthritic disease of the TMJ's, neuropathy, epilepsy, intraoral lesions, and odontalgia (toothache).

The total of 188 patients who met the criteria of the control group were 58±14 years of age (range 21-84). The control group contained 98 males (52%) and 90 females (48%) with a BMI of 27.5±5 kg/m^2.The patient demographics are summarized in Table 1.

Table 1: Patient demographics

Table 1	Study Group	Control Group
Number of patients,	155	188
Age (years)	59± 14	58±14
Male/female, N	81/74 (M: 53%- F: 47%)	98/90 (M: 52%- F:48%)
Apnea Hypopnea Index (AHI), (N/h)	11.87±6.23 Mild OSA: 107 Pt (69%) Moderate OSA: 48 Pt (31%)	N/A
Body Mass Index (BMI kg/m²)	27.7± 6.3	27.5 ±5
Tried C-PAP	77 (50%)	N/A

2-1-2. Clinical Examination:

All subjects were examined by calibrated examiners following an American Academy of Orofacial Pain standardized protocol [22]. To detect myalgia, masticatory muscles were palpated with a force between 0.5 and four kg/cm^2, and the force was maintained for about 5 to 20 seconds. A force range between 0.5 to 1 kg/cm^2 was used for TMJ assessment to detect

arthralgia. Painful TMD was defined as pain, as indicated by the patient, in the masticatory musculature or the temporomandibular joints when palpating these structures. Joint clicks assessment was performed by palpation and using a stethoscope for auscultation, and sounds were detected on repetitive opening and closing of the jaw. Mouth opening was measured between the central incisors using a ruler.

2-2. Painful TMD During MAD Therapy

2-2-1. Subject Selection:

OSA patient data were reviewed for evaluation of painful TMD during MAD therapy. Inclusion criteria for this study group were as follows: subjects that had received an MAD device, wore the device at least five hours a night and five nights a week, and had at least one follow-up after the delivery of appliance. Since nonpainful joint click did not necessarily need to be treated, patients with nonpainful click were excluded from this category. The data used for this observational study were obtained from chart entries made after the patient received an MAD device.

Among the 155 subjects selected above as the study group (3.1.1) a total of 104 subjects met the criteria for “painful TMD during MAD therapy”. The 51 remaining subjects either did not receive an MAD appliance for a variety of reasons such as financial difficulties or they did not return for the follow-up visits and were therefore excluded from the analysis of painful TMD during MAD therapy.

Patients were treated with different intra-oral MAD including: Adjustable Herbst Appliance, Adjustable Dorsal Appliance, EMA (Elastic Mandibular Advancement), or a Good Air Oral Appliance. In the delivery visit, all types of MADs were advanced at 60-70% of

patients' protrusive capacity as determined with a George Gauge (Peter T. George, Honolulu, Hawaii) during bite registration. In the follow-up visits, more advancements would be added to the MADs according to patients' signs and symptoms such as sleepiness and snoring.

2-2-2. Symptoms of Painful TMD and Posterior Open Bite (POB)

The presence of signs and symptoms of TMD and POB were evaluated before delivery of the MAD at baseline, and any follow-up visits after delivery of the MAD appliance. Examinations were standardized and performed by calibrated examiners. All patients were instructed in simple jaw position correction exercises and physical medicine exercises for painful TMD problems. At each visit, by using 12-μm shim stock foil, the presence of a posterior open bite (POB) was determined and monitored. POB was defined as no occlusal contact between premolars and molars of the opposite jaws when the patients were holding their jaws in maximum intercuspation position. This was further confirmed by sliding a shim stock through the interocclusal area of the posterior teeth. Bite changes were considered transient if patients reported it lasted for less than 12 hours.

At every visit, the patients were asked to demonstrate the jaw position correction exercise and physical exercises for painful TMD to evaluate the patients' compliance with the physical exercise protocol. If a patient was not able to demonstrate the physical exercises correctly, the examiner would review all exercises with the patient again as mentioned in the introduction section. Patients who presented with POB at baseline were eliminated from the analysis as this was not a consequence of wearing the MAD.

2-2-3. Effectiveness of MAD

OSA treatment success and efficacy of MAD is considered as a percentage reduction in AHI of more than 50%, from the baseline. In order to compare the baseline and follow-up AHI, patients' data were reviewed to retrieve follow-up PSG data. Due to the high cost of PSG testing and difficulty of overnight PSG test in the sleep lab, only 16 out of 104 patients who received MAD had follow-up PSG with MAD.

2-3. Statistical Analysis

Demographic variables such as age, gender, and BMI were analyzed with independent-samples t-test between study and control groups. The Chi-square test was applied to compare prevalence of TMD and painful TMD at baseline between study group and control group. The Chi-square test was also used to determine the effectiveness of instructed daily physical medicine exercises to prevent posterior open bite and to manage painful TMD during MAD therapy.

Archival data of 104 OSA patients wearing MADs were included to determine the effect of MADs on painful TMD and POB. Wilcoxon Signed Ranks Test was employed to compare the signs and symptoms of painful TMD at baseline with follow-up visits.

Statistical analysis was performed using the IBM Statistical Package for Social Sciences (SPSS version 26.0) for windows, and Microsoft Excel software were used for statistical analysis and generation of figures and graphs.

3. Results

The aim of this study was to present the incidence and prevalence of TMD and painful TMD in OSA patients in comparison to a control group not suffering from these conditions, and to evaluate the effect of MADs on TMD. The incidence and prevalence of POB during MAD

treatment for OSA patients were also examined. Furthermore, this study tried to assess the role of physical medicine exercises to manage painful TMD and POB during MAD treatment. At their follow-up visits, 91.2% of the patients reported that they were wearing their appliance more than five hours a night, and at least for five nights a week. Forty-seven patients (45%) used a hard Modified Herbst appliance, 43 patients (41%) used the Adjustable Dorsal appliance, and 14 patients (14%) received other appliances such as GoodAir or EMA (Figure 1). Since this is a retrospective sturdy and data were extracted from existing medical records, patients' charts evaluated in this study presented variations in the amount of data and examination executed. Therefore, missing data will be reflected in an uneven amount of information for each study aim. Consequently, not all denominators represent the total amount of patients in each particular aim. One-hundred-fifty-five OSA patients' medical records were reviewed at baseline. There was no statistically significant difference in age, gender and BMI between the study group and the control group (Table 1).

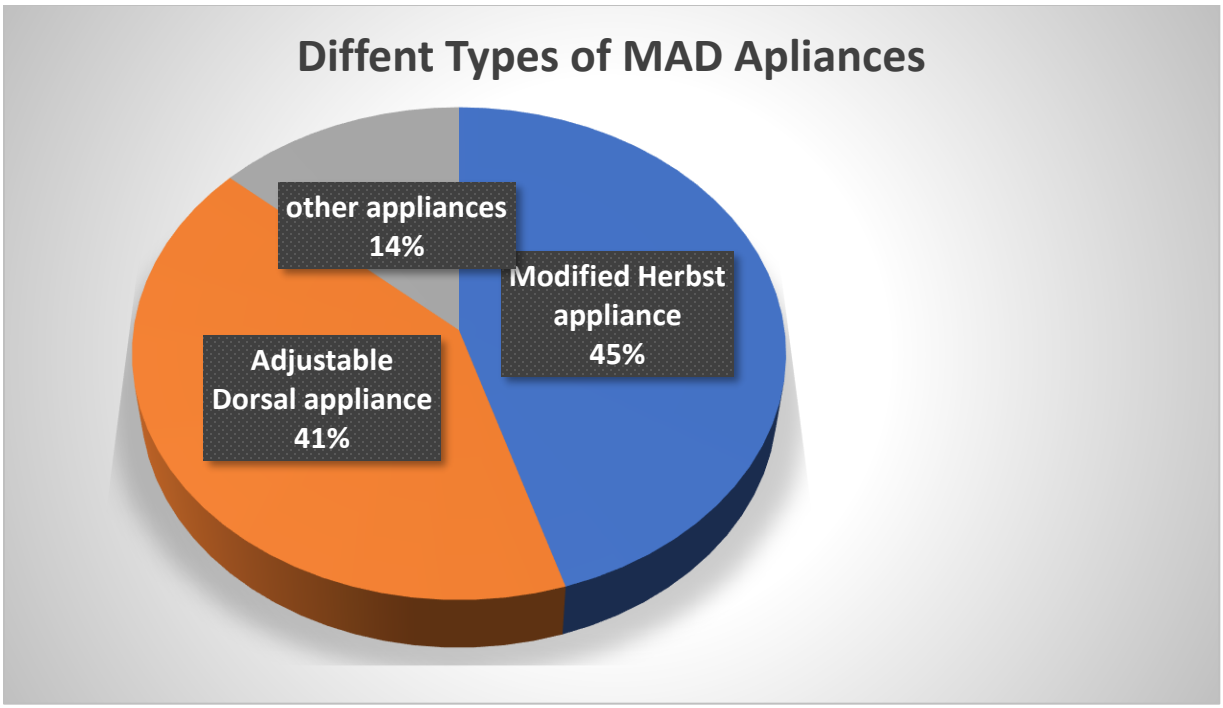

Figure 1: Distribution of different MAD appliance types that patients received in this study.

3-1. Prevalence of TMD and Painful TMD at Baseline

At the baseline visit, TMD symptoms were present in 146 patients among the 155 qualifying OSA patients (94 %). All of the 146 patients included in the study group had painful TMD. Fifty-three of these patients only had myalgia, while three only had TMJ pain (Arthralgia).

In the control group 53 of the 188 patients had TMD (28%), and 10 of the 188 patients had painful TMD. Five patients only had myalgia, and five patients had both arthralgia and myalgia. None of the control group patients had solely TMJ pain.

The Chi-squared test was used to compare prevalence of TMD and painful TMD between the study group and the control group, and it showed that the OSA patients (study group) had

statistically significant higher levels of TMD and painful TMD compared to the control group ($p < 0.05$). Five percent of the control group showed painful TMD and 94% of the study group had painful TMD. (Figure 2)

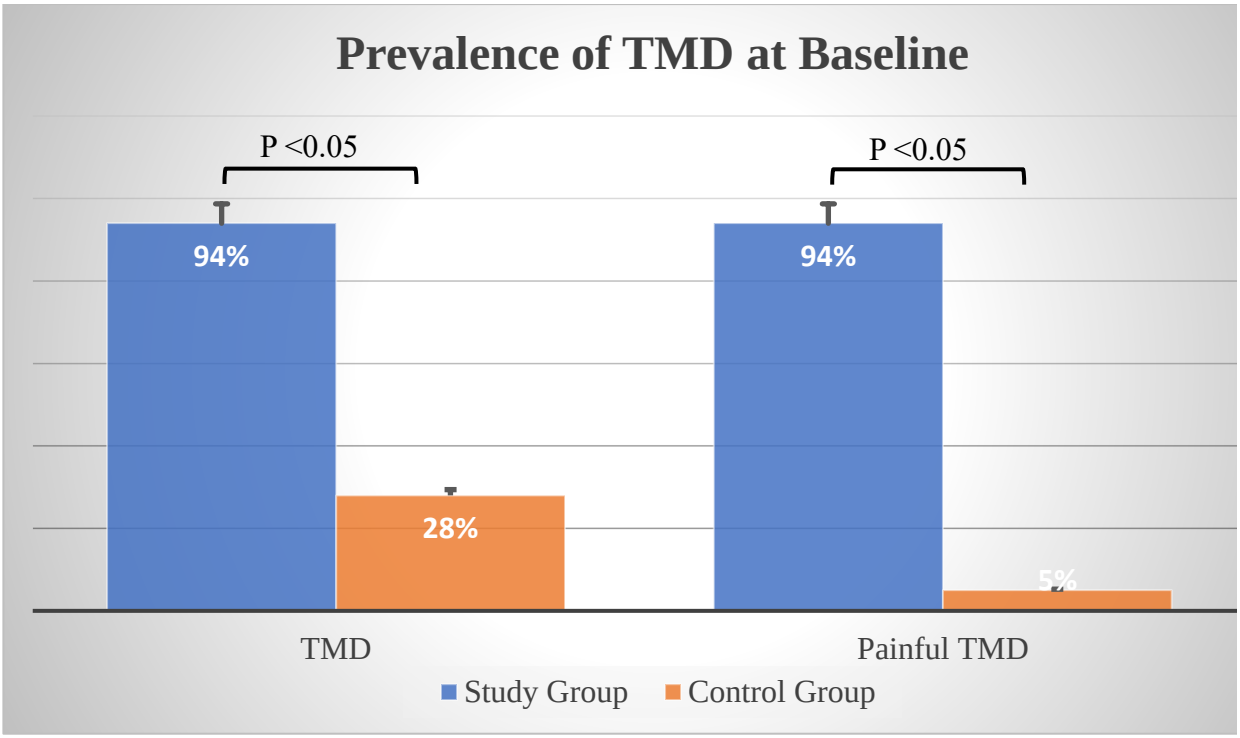

Figure 2: Comparison of TMD and painful TMD between control group and study group at baseline. TMD and painful TMD were significantly higher in the OSA patients ($p < 0.05$).

3-2. Prevalence of Painful TMD During MAD Therapy

Due to dropouts at follow-up visit, the patient number decreased from the initially included 155 TMD patients to 104. Twenty-four of 51 drop out patients did not return for follow-up visit and 27 did not receive a MAD. Therefore, 104 patients met the criteria for inclusion in the study group after receiving MAD. The time interval to the follow up visit was 8±5 months.

This study also determined the prevalence of painful TMD during MAD therapy in both patients with preexisting TMD problems as well as those who developed painful TMD signs and symptoms during MAD therapy. Sixty-nine patients (66%) of OSA patients who received MAD did not experienced painful TMD during MAD therapy. Thirty-five of the 104 patients in the study group experienced painful TMD during MAD therapy. Twenty four of these patients had myalgia (23%) only, two patients (2%) had TMJ pain (arthralgia) only, and nine patients (9%) had both myalgia and arthralgia (TMJ pain). (Figure 3)

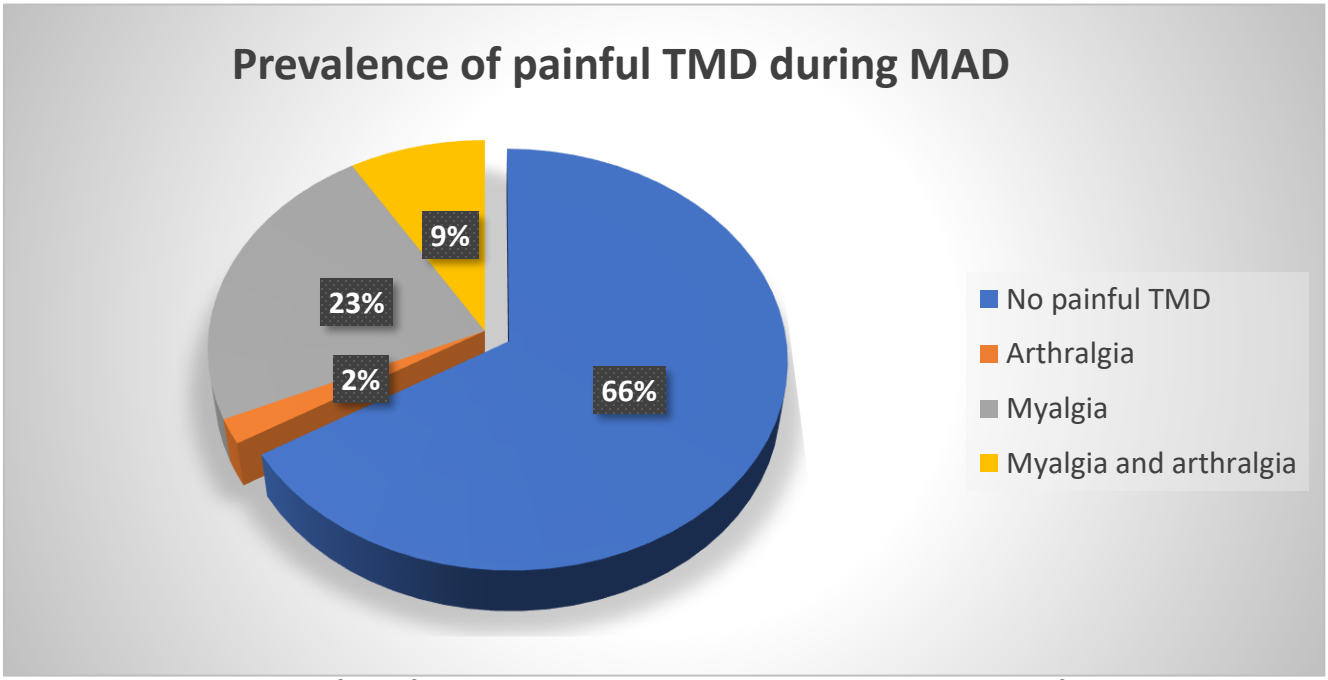

Figure 3: Prevalence of painful TMD during MAD therapy. Sixty six percent of patients were pain free during MAD therapy.

Recurrence of pain in TMJ and/or masticatory muscles after receiving an MAD, and effectiveness of daily physical medicine exercise instructions to manage painful TMD signs and symptoms were explored in order to evaluate the impact of the MAD on painful TMD. Prior to receiving MAD therapy, 98 of the 104 patients had painful TMD. The number of patients with painful TMD reduced to 34 patients after receiving MAD. Only two patients did not have painful TMD before MAD and developed painful TMD (solely myalgia) after receiving their MAD. There were only two patients that did not have TMJ pain before MAD and developed TMJ pain after receiving their MAD. Wilcoxon Signed Ranks Test showed a statistically significant reduction in painful TMD after receiving MAD therapy. (Figure 4)

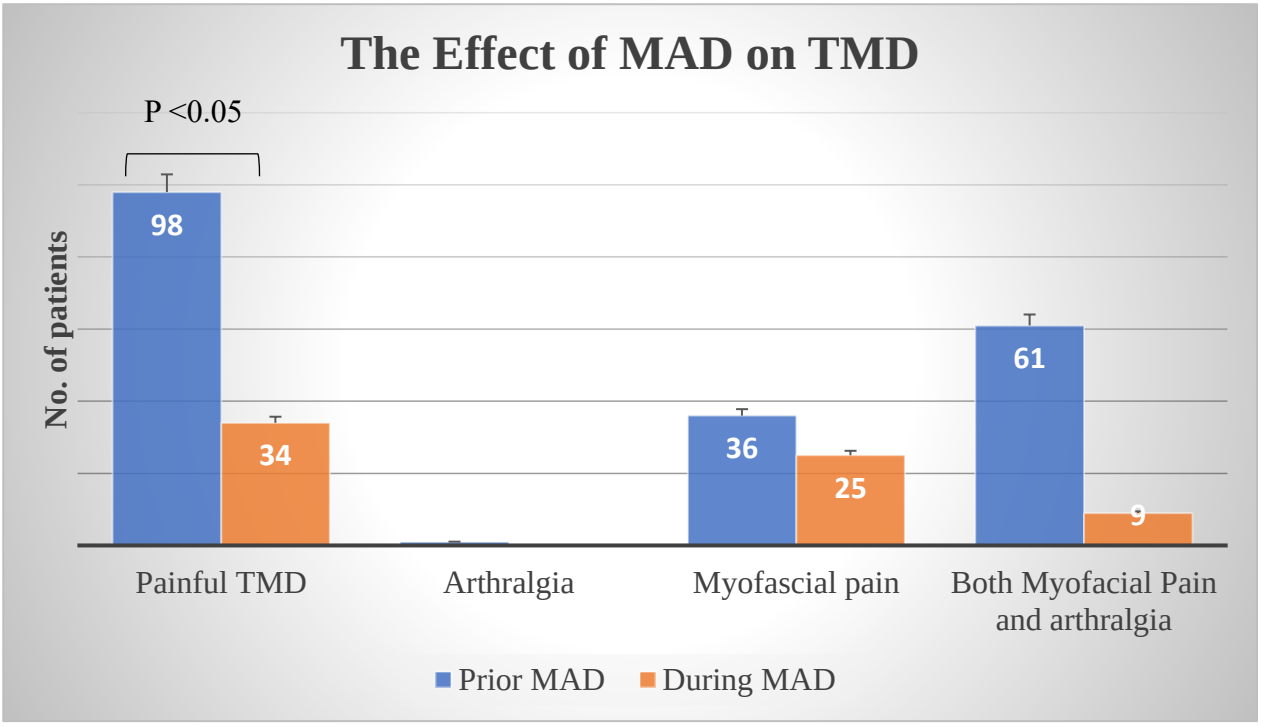

Figure 4: The effect of MAD on painful TMD. Significant reduction of painful TMD during MAD therapy ($p<0.05$).

In order to study the effectiveness of physical exercises on painful TMD during MAD therapy, patient charts were reviewed. Three of the 104 patients were excluded from this study group due to lack of information about their compliance with daily physical exercises. The information of 101 patient charts were included in this part of study. Thirty-four of the 101 patients that received a MAD were not compliant with the daily physical medicine exercise instructions (physical medicine protocol), and 17 of these 34 patients had painful TMD. Sixty-seven of the 101 patients followed the instructed daily exercises, and only 19 of these 67 had painful TMD during MAD therapy. Chi-square test showed that practicing daily physical medicine exercises as instructed had a statistically significant effect in reduction of painful TMD during MAD therapy (P= 0.03) ($p < 0.05$) (Figure 5).

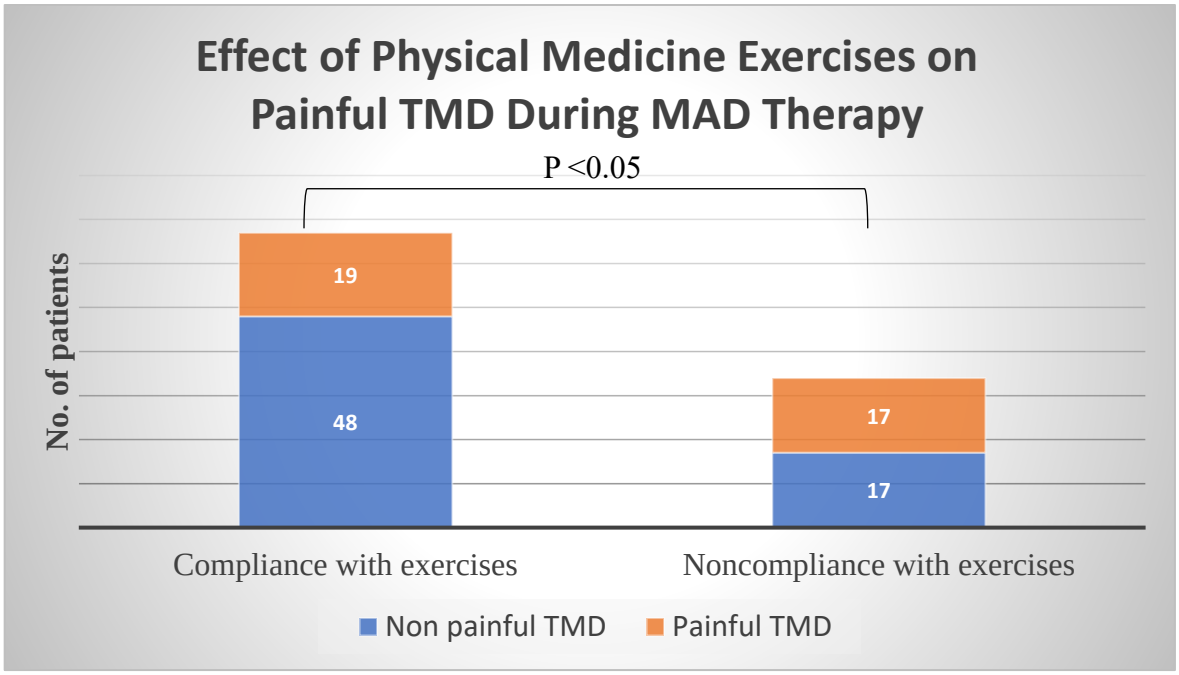

Figure 5: The effect of physical exercises on painful TMD during MAD therapy. Significant effect of practicing daily exercises on reduction of painful TMD during MAD therapy * (P= 0.03) ($p < 0.05$).

Next, the incidence and prevalence of POB associated with MAD, and the effectiveness of daily physical medicine exercise instructions to prevent POB was evaluated. Twelve of the 104 patients developed transient posterior open bite during MAD therapy (11.5%). Six of 67 patients that were compliant with the instructed daily exercises still developed posterior open bite during MAD treatment (9%). Six of the 34 patients who were not compliant with the daily exercise instructions developed posterior open bite during MAD treatment (18%) (Figure 6).

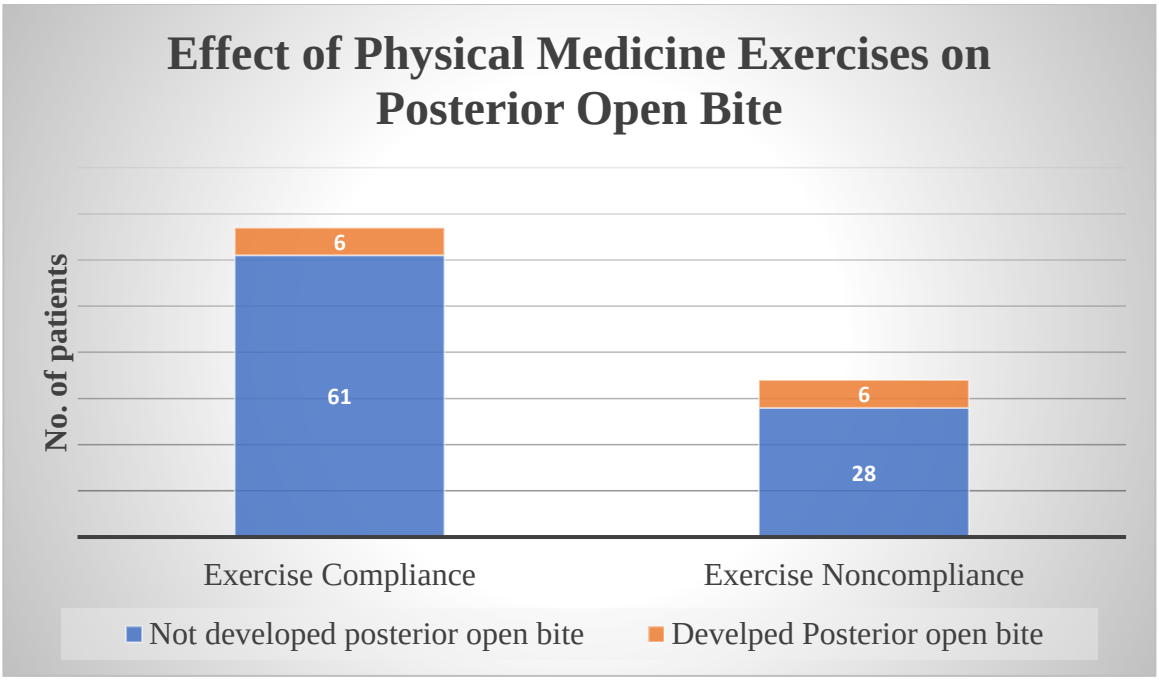

Figure 6: The effect of physical medicine exercises on posterior open bite during MAD therapy

3-3. Effectiveness of MAD Therapy

For evaluation of the effectiveness of MAD therapy, follow-up PSG with MAD in place were available for only 16 patients as already explained above. These limited data were used to

detect the efficacy of MAD in reduction of AHI. At follow-up PSG, across all 16 patients, 75% of patients achieved a 50% AHI reduction compared to their respective baseline AHI by using MAD. The mean percentile of AHI reduction was 65%± 32. (Figure 7 and 8)

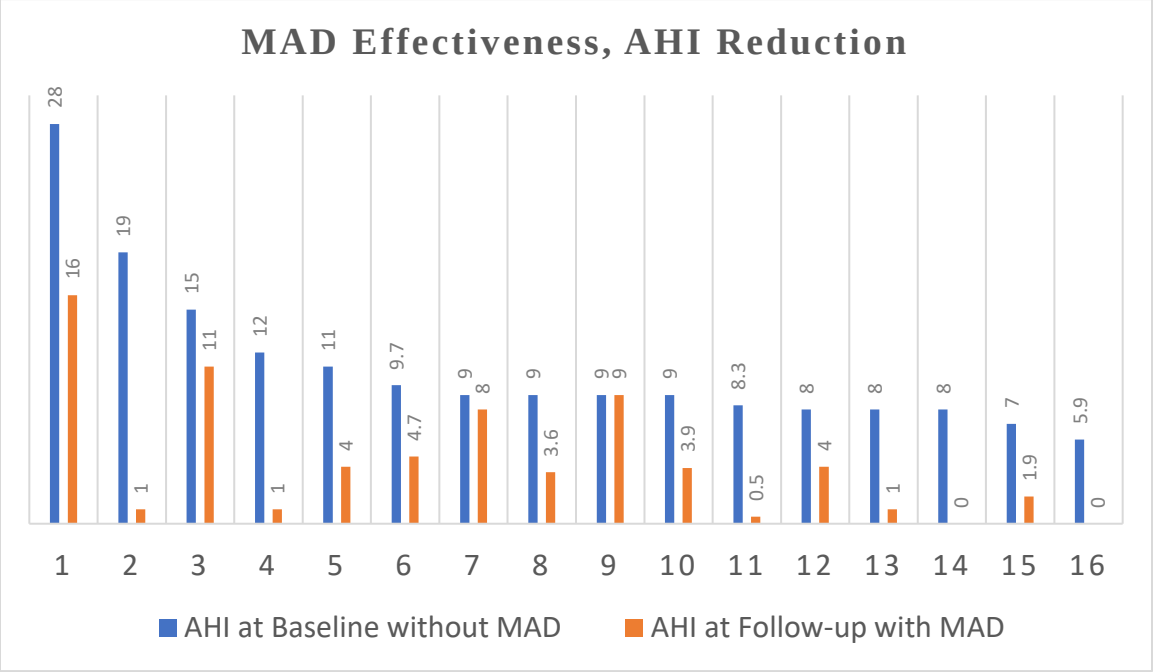

Figure 7: Comparison of AHI without MAD at baseline and AHI at follow-up with MAD.(n=16)

50% AHI reduction in 75% of patients by MAD therapy.

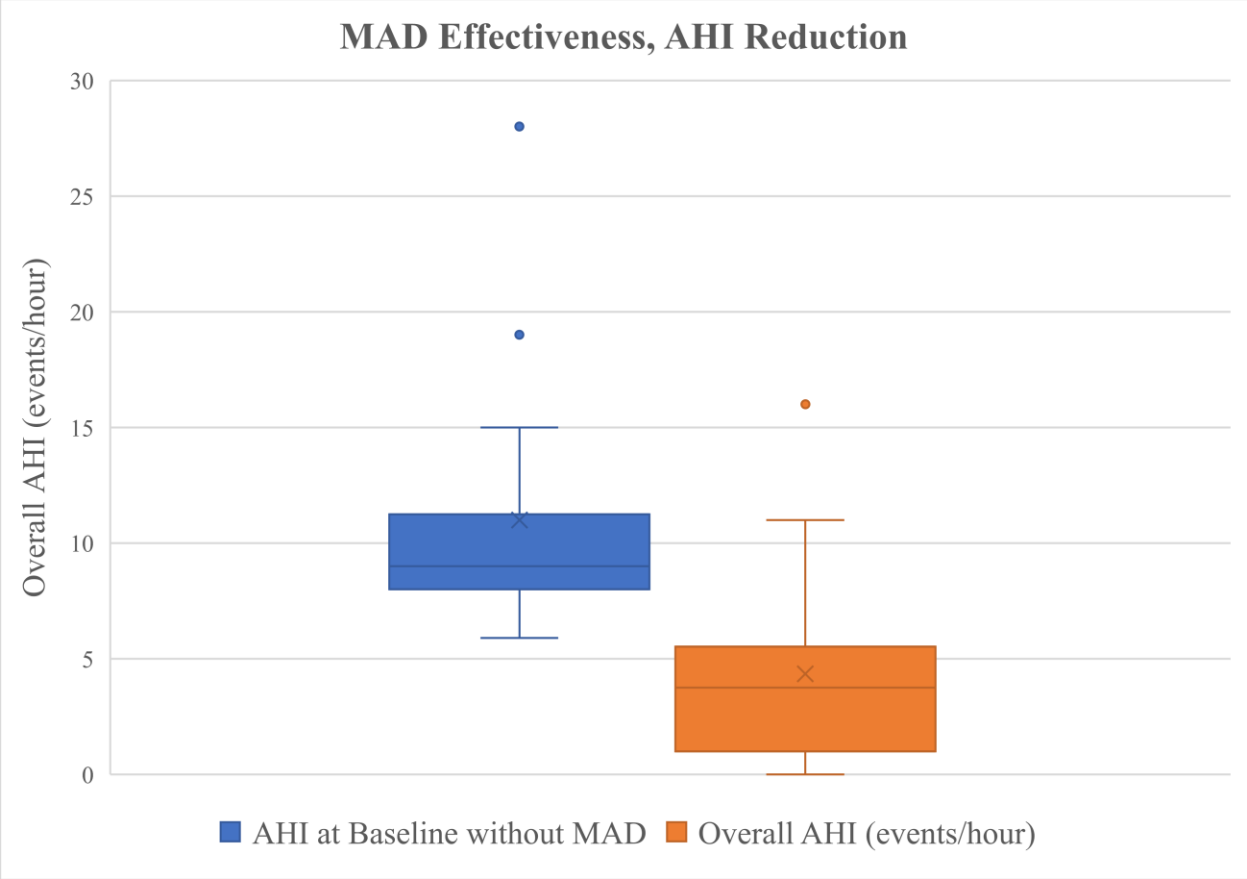

Figure 8: Box plots for MAD effectiveness. Comparing baseline AHI and follow-up AHI with MAD in place. The upper and lower margins represent the 75th and 25th percentiles. The mean is denoted by the "X" marker in the chart and represents the average of all the data points, and the median values by the horizontal line. Whiskers represent the maximum value (top) and the minimum value (bottom) of the dataset. Outliers are represented by a point.

4. Discussion

The results of this study showed that OSA patients had a significantly higher pre-treatment prevalence of TMD (94%) compared to the control group (28%) (Figure 2). Additionally, all of the OSA patients who had TMD showed painful symptoms, while only a

fifth of the TMD patient in the control group presented with painful TMD. Patients with OSA need to posture their mandible forward and hold their mouth open during sleep in order to maintain a patent airway. This constant strain on the muscles of mastication, especially the lateral pterygoid in translating the condyle forward in the fossa, is most likely the cause of TMD during MAD treatment.[62] Only a few studies investigated the prevalence of TMD in OSA patients and showed that OSA has a significant correlation with TMD, [25,62,63] which is consistent with the findings of this study that showed higher prevalence of TMD in the OSA patients.

Due to the high prevalence of TMD in OSA patients, Merrill et al.[24] suggested that a thorough head and neck examination should be performed before initiating MAD therapy in order to assess and document joint dysfunction, pain in joints or muscles, and bite discrepancies. All signs and symptoms of TMD should be discussed with the patient, and if there is any indication, TMD should be managed prior to initiating OSA therapy with a MAD.[24] Cunali et al.[63] also suggested that the high prevalence of TMD in OSA patients, referred for oral appliance therapy, indicates that OSA patients require specific TMD evaluation at the baseline.[63] Clark et al.[64] strongly advised when an OSA patient is referred to a dental practitioner, careful clinical examination is necessary. In the initial examination, clinicians should document range of motion of the jaw, including active maximum mouth opening, right and left lateral and protrusive jaw movement and indicate any pain or restriction during function. In addition, to detect any TMJ problems, auscultation and palpation of the TMJ for evidence of derangement or degenerative sounds needs to be conducted. Careful palpation of the right and left masseter, temporalis and TMJ capsule for tenderness needs to be performed and documented to record any preexisting TMD. Therefore, high prevalence of TMD in OSA patients indicates that the clinician providing

MAD therapy should have enough training and background for assessment, documentation, and management of TMD prior to administering the therapy.

There is controversy surrounding oral appliance contraindications and adverse effects of its use to treat OSA patients who have TMDs. Some articles studied the side effects of MADs, and a few studies reported TMD as the side effects of MAD usage. Reported incidence of TMD during MAD therapy ranges from 10% to 77% [64,65,66,67,68]; however, those studies reported that TMD symptoms were not clinically significant. Others have reported that due to development of TMD related to MAD therapy, OSA patients became noncompliant with MAD usage. As a result, those studies have contraindicated the MAD therapy for OSA patients when TMDs are present.[69] These studies probably concluded that the TMD was caused by the MAD appliance, since signs and symptoms of TMD were observed during MAD therapy.[55,69,64] Such conclusions, however, have been made in the absence of reproducible, systematic diagnostic criteria for TMD, and those studies did not consider the role of proper management of TMD prior to and during MAD therapy including instructed physical medicine exercises that can effectively manage TMD. In contrast, Cunali et al.[60] believe that there is no contraindication for MAD therapy in OSA patients who have TMD, and that those patients are still eligible for MAD therapy. The present study showed that the majority (66%) of OSA patients that received MAD did not experience any painful TMD during MAD therapy (Figure 3). Furthermore, adherence to daily physical medicine exercise instructions had a significantly positive impact on management of TMD prior to and during MAD therapy (Figure 5). This is consistent with findings by Cunali et al.[60] who also reported that mandibular exercises enable OSA patients with TMD to use MAD. They found that physical medicine exercises were effective in reducing pain, increasing MAD

compliance, and producing a significant improvement in the quality of life and quality of sleep.[60,51]

Increased occurrences of TMD signs and symptoms generally are not associated with use of MADs in the treatment of OSA. Perez et al.[25] reported that a reduction in joint clicks as well as painful TMDs were observed during MAD therapy as a result of mandibular anterior positioning. The present study's findings confirm that there was a significant reduction in painful TMD after receiving MAD (Figure 4). Therefore, daily physical medicine exercises are an effective tool to manage TMD prior to and during MAD therapy.

The development of POB is another possible side effect of using MADs. Perez et al.[25] reported that POB developed with the use of the MAD. Even though the initial incidence of POB was only 5.4%, prevalence of POB increased with long term usage of MADs. They assumed that POB development was due to a transient shortening or contracture of the inferior portion of the lateral pterygoid muscle. When this muscle is not stimulated to return to its normal length, it may develop a myofibrotic contracture that decreases its ability to return to its habitual length. This present study found that the incidence of POB was 11.5%; however, daily physical exercises including lateral pterygoid muscle stretches reduced the incidence and prevalence of POB during MAD therapy (Figure 6). These exercises should start after MAD removal in the morning by trying to reestablish tooth contact in the occlusion and accelerate the repositioning of the mandible to its normal position.

To assess the efficacy of MAD on AHI reduction in OSA patients, Vecchierini et al.[70] compared baseline and follow-up PSGs and found that 60% of their patients had a more than

50% decrease in AHI. Dieltjens et al.[71] also investigated the efficacy of MAD and reported 68.8% AHI reduction in their patients. The results presented here showed that 75% of patients had a more than 50% AHI reduction by MAD therapy (Figure 7), which is consistent with other studies' findings.

Lawrence et al.[72] recommended that once optimal placement and titration of the MAD is achieved, the clinician should establish regular every six months follow-up visits for the first year, and at least an annual visit thereafter. Compliance with follow-up visits at regular intervals was one of the limitations in the present study.

Among other limitations, the follow-up PSG data with oral appliances in place to confirm the efficacy of MADs in reduction of AHI were not available for most patients. Reasons for this may be due to the associated costs or reluctance of patients to go through an overnight PSG in a sleep lab. This information would have been ideal to assess the overall success of MAD treatment in OSA patients.

The current retrospective study already provides encouraging evidence that physical medicine exercises support a positive outcome on TMD and POB incidence. Nevertheless, a well-designed prospective study would provide more information about the effect of adherence to physical exercise instructions on management of possible side effects of MAD therapy. In addition, it would be of interest to study oral health during OSA treatment, i.e., whether oral health improves or deteriorates as a result of the MAD therapy.

5. Conclusion

The prevalence of preexisting painful TMD were high in OSA patients who were referred for MAD therapy. If preexisting TMD was diagnosed and managed properly by supporting treatment including instructed physical medicine exercises, prevalence of painful TMD would be significantly reduced during MAD therapy. POB can develop by using MAD as well but by instructing the patients to do the physical medicine exercises, the incidence of POB could be reduced. Therefore, these findings suggest that TMD in the OSA patients is not an absolute contraindication for MAD therapy if all OSA patients received a comprehensive physical assessment of TMJ and associated structures at the baseline and at each follow-up visit to allow documentation and discussion of preexisting or occurrence of TMDs in the patients. This study also recommended that MAD therapy for OSA patients should be provided by a qualified dentist who is well trained and experienced in diagnosis and management of TMD and orofacial pain. The clinician should be able to diagnose preexisting TMD and have a good background to provide proper TMD supportive treatment before MAD delivery. Additionally, management of recurrence or development of TMD during MAD therapy is a necessary part of treatment. Regular interval follow-up visits and supportive therapy including instructed daily physical medicine exercises could prevent or reduce possible MAD side effects such as painful TMD and POB. The MAD therapy is an effective way to manage mild or moderate OSA. Follow-up polysomnography with and without MAD is necessary to verify its efficacy for each patient.

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