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CLINICAL REVIEW

Effects of mandibular advancement device for obstructive sleep apnea on temporomandibular disorders: A systematic review and meta-analysis

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SUMMARY

The clinical practice guidelines do not give precise indications on the use of mandibular advancement devices (MAD) for obstructive sleep apnea (OSA) patients when they suffer from temporomandibular disorders (TMD). The aim of this systematic review was to evaluate the effects of MADs on prevalence of TMD signs and symptoms in adult OSA patients. The study protocol was registered under the PROSPERO register and an electronic search was performed in several databases. All types of studies evaluating TMD prevalence on adult patients wearing MAD for OSA were included and independently evaluated by two investigators. The quality of evidence was evaluated using the grading of recommendations assessment, development and evaluation and the risk of bias by the risk of bias in non-randomized studies of interventions tool or the Cochrane collaboration's tool. For each study included, the difference in means and 95% CI was calculated between baseline and follow-up. Twelve studies were included. The meta-regression analysis showed that patients with pre-existing signs and symptoms of TMD do not experience significant exacerbation of symptoms using the MAD. The presence of TMD does not appear to be routine contraindication for the use of MAD used for the management of OSA.

Introduction

Obstructive sleep apnea (OSA) is a common chronic sleep disorder, affecting from 9% to 49% of the overall population [1,2] and characterized by repeated pauses in breathing during sleep due to collapse of the upper airway [3]. OSA is defined as the occurrence of five or more episodes of complete (apnea) or partial (hypopnea) upper airway obstruction per hour during sleep, in the presence of sleep related symptoms and its severity is described by the apnea-hypopnea index (AHI) and by the respiratory disturbance index (RDI) [4]. The conventional clinical cut-off levels are of >5 events/h AHI/RDI, >15 events/h AHI/RDI, or >30 events/h AHI/RDI for respectively mild, moderate or severe sleep apnea.

It is considered to be a systemic life-threatening disease as patients with untreated sleep apnea have an increased risk of mortality [5,6] even though the severity of AHI or RDI indexes are proxy and not unequivocally related to health consequences [7–9].

Continue positive airways pressure (CPAP) is the most efficacious and commonly used treatment for patients with OSA [10], however long-term adherence has been reported to be as low as 50% [11,12]. For many patients which are not compliant with the CPAP, for patients with primary snoring, mild or moderate OSA [13] and for those who have a clear preference for oral appliances, mandibular advancement devices (MAD) are a valid alternative and have been proven to be associated with a greater therapeutic adherence [14–18]. Moreover, MADs are reported to be superior to CPAP in improving sleep quality among bed partners.

MAD have been proven to be effective in significantly reducing snoring and obstructive respiratory events, by mechanically protruding the mandible, widening the oropharyngeal area and

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Abbreviations

AADSM	American academy of dental sleep medicine
AASM	American academy of sleep medicine
AHI	apnea-hypopnea index
CI	confidence interval
CPAP	continue positive airways pressure
GRADE	grading of recommendations assessment, development and evaluation
MAD	mandibular advancement device
OSA	obstructive sleep apnea
PRISMA	preferred reporting items for systematic reviews and meta-analyses system
RCT	randomized controlled trial
RDC/TMD	research diagnostic criteria for temporomandibular disorders
RDI	respiratory disturbance index
TMD	temporomandibular disorders
TMJ	temporomandibular joint

stretching the tongue muscles to avoid its collapse against the pharyngeal wall [19,20].

Considering the protruded mandible position, MAD have often been discussed and some have suggested that they are contra-indicated for patients suffering from musculoskeletal disorders of the masticatory system, called temporomandibular disorders (TMD) [21–26]. TMD is a collective term defining a number of clinical conditions involving the masticatory muscles, the temporomandibular joint (TMJ) or both [27]. TMD prevalence has been reported to be as high as 30% [28–30], occurring more frequently in women than in man [31,32], and tending to arise in the early twenties and to continue intermittently into middle age [33]. It is generally characterized by chronic, fluctuating, non-progressive pain and it forces a significant number of patients to seek treatment, lowering their quality of life and effecting social costs.

The clinical practice guidelines of the American academy of sleep medicine (AASM) and American academy of dental sleep medicine (AADSM) mention that oral appliances may aggravate TMD [32], but this statement is not well supported with scientific literature.

Since the management of OSA is likely to be life-long, understanding the effects of MADs on the masticatory structures and TMD is an important issue. The aim of this systematic review was to evaluate the effects of MADs on prevalence of TMD signs and symptoms in OSA patients.

Materials and methods

This systematic review protocol was registered under the PROSPERO register with the number CRD42019116702 (http://www.crd.york.ac.uk/prospero) and follows the preferred reporting items for systematic reviews and meta-analyses system (PRISMA) [35].

The methodological characteristics of the selected papers were summarized according to PICO (patients, intervention, comparison and outcome) [36].

In order to perform a comprehensive evaluation, the decision was made to analyze both studies which included TMD patients at baseline and evaluate their variation over time, as well as those who excluded TMD patients at baseline and evaluated the incidence of TMD signs and symptoms during MAD treatment.

Search strategy

The search strategy used for MEDLINE including MeSH and text words was ("Sleep Apnea, Obstructive" [Mesh] OR "Sleep Apnea Syndromes" [Mesh] OR (sleep apnea) OR (sleep apnea)) AND ("Temporomandibular Joint Disorders" [Mesh] OR "Temporomandibular Joint Dysfunction Syndrome" [Mesh] OR "Craniomandibular Disorders" [Mesh] OR "Myofascial Pain Syndromes" [Mesh] OR "Facial Pain" [Mesh]) AND ("Mandibular Advancement" [Mesh] OR (Mandibular Advancement device) OR (oral appliance) OR (oral device)).

The last search was performed on the 15Th of March 2019.

Screening and study selection

In order to be as inclusive as possible, all types of studies were included, except for case series, case reports and expert opinions. Participants were adult subjects (>18 y of age) seeking treatment for sleep apnea. Intervention was the therapy with MAD and comparison was of TMD or orofacial pain before and during therapy. Primary outcomes were TMD signs and symptoms.

In order to retrieve lists of potentially relevant studies to be included, a systematic research was carried out analyzing the following electronic databases: MEDLINE, Scopus, ISI Web of Knowledge, Cochrane Database of Systematic Reviews, LILACS and Google Scholar. The gray literature was also searched. Bibliography lists of all retrieved article were further analyzed and potentially relevant studies retrieved as well.

The search was conducted independently of language and year of publication.

Articles and abstracts from the search were independently analyzed by two researchers (A.A.B. and F.B.) in order to select the relevant ones. Full texts of potentially eligible studies were further analyzed for conformity to the inclusion and exclusion criteria. Any intra-examiner doubts or disagreements were solved by a third researcher (G.A.B.).

Data items and collection

The following data items were collected from each study: study design, sample size, mean age, gender, mean body max index, type of oral appliance, assessment method, pre-treatment pain and dysfunction score, during treatment pain and dysfunction score, mean time of each follow-up, withdrawal patients and the authors' main conclusions.

Risk of bias in individual studies and across the studies

In order to assess the methodological soundness of each paper, the quality assessment tool for quantitative studies by effective public health practice project was used [37].

Concerning the assessment of risk of bias in individual cohort studies, the risk of bias in non-randomized studies of interventions tool (ROBIN-I) was used [38].

In order to assess the risk of bias in individual randomized control trials (RCT) studies, the Cochrane collaboration's tool for assessing risk of bias in randomized trials (RoB 2.0) was used [39].

To evaluate the quality of body evidence, the grading of recommendations assessment, development and evaluation (GRADE) was performed [40].

Two assessors (A.A.B. and F.B.) independently performed the quality evaluations; when a disagreement existed, a conjunct evaluation was performed to reach a consensus.

The risk of bias across the studies was evaluated by means of Egger's test and Funnel plot. The heterogeneity among studies was assessed using a χ^2-based Q statistic test and I^2 index; however, because of the moderate insensitivity of the Q statistic, only an I^2 index greater than 50% was considered associated with a substantial heterogeneity among the studies. The tau^2 was also calculated for the heterogeneity assessment.

Methodology of synthesis of the results of the individual studies

Odds ratio and 95% confidence intervals (CI) to develop TMD over the follow-up were computed for each study. A fixed effect model was used if homogeneity was proved ($p > 0.10$); if homogeneity was rejected ($p < 0.10$), a random effects model was used to better aggregate data [41].

Calculations were carried out by means of comprehensive meta-analysis software (Biostat Inc, Englewood, NJ).

Results

The search identifies 2474 citations, of which 12 met the inclusion criteria.

Fig. 1 reports the selection process and Table 1 describes the studies included. Among these, three studies were RCT [42–44], eight were prospective cohort studies [45–52] and one was a retrospective cohort study [53].

Regarding follow-ups: one study had a 2-mo follow-up [52], eight [42–47,51,53] had a follow up from 6 to 24 mo. Two studies [48,49] had a 3 y follow-up, and one [50] reached 5 y follow-up. Concerning the assessment methods, five [42,49,50,52,53] studies used the research diagnostic criteria for temporomandibular disorders (RDC/TMD) [54]; four studies [45,46,48,50] used Helkimo's index for anamnestic and clinical dysfunction [55]; while three [43,44,47] examined patients using different types of questionnaires and clinical examination.

Nine studies [45–53] evaluated variation in incidence and prevalence of TMD during follow-ups. Two studies [43,44] analyzed the number of adverse events in the stomatognathic system in patients treated by oral appliances at different degrees of mandibular protrusion; while Doff et al. [42] compared the variation in occurrence of TMDs and function impairment in OSA patients treated with MAD or CPAP.

Quality analysis and risk of bias in individual studies

The methodological soundness of the studies included was found to be strong in three [42,44,48], moderate in seven [43,45–47,49,52,53] and weak in two [50,51]. The control of the confounders and the withdrawals are the most frequent domain that lowered the quality of methodology. The results of the effective public health practice project analysis are summarized in Table 2.

The risk of bias analysis showed that the overall bias evaluation was considered to have some concerns in the RCTs and to be at moderate risk for all the cohort studies included apart from one which was at serious risk. As far as the RCTs, these results were mainly consequences of bias due to deviations from the intended intervention and in the randomization process. The risk of bias in the cohort studies resulted to be moderate mainly because deviation from the intended intervention.

The risk of bias analysis is reported in Tables 3 and 4.

The GRADE scores calculated with the GRADEpro software (McMaster University and Evidence Prime Inc., Hamilton, ON, Canada) are shown in Table 5. The reasons for lowering the quality of evidence were related again to the risk of bias.

Results of individual studies

Table 1 reports the results of individual studies. The results of different studies are consistent in stating that patients with pre-

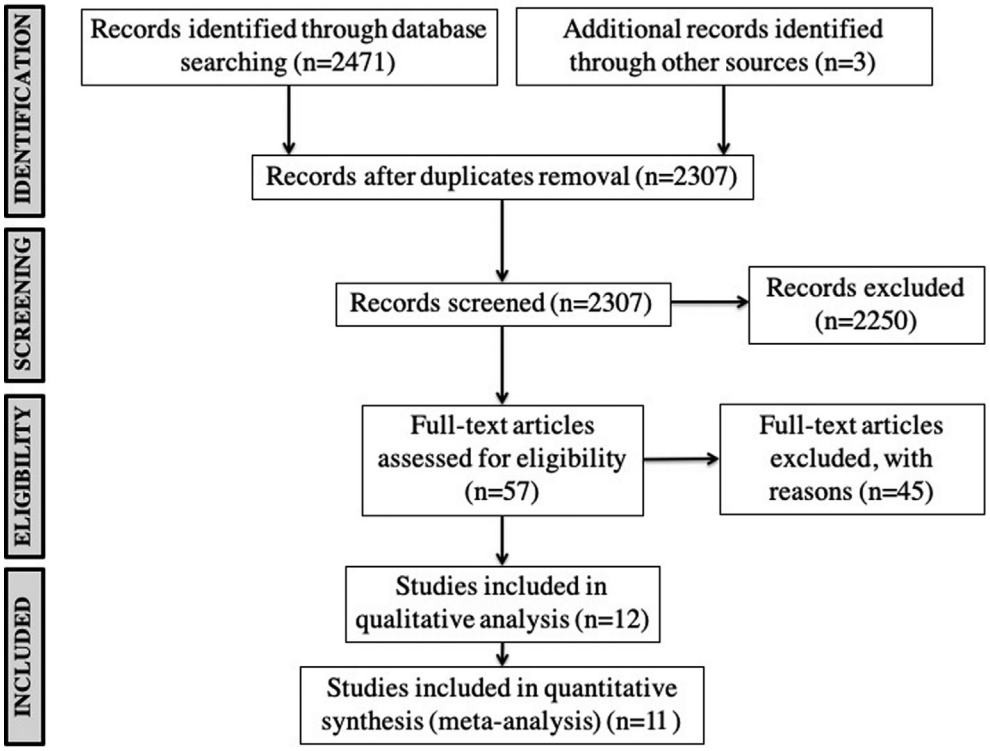

Fig. 1. PRISMA flow diagram regarding the selection process.

Table 1
Description of studies included in the systematic review.

Study included	Study design	Sample size	Mean BMI	Type of appliance	Advancement	Assessment method	Follow up	Withdrawal	Authors main conclusions
Bernhold et al., 1998 [45]	PC	25 (54.1 ± 11.44 y, 25M, 0F)	28	Magnetic appliance	50%–70%	Helkimo index	6 mo	0	MAD treatment had no aberrant effects on the TMJ status
Bondemark et al., 2000 [46]	PC	32 (54.4 ± 8.78 y, 23M, 9F)	Not stated	Monobloc	50%–70%	Helkimo index	24 mo	0	The study showed no adverse effects on the TMJ or stomatognathic system after 2 y nocturnal use of MAD
Doff et al., 2012 [42]	RCT	103 (49 ± 10 y, 43M, 8F)	32	Thornton adjustable positioner	Mean 76%	RDC/TMD	2, 12, 24 mo	15, none because of TMD	MAD therapy results in more pain-related TMDs in the initial period of use compared with CPAP therapy, because of the transient nature, this pain is not a reason
Fransson et al., 2004 [47]	PC	77 (55 y, 64M, 14F)	29	Monobloc	75%	questionnaire	6, 24 mo	12, not specified if some of them were due to TMD	Signs and symptoms from the masticatory system were reduced and the mean range of mandibular mobility increased slightly in patients who underwent long-term treatment with MADs
Gianassi et al., 2009 [48]	PC	42 (49 ± 12y, 33M, 9F)	26	PMPositioner	Mean 9.6 ± 0.3 mm	Helkimo Index	36 mo	8, of which 1 because of TMD	Long-term usage of MAD did not aggravate TMD symptoms. TMD symptoms lessened and use of MAD did not cause impairment to the TMJ.
Knappe et al., 2017 [49]	PC	43 (54 y, 30M, 13F)	Not stated	Hard acrylic device	Mean 77%	RDC/TMD	3–6, 12, 36 mo	29, of which 6 because of TMD	Treatment with MAD is beneficial to some OSA patients, but might induce changes in the occlusion, TMJs and oral function. Fluctuations in the occurrence of joint sounds might develop.
Martinez-Gomis et al., 2010 [50]	PC	40 (54.1 ± 8.7 y, 31M, 9F)	Not stated	Herner guiding telescopes	Mean 83%	RDC/TMD	6 wk, 6, 72 mo	25, of which 4 because of TMD	The use of MAD does not affect TMD prevalence
Napankangas et al., 2012 [51]	PC	15 (51 y, 9M, 6F)	28	Hard acrylic devices	50%	Helkimo Index	1, 3, 6, 24 mo	17, of which 7 because of TMD	Signs and symptoms of TMD do not increase during long-term mandibular advancement device therapy. However, patients with clinically assessed TMJ crepitation may discontinue their MAD therapy due to TMD
Perez et al., 2013 [53]	RC	167 (54 ± 12.9 y, 91M, 76F)	28	Hard modified Herbst	60–70% + titration	RDC/TMD	4, 7, 14 mo	82, of which 13 were suffering from TMD	Treatment with MAD is beneficial to some OSA patients, but might induce changes in the occlusion, TMJs and oral function. Fluctuations in the occurrence of joint sounds might develop symptoms with MAD use. Furthermore, these may decrease over time
Ranieri et al., 2009 [52]	PC	14 (42.5 y, 8M, 6F)	78	monobloc	Not stated	RDC/TMD	2 mo	0	Patients did not show prior myofascial pain or 60 d after use of the intra-oral appliance. Four patients reported TMD pain, lasting less than 15 d.
Tegelberg et al., 2003 [43]	RCT	74 (53 y, 74M, 0F)	/	Heat-cured acrylic appliance	50% or 75%	questionnaire	24 mo	19, of which 2 suffering from TMD	Together with few adverse events in the stomatognathic system or other complications we can recommend MAD treatment
Walker-Engstrom et al., 2003 [44]	RCT	86 (52 y, 86M, 0F)	/	Heat-cured acrylic appliance	50% or 75%	questionnaire	6 mo	9, but none because of TMD	Dental appliance treatment could be an alternative to CPAP for some patients with severe OSA

BMI = body mass index CPAP = Continuous Positive Airway Pressure; MAD = Mandibular Advancement Device; OSA = Obstructive Sleep Apnea; PC = prospective cohort; RC = retrospective cohort; RCT = randomized controlled trial; RDC/TMD = research diagnostic criteria for temporomandibular disorders; TMD = temporomandibular disorders; TMJ = Temporomandibular Joint.

Table 2
Quality assessment components and ratings (effective public health practice project).

Study	Selection Bias	Design	Confounders	Blinding	Data collection methods	Withdrawal	Overall bias
Bernhold et al., 1998 [45]	moderate	moderate	weak	moderate	strong	strong	moderate
Bondemark et al., 2000 [46]	strong	moderate	weak	moderate	strong	strong	moderate
Doff et al., 2012 [42]	strong	strong	strong	moderate	strong	moderate	strong
Fransson et al., 2004 [47]	moderate	moderate	weak	moderate	moderate	strong	moderate
Gianassi et al., 2009 [48]	strong	moderate	strong	moderate	strong	strong	strong
Knappe et al., 2017 [49]	moderate	moderate	moderate	moderate	strong	weak	moderate
Martinez-Gomis et al., 2010 [50]	strong	moderate	weak	moderate	Strong	weak	weak
Napankangas et al., 2012 [51]	moderate	moderate	weak	moderate	strong	weak	weak
Perez et al., 2013 [53]	strong	moderate	strong	moderate	strong	weak	moderate
Ranieri et al., 2009 [52]	strong	moderate	weak	moderate	strong	strong	moderate
Tegelberg et al., 2003 [43]	moderate	strong	strong	moderate	weak	moderate	moderate
Walker-Engstrom et al., 2003 [44]	moderate	strong	strong	moderate	strong	strong	strong

Table 3
Risk of bias in individual cohort studies (ROBIN-I).

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended intervention	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Overall risk of bias
Bernhold et al., 1998 [45]	No information	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Moderate
Bondemark et al., 2000 [46]	No information	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Moderate
Fransson et al., 2004 [47]	No information	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate
Gianassi et al., 2009 [48]	No information	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate
Knappe et al., 2017 [49]	No information	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate
Martinez Gomis et al., 2010 [50]	No information	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Moderate
Napankangas et al., 2012 [51]	No information	Low risk	Low risk	Serious risk	Moderate risk	Low risk	Low risk	Serious
Perez et al., 2013 [53]	No information	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk	Moderate
Ranieri et al., 2009 [52]	No information	Low risk	Low risk	Low risk	Low Risk	Low risk	Low risk	Low

Table 4
Risk of Bias in individual randomized controlled trial (RoB 2.0).

Study	Bias in arising from the randomization process	Bias due to deviations from intended intervention	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Overall risk of bias
Tegelberg et al., 2003 [43]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Walker-Engstrom et al., 2003 [44]	Some concerns	Low risk	Low risk	Low risk	Low risk	Low risk
Doff et al., 2012 [42]	Some concerns	Some concerns	Low risk	Low risk	Low risk	Some concerns

Table 5
Quality assessment and summary of findings across studies (GRADE).

Quality assessment						Summary of findings			Quality
Number of Studies (Design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias (Egger's test)	Number of patients	Odds ratio (95% CI)	Standard mean difference (95% CI)	
RDC/TMD									
4 (1 RCT)	Serious	Not serious ($I^2 = 48.667$, $p = 0.119$, $\tau^2 = 0.035$)	Not serious	Not serious	Serious ($p = 0.020$)	184	0.720 (0.603−0.861)	−0.181 (−0.279−−0.083)	Low
Helkimo index									
4 (Non-RCT)	Serious	Not serious ($I^2 = 0.000$, $p = 0.733$, $\tau^2 = 0.001$)	Not serious	Not Serious	Not serious ($p = 0.465$)	103	0.877 (0.673−1.143)	−0.072 (−0.218−0.074)	Moderate
Signs and symptoms questionnaire									
3 (1 RCT)	Serious	Not serious ($I^2 = 0.000$, $p = 0.840$, $\tau^2 = 0.001$)	Not serious	Not serious	Not serious ($p = 0.585$)	195	0.937 (0.773−1.136)	−0.036 (−0.142−0.070)	Moderate

CI = confidence interval; RCT = randomized controlled trial; RDC/TMD = research diagnostic criteria for temporomandibular disorders.

existing signs and symptoms of TMD do not experience significant exacerbation of symptoms using the MAD.

Bernhold and Bondemark [45] and Bondemark and Lindman [46] reported that most of patients did not show any change in anamnestic and clinical pain-dysfunction index. In one study two patients out of 25 reported improvement in symptoms and only one got worse. In the other study, two patients out of 32 were improved and only one got worse.

Two studies [42,53] reported an initial increase of TMDs at the first follow-up; followed by a significant decrease at 1-y follow-up.

Fransson et al. [47] and Gianassi et al. [48] reported a significant decrease in TMD symptoms throughout the study period when compared to baseline.

Five studies [43,44,50–52] did not report a significant variation in TMD prevalence.

Knappe et al. [49] reported that in subjects with no pre-existing symptoms of TMD, MAD treatment might induce changes in the temporo-mandibular joints and in the oro-facial function.

Synthesis of results

The quantitative analyses have been conducted to evaluate the effect of MAD therapy on TMDs. As assessment method four studies used RDC/TMD, four studies used Helkimo anamnestic Index and three studies used a dedicated questionnaire. The study by Ranieri and coworkers [52] was excluded from the quantitative analysis because it did not include TMJ disc displacement as a possible diagnose. In all the comparisons homogeneity was proved, consequently a fixed effect model was used. Figs. 2–4 report the odds ratio and 95% confidence intervals (CI) to develop TMD over the follow-up. In all the analyses the odds ratio is lower than one, suggesting that MAD therapy is not a risk factor for TMD development or worsening.

Risk of bias across studies

Concerning the publication bias, the results of Egger's test show no significant deviation of the intercept from the symmetry for questionnaire and Helkimo index analyses, while there is a significant publication bias in RDC/TMD analysis, as showed in Table 5.

Discussion

The aim of this systematic review was to evaluate the effects of MADs on prevalence of TMD signs and symptoms in OSA patients. There remains a lack of clear direction on this topic: some scientific associations have suggested that MADs are contraindicated in TMD patients [21,25], while the clinical practice guidelines of both the AASM and AADSM [34] mention that oral appliances may aggravate TMDs, but avoid stating whether they should or should not be used.

Twelve studies met the inclusion criteria and therefore were included in the analysis. The methodological soundness was found to be moderate overall, where the main reasons to lower the quality of methodology were the control of the confounders and the withdrawals.

The risk of bias analysis showed that the overall bias evaluation was considered to be at moderate risk in most studies, where the main reason for lowering the quality was the deviations from the intended intervention. Therefore, the main weakness of the studies included is due to the high dropout rate.

The meta-analysis was carried out to and the odds ratio evaluation revealed that MADs do not represent a risk factor for TMD signs and symptoms. On the contrary, most of the studies showed that the use of MAD might represent a protective factor for TMDs.

TMDs are classified in pain-related TMD and headache and intra-articular joint disorders and degenerative joint disorders [56]. When the joint component is predominant, an anterior positioning appliance, by slightly moving the condyle forward in the glenoid fossa, may play a significant role in alleviating pain in cases of arthralgia, capsulitis, retrodiscitis, painful disc displacement and chronic intermittent locking [57–59]. Its action is likely achieved by reducing the loading forces on painful retrodiscal tissues, allowing adaptation of

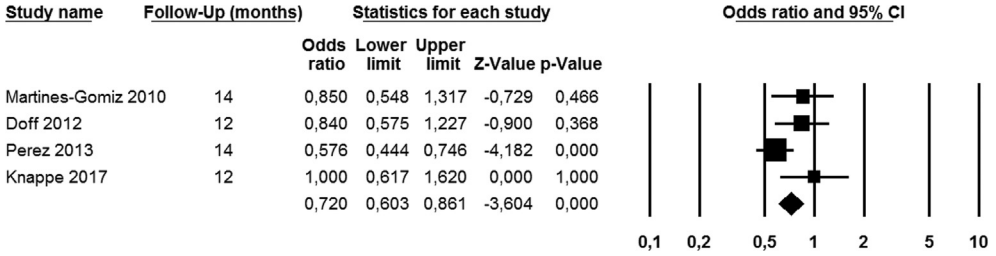

Fig. 2. Quantitative analysis of studies using RDC/TMD.

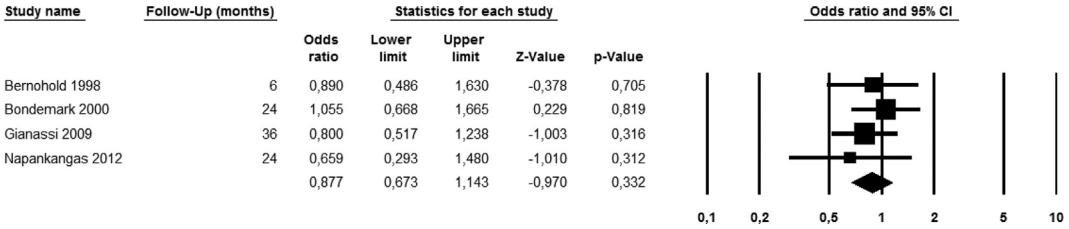

Fig. 3. Quantitative analysis of studies using Helkimo anamnestic and clinical dysfunction index.

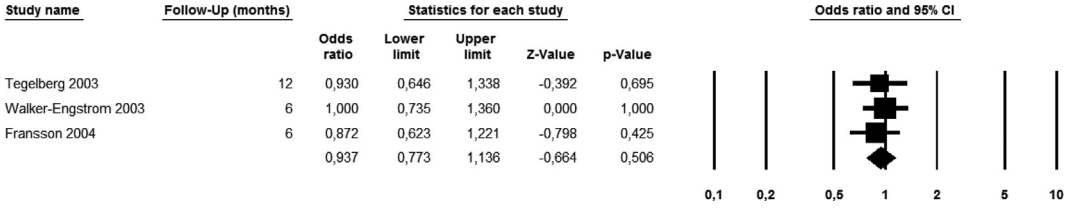

Fig. 4. Quantitative analysis of studies using questionnaires.

these tissues. The therapeutic condylar position used in anterior positioning appliance therapy for intracapsular TMD is similar to that used with the MADs and consequently, in some patients, a reduction in the signs and symptoms of both TMD and OSA can be expected; therefore, the results of the studies included are not surprising.

A lower pain pressure threshold of masticatory muscles and a consequently higher pain incidence has been reported during the first months of MAD therapy, but this tends to decrease with time [60]. In fact, a reduction in both incidence and prevalence of TMD was reported [52], as well as a reduction in the number of patients who drop-out at following follow-ups. It has to be considered that CPAP, like MAD, may induce orofacial pain in some individuals [42], but no systematic investigation was carried out on this topic. Future studies are needed to evaluate this association. TMD pain and dysfunction may be acute, transient or chronic [27] and may be present before or on onset or be exacerbated by the treatment, as became evident from this review. Since the different individual ability of adaptation may play a role, in order to help the masticatory structures adapt, slow titration of the appliance should be used [34] and slow advancement should be performed, stopping at the minimum advancement needed to manage the OSA. This is also supported by the evidence that increasing the mandibular advancement does not always produce significant improvement in success rate [61].

It has also been demonstrated that TMD symptoms arise in the early twenties and continue intermittently into middle age [33]. In fact, pain and functional problems tend to fluctuate and symptomatology often resolves with time. These findings may provide another possible explanation for the disappearance of TMDs in some patients and the development of TMD in others, since the mean age of the patients included in the studies reviewed [42–53] is 45–55 y.

It is well established that TMDs occur more frequently in women than in man [31,32], while OSA is reported to be more frequent in men than in women [62]. Of the studies included in the review, three analyzed only male patients [43–45], and the others presented a mix of different sexes, with a far greater prevalence of males than females.

It would have been interesting to report on any differences of the effects of MADs on TMDs, in men and women, since an underestimation of TMDs can be possible in the sample analyzed; however, this review was unable to provide these data. It has to be considered that although an association between TMD and MAD treatment is possible, no causal association can be gained from the present data.

A strength of the present review is the decision of analyzing TMD signs and symptoms variation during MAD treatment, by including both studies which analyzed patients with TMD at baseline, as well as those who excluded TMD patients at baseline. When analyzing studies which included patients who received a positive diagnose of TMD patients prior to beginning MAD treatment, the results demonstrated that often there was a reduction of TMD signs and symptoms, some patients did not show a significant change in the symptomatology and only small group tended to get worse. At the same time, when analyzing studies which excluded patients with signs or symptoms of the TMD prior to the treatment beginning [49,63–66], it became evident that some patients did develop some type of TMD symptoms during treatment, where the incidence varies from 18.6% to 40.9% during MAD therapy.

Despite the high dropout rate, MADs are well tolerated by the general population. In fact, side effects causing patients to discontinue treatment, are less common than the ones causing them to discontinue the use of CPAP [34]. Moreover, considering that OSA is a systemic life-threatening disease, the side effects related to MADs use are not serious enough to contraindicate the treatment in either TMD or non-TMD patients.

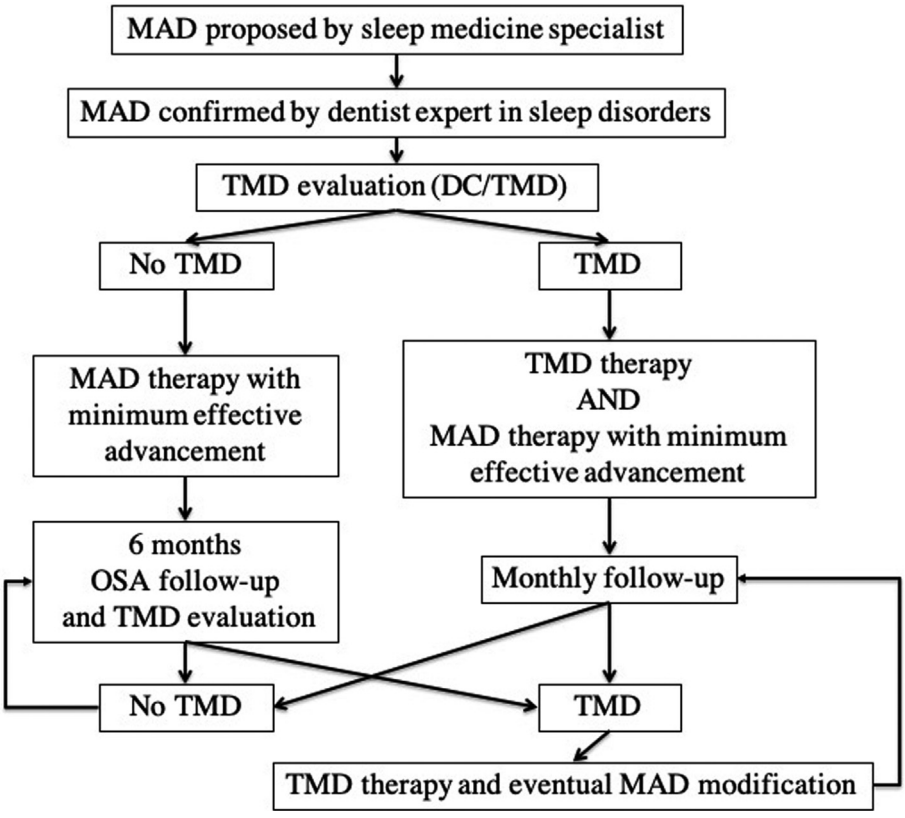

Fig. 5. Decision tree for MAD therapy in relation to TMD.

Since TMD may arise in any moment with fluctuating signs and symptoms, and considering that MADs strain masticatory structures, OSA patients need to be closely monitored by an orofacial pain specialist. When examining a candidate for MAD therapy a complete TMD evaluation should be performed. The DC/TMD protocol [56] represents today the gold standard for clinical and research purposes and should therefore be universally used for TMD assessment prior to the treatment beginning and during MAD therapy. It consists of several anamnestic questionnaires and a clinical examination involving records of mandibular movements, TMJ noises during movements and muscle and TMJ palpation.

Based on available data, in order to sum up the decision process for MAD use related to TMD, the following decision tree is proposed (Fig. 5). If the sleep specialist indicates MAD treatment, the patient needs to be evaluated by a dentist expert in sleep disorders and orofacial pain and undergoes dental and TMD examination during the first evaluation as well as at every follow-up appointment. Regarding TMD evaluation, DC/TMD is used [56]. If the patient does not suffer from TMD, MAD therapy may be started, stopping the titration at the minimum effective advancement. In absence of symptoms, the patient is set in a 6 mo follow-up. In case of an onset of TMD during titration or follow-ups, TMD therapy and eventual MAD modification are provided.

If the patient suffers from TMD before starting MAD treatment, TMD therapy may be provided. Depending on TMD diagnosis, the dentist needs to treat TMD before MAD therapy, or may treat TMD taking advantage of the MAD. After the titration period, monthly TMD follow-ups are provided until TMD resolution; then the patient is set in a regular 6 mo follow-up.

Furthermore, considering that MAD therapy is likely to be lifelong and since it is associated with dental side effects [67–69], the dentist is crucial in the management of this treatment.

Future studies are needed to identify adverse side effects created by the use of MADs on healthy masticatory structures, as well as in patients suffering from TMD.

Conclusion

The analysis of scientific literature evaluating the effects of MADs on TMD in patients with and without pre-existing signs and symptoms showed that there is a moderate to low quality evidence that MAD therapy is not a risk factor for TMD signs and symptoms. Therefore, the presence of a TMD should not be considered a routine contraindication for the use of MADs in the management of OSA.

Conflicts of interest

The authors do not have any conflicts of interest to disclose.

Practice points

1. The presence of signs or symptoms of temporomandibular disorders is not a reason to contraindicate the use of mandibular advancement device in patients affected by obstructive sleep apnea.
2. Mandibular advancement device for the treatment of obstructive sleep apnea may cause temporomandibular disorders in patients who were temporomandibular disorder-free prior to the treatment beginning
3. A temporomandibular disorder specialist should closely monitor patients undergoing treatment with mandibular advancement device

Research agenda

1. Future studies regarding mandibular advancement devices and temporomandibular disorders need to better control confounding factors and withdrawals, which are the most frequent domains that lower the quality of methodology.
2. Some studies presented a small sample size. Future studies need to ensure that their samples are adequate in size to provide valuable information.
3. Future research needs to determine which conditions are more likely to improve temporomandibular disorders signs and symptoms with mandibular advancement device therapy and which ones are not.
4. Future research needs to understand which patients present a higher risk of developing temporomandibular disorders during obstructive sleep apnea treatment with mandibular advancement device.

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