REVIEW ARTICLE

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Anteroposterior and Vertical Effects of Mandibular Advancement Devices in Sleep-Disordered Patients: A Systematic Review

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Study Objectives: To perform a systematic review of the current evidence regarding the anteroposterior and vertical effects of mandibular advancement devices (MADs) in sleep- disordered patients.

Methods: A systematic review of relevant articles retrieved from online databases (PubMed, Medline, Embase, Cochrane, and LILACS) was conducted. All relevant studies published prior to January 5, 2020 that examined the anteroposterior and vertical dentoskeletal effects of MAD on patients with sleep apnea were included.

Results: Sixteen articles were included in this systematic review. MAD therapy mostly did not affect the SNA value; three articles found a significant reduction, one article a significant increase, and three articles no change of the SNB value; the facial height and mandibular plane angle were generally found to be significantly increased; the overjet and overbite were commonly found to be significantly decreased; usually the upper anterior teeth position was significantly retroclined or retruded and the lower anterior teeth were found to be significantly proclined and protruded.

Conclusion: MAD therapy showed anteroposterior and vertical effects on dentoskeletal structures in patients with obstructive sleep apnea over the short and long term. A posterior rotation of the mandible together with an increase in the vertical dimension, overbite and overjet decrease, and retroclination of upper incisors and proclination of lower incisors were typically found.

Keywords: dentoskeletal effects, mandibular advancement device, obstructive sleep apnea, oral appliance therapy

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INTRODUCTION

Obstructive sleep apnea (OSA) has been defined as the presence of repeated episodes of obstructive apneas and hypopneas during sleep accompanied by snoring, dyspnea, asphyxia or suffocation, and sleep fragmentation.[1,2] OSA has been also associated with arterial and pulmonary hypertension[3] and traffic and work-related accidents.[4]

Because of its high morbidity, many treatment modalities have been used to address OSA including but not limited to: weight loss, pharmacologic therapy, pharyngeal and jaw surgery, and continuous positive airway pressure (CPAP) therapy.[5] Mandibular advancement devices (MADs) have also been reported as an effective nonsurgical treatment option for patients with OSA, especially for those who are unable to tolerate CPAP treatment.[6] According to the American Academy of Sleep Medicine, MADs are indicated in patients with mild to moderate OSA.[7] The overall use and therapeutic effect of MADs is evident and well documented.[8,9] Furthermore, over the past 20 years, MADs have been proven to reduce the apnea-hypopnea index, improve oxygen saturation during sleep, reduce snoring, and reduce arterial blood pressure.[10] Nonetheless, MADs have shown side effects that might affect the masticatory system, altering the vertical and/or sagittal position of either the mandible or dentition. Moreover, little is known about their short- and long-term effects.[11] Therefore, knowing the side effects of MADs will be both helpful and beneficial for clinicians in terms of preventing its undesirable effects on patients' profile and functional ability.

Many cephalometric studies have been performed to determine side effects on the dental and skeletal structures after OSA treatment with MADs; yet, there is no agreement on their results.[12-21] The findings in this review provide clinicians with information about side effects of MAD therapy for patients with sleep apnea and general knowledge about the sagittal and vertical dentoskeletal effects of MADs in patients with OSA. Through an evidence-based approach, the aim of this systematic review was to extensively evaluate the current bibliographic data assessing, over the short and long term, the anteroposterior and vertical effects of MADs in sleep-disordered patients.

METHODS

Eligibility Criteria

Observational studies based on general population, randomized clinical trials (RCTs), and nonrandomized clinical trials (NRCT) that investigated the anteroposterior and vertical effects of MADs in sleep-disordered patients in adults (age 18 years or older) were included. There was no restriction to the language or publication year.

Case series, case reports, reviews, letters, conference abstracts, and personal opinions were not included. Also excluded were the following studies: those that reported outcomes immediately after MAD delivery; those in which patients had previously used MADs at the time of enrollment; those in which MADs had been indicated for purposes other than treating OSA; those in which the examination was not done by a dentist; and those that did not report the anteroposterior and vertical changes in either radiographs or dental casts.

Information Sources: Search Strategy

Search strategy, including word combinations and truncation, was made for each one of the following databases: Cochrane, EMBASE, LILACS, MEDLINE, and PubMed. Reference lists were also reviewed to verify whether any articles had been missed from the searches. All searches were conducted up to January 5, 2020 (Appendix 1). The references were organized, and the duplicates were removed manually. Two independent reviewers (N.A.P. and M.L.V.) proceeded with the search on the selected databases after consultation with a health sciences librarian.

Study Selection

The study selection was conducted in two phases. In the first phase, two reviewers (N.A.P. and M.L.V.) independently checked the titles and abstracts of all records identified. Any studies that did not match the inclusion criteria were excluded. This phase was blinded by the two examiners. In the second phase, the same two reviewers evaluated the remaining articles, analyzing the full text to identify the ones that fulfilled the eligibility criteria. Disagreements, if presented, in both phases were discussed with the third reviewer (M.M.).

Data Collection Process

The data were extracted by one author (N.A.P.) and cross-checked by a second one (M.L.V.); any disagreement was discussed between them and the third reviewer (M.M.). The following key features were extracted: authors, nationality, year, sample size, age, sex, and sagittal and vertical changes of the mandible and/or dentoalveolar structures.

Risk of Bias in Individual Studies

Two authors assessed the methodologic quality of the included studies using the quality index of individual studies.[22] The results obtained from the index indicated that 4 studies were of good quality, 10 studies were fair, 2 studies were of poor quality, and no studies presented excellent quality (Table 1).

RESULTS

Selection of Studies

Following the electronic databases search, 654 articles were identified and screened for retrieval. After removing duplicates, a total of 605 studies were found. In the first selection phase, the studies were selected through their title and abstracts and 570 studies were excluded. In the second phase, the reviewers screened the papers by reading their full text; 35 were analyzed and 19 were excluded. At the conclusion of the screening, 16 studies met all the inclusion criteria. Figure 1 maps the selection process.

Study Characteristics

Sixteen studies were included in this systematic review with the sample size ranging from 15 to 155 patients and the mean age ranging from 46.9 to 54.1 years. Studies came from Denmark,[23] China,[17,21,24] Holland,[14] Canada,[12,24] United Kingdom,[25] Sweden,[15,18,26,27] New Zealand,[19] France,[13] Brazil,[20] Spain[28] and Australia.[16] Papers included observational studies as well as RCTs and NRCTs.

Two main parameters were discussed in the selected papers: anteroposterior and vertical effects, which are indicative of the skeletal and dental transformation following the treatment with MADs. The common assessment method used in these studies was cephalometric analysis before and after treatment, and comparison of dental casts as well as clinical examinations based on patients' perspective after MAD therapy.

Results of Individual Studies

Two main topics were examined: anteroposterior and vertical effects of MADs in terms of SNA, SNB, ANB, facial height, mandibular plane angle, overjet (OJ), overbite (OB), and upper and lower incisors position. The treatment time and summary of outcomes per each study are presented in Table 2.

Anteroposterior Changes

In terms of the anteroposterior skeletal effects of MADs, the most prevalent findings were either no statistically significant change or statistically significant but clinically negligible change. In regard to SNA value, 7 of 16 studies found no significant changes in SNA values, whereas the study by Robertson et al.[19] found an increase of 0.32°and Almeida et al.[12] found a progressive decrease from 0.9° (< 6 years of MAD treatment) to -0.8° (> 8 years of MAD therapy) in the class I subgroup. Additionally, 7 of 16 studies did not provide any information regarding SNA value changes. In terms of the change in SNB, 3 of 16 studies found no significant change, another 9 studies did not demonstrate any information regarding the SNB, 2 studies[14,15] indicated a decrease in SNB of 0.4°, 1 study[18] displayed a backward movement of 0.6 mm at B point, and only 1 study presented an increase in SNB values.[13] When it comes to the ANB angle, 12 of 16 studies did not investigate the changes in this parameter and did not present any information regarding the ANB angle. The other two studies indicated no significant change in ANB angle, whereas two other studies found an increase in ANB values ranging from 0.29° to 0.5°.[12,19]

After a thorough investigation of the studies in terms of the anteroposterior dental effects of MADs, the following outcomes were collected. The studies showed a range of variation in the prevalence of a decrease of OJ ranging from 0.2° to 2.6°. Nevertheless, Ringqvist et al.[18] found no change and two studies provided no information on OJ changes. The position and inclination of the upper and lower incisors were also analyzed, and the following results were presented; 4 of 16 studies found significant retroclination of upper incisors ranging from 1.41° to 3.5°. Thus, Ringqvist et al.[18] and Hammond et al.[16] demonstrated no change in position of the upper anterior teeth. The rest of the reviewed studies presented no information on the positional changes of the incisors. In regard to the lower incisor positions, 7 of 16 studies demonstrated proclination of the lower anterior teeth ranging from 0.94° to 6.6°. However, eight studies gave no information on lower incisor movements. Only one study, that of Ringqvist et al.,[18] indicated no change in the position of lower anterior teeth. A more detailed analysis is provided regarding the dental and skeletal effects of MADs in the following Discussion section.

Vertical Changes

Concerning the changes in vertical dimensions, studies showed a range of variation in the increase in total anterior facial height (TAFH) ranging from 0.7 to 7.4 mm. Four of 16 papers found an increase in anterior lower facial height (ALFH), ranging from 0.8 to 1.8 mm. Eight studies reported no information concerning vertical changes and only Hou et al.[17] showed an increase in lower posterior facial height (LPFH). Only one study indicated no significant change in facial height.[16] The findings from the reviewed papers build up a general consensus that vertical dimensions increased after MAD treatment. In association with the vertical changes, the findings from 6 of 16 studies show a noticeable increase in mandibular plane angle ranging from 0.3° to 3°. However, nine studies reported no information about the mandibular plane angle value. Only one study indicated no significant change in mandibular plane angle.[16]

In terms of the OB, across studies, it decreased from 0.3 mm to 2.8 mm. Ringqvist et al.[18] reported no change in OB, and Bacon[13] provided no information regarding OB.

DISCUSSION

Interpretation of Results

Anteroposterior Changes After MAD Therapy

In this review, the most prevalent finding about the SNA angle was no significant change.[13-18,21] However, Robertson et al.[19] evaluated 100 participants with a mean age of 49 years for males and 51 years for females. A clinically negligible but statistically significant change of + 0.32º was found after 2 years of treatment. This could be related to a measurement error or larger sample sizes when compared to the other studies, which have relatively smaller sample sizes.

Interesting results were described by Almeida et al.[12] who found no significant changes in terms of the SNA value after MAD therapy when evaluating 71 samples of class I and class II patients. However, they found significant changes between the class I subgroup after less than 6 years of treatment (+0.9º), and the class I subgroup after more than 8 years of treatment (-0.8º). According to the study by Almeida et al.,[12] it could be determined that class I patients with less than 6 years of treatment with MAD have forward movement of the A point. Later, if using MAD for more than 8 years, the A point will turn its direction backward. According to the authors' hypothesis, this could be attributed to an initial retroclination of upper incisors that will account for a slight forward movement of the A point. However, after the cortical resistance is overcome, root resorption or bone fenestration could be found along with a slight backward movement of the A point.

Although Robertson et al.[19] reported an increase of 0.95 mm between ANS-PNS distance after MAD application, measuring the palatal length is somehow problematic: this is because locating either the ANS, PNS or both points is difficult to do. However, this increase in distance could be because of remodeling of ANS secondary to retroclination of the upper incisors or it could be basically a chance finding.

When it comes to change of the SNB value, studies by Doff et al.[14] and Fransson[15] claimed a reduction of 0.4° with a mean of 2 years after treatment. These findings are in agreement with Ringqvist et al.[18] who reported that the B point moved backward by 0.6 mm after 4 years of MAD therapy. These findings could be related to a more marked clockwise rotation of the mandible that counteracts the actual forward movement of the mandible. In contrast, Bacon et al.[13] noticed an increase in the SNB angle of 1.7° after 2 years. This could be attributed to a more pronounced anteroposterior than vertical mandible change position. Moreover, Bacon et al. reported that the hyoid bone adopted a more distant position from the cervical vertebrae, which could facilitate a more pronounced anterior movement of the mandible.

In general, the reviewed studies did not specify the ANB changes.[13-15,17,18,20,23-28] However, Hammond et al.[16] and Wang et al.[21] found no significant change. Almeida et al.[12] suggests an increase of 0.5° after a mean of 7.3 years of treatment. In agreement with the previous study Robertson et al.[19] found a significant increase of 0.29° of ANB angle after a mean of 2 years of treatment. The ANB angle could have been increased because of a mandibular clockwise rotation or an anterior direction remodeling of the A point.

Regarding changes in OJ, most of the studies are in agreement with the fact that a decrease in OJ ranging from 0.2 mm to 2.6 mm is the common finding after MAD treatment.[12,14-17,19-21,24-28] This could be attributed to the forward movement of the mandible as well as retroclination of the upper incisors and proclination of the lower incisors after using MADs. These changes might occur because of a labially directed force to the lower incisors and a lingually directed force to the upper incisors while the appliance is in use.

There is an overall prevalent retroclination of the upper incisors, which ranges from -1.41° to -3.5°.[12,14,19,21] Also, studies suggested proclination of the lower incisors, ranging from 0.94° to 6.6°, as a dentoalveolar effect of MADs.[12,14-16,19-21] Almeida et al.[12] evaluated 71 participants (mean age of 49.7 years) after treatment with the Klearway advancement device (Klearway, Vancouver, British Columbia, Canada) and reported the biggest increase in the proclination of the lower incisors by 6.6°. This could be interpreted as a consequence of the increased prevalence of OSA with age. OSA has a tendency to worsen with age and this situation shows the need for more mandibular advancement over time. Long-term effects over a mean period of 7.3 years were also evaluated. The authors stated that most orthodontic effects of MAD were related to mandibular advancement and not to the appliance design or material. However, they mentioned that more research is needed with the Klearway advancement device to prevent the unwanted proclination of lower anterior teeth. It can be speculated that if the design of the MAD used were analyzed, perhaps the adverse effect could be understood. Consequently, different designs may cause different adverse effects. Finally, it is probable that Almeida et al.[12] found a decrease in the interincisal angle of 4.1° as a result of proclination of the lower anterior teeth and retroclination of the upper incisors.

Vertical Changes After MAD Therapy

There is a general consensus in the literature[12,13,15,17,18,21] in terms of the increase of the mandibular plane angle ranging from 0.3° to 3°. Similarly, Wang et al.[21] found a 1.25° increase in less than 3 years, and a 1.48° increase in more than 3 years of treatment. In addition, Bacon et al.[13] found 3° of increase after 2 years of MAD treatment. All of these reviewed studies show a slight increment tendency of the mandibular plane angle the longer the MAD device is used. Only one study's subgroup (less than 6 years of MAD treatment) was found to present a clinically negligible decrease of -0.1° when evaluating the mandibular plane angle.[12] This minimum difference could be attributed to error measurement. As a most prevalent outcome, it could be inferred that a natural effect of the MAD is the posterior rotation of the mandible. This is probably because of the natural result of the protrusion of the mandible after the treatment.

Moreover, the reduction in overjet after MAD therapy can lead to premature anterior contact with posterior open bite, which also can contribute to posterior rotation of mandible. In addition to this phenomenon, and following the posterior mandibular rotation, the overeruption of molars may be indirectly induced by the space created between the mandibular and maxillary molars. These factors might account for the general agreement regarding an increase in the ALFH,[12,14,17,21] TAFH,[12-15,17,19,21] total posterior facial height (TPFH), and LPFH[17] after use of the MAD. In addition, Hou et al.[17] hypothesized that some changes were too small to be observed at annual intervals. Thus, based on these presumptions, the LPFH and TPFH changes were observed at 3-year follow-up but not in annual or biannual evaluations.[17]

According to Wang et al.[21] there was an increase in lower anterior facial height by 1.46 mm and 1.52 mm and an increase in the TAFH by 1.21 and 1.56 mm in less than 3 years and more than 3 years of treatment, respectively. Because values are very similar in the two groups, it could be deduced that significant changes can be seen in less than 3 years, but if the appliance is used more than 3 years, the vertical dimension would not be affected on a large scale.

In reference to all the studies, an inference could be drawn that the longer the use of the MAD, the greater the increase in the vertical dimension. Unexpectedly, Bacon et al.[13] observed, after only 2 years, an increase of 7.4 mm in the TAFH in 21 patients treated successfully with a MAD. This value represents the highest value among all the studies' results. It is worth mentioning that a single device that was previously composed of upper and lower acrylic plates was used. These plates were later bonded in a protrusive position that was most tolerable and comfortable for the patients. No specific value for acrylic height or protrusion posture are mentioned, and these variables could affect the vertical changes. The face height increment also could be related to two additional factors: the depth and curvature of the mandibular fossa in its anterior portion, and the amount of OB of the sample. If the curvature of mandibular fossa is pronounced or the deep bite is severe, then the vertical change could be larger in magnitude when moving the mandible forward. However, there is no clear description in the study about the facial type and OB of patients at screening and/or before treatment. More research can be done to determine the effect of temporomandibular joint anatomy and deep bite over facial type increment when wearing MADs.

Additionally, only Hammond et al.[16] demonstrated no significant change in facial height as well as mandibular plane angle. This might be because of upward movement of the condyle as it compensates the vertical increase of facial height. In reference to this hypothesis, Robertson[29] demonstrated vertical repositioning of the condyle with respect to the cranial base as early as 6 months within MAD treatment.

There is a general consensus in the literature[12,14-17,19-21,23-28] in terms of the decrease in OB ranging from 0.3 mm to 2.8 mm after MAD treatment. Meanwhile, Battagel and Kotecha[25] noticed a small, statistically significant reduction in both vertical (0.4 mm) and horizontal (0.5 mm) overlap of the incisor teeth with the median duration of 3.6 years of mandibular advancement splint wear. These authors found a correlation between these values and the degree of vertical opening of the mandibular advancement splint. However, no correlation was found with the amount of mandibular protrusion or duration of appliance wear.

Similarly, Robertson et al.,[19] with a nonadjustable rigid splint, found changes in OB (-0.61 mm) occurring as early as 6 months. In the same study, significant positive correlations were found in the amount of anterior opening with each appliance and OB changes at 24 and 30 months. It should be noted that because a nonadjustable appliance was used, care should be taken when attempting to compare to adjustable appliances.

Despite the studies that found significant changes in OB and OJ, one particular study reported no significant changes in OJ and OB as well as in the horizontal position of the maxillary and mandibular incisors at 4-year follow-up.[18] This might be because of extrusion of the molars and incisors on the upper and lower jaw as a consequence of posterior rotation of the mandible after MAD treatment. In this particular study, the downward movements of the maxillary incisors were able to be observed because the construction of the MADs allowed for minor movement of the incisors because there was no acrylate covering on the teeth. As a result, eruption of incisors might compensate for the decrease in OB and OJ. This finding, which opposes other studies, shows the importance of appliance design. There is no consensus in the literature regarding the construction of dental devices for the treatment of OSA. More studies are needed to clarify the significance of the composition of the MADs.

The aforementioned orthodontic changes are thought to be related to the amount of mandibular advancement, duration of MAD use, and periodontal condition of teeth. However, the sleep apnea specialist decides the amount of mandibular advancement and the duration of the therapy in the treatment of patients with OSA. In that sense, the sleep apnea specialist has to be aware of all dentoskeletal side effects. More investigations are needed to compare appliance designs or materials.

Limitations of the Study

The goal of this study is to help clinicians gain insight into potential effects of MADs on dental and skeletal structures over the short and long term. Nevertheless, there are some points that decrease the quality of the studies. The most frequently noticed limitation among the reviewed studies was the compliance reported by the patients because it was not objectively measured.[12,13,21] Another important limitation was the peak time for periodontal disease, which mostly increased at the mean age of the patients undergoing treatment with MADs. Because most of the patients using MADs were older than 40 years, which is when periodontal disease usually peaks, more detailed studies with a comprehensive periodontal examination are required.[12,21] Thus, patients with less bone support may be expected to present more dentoalveolar than skeletal changes. Also, only two studies[23,28] used a digital caliper directly in the mouth to assess OB and OJ, which could be subject to measurement error.

Another point is that 75% of the studies reviewed in this study were of either fair or poor quality. Most of the studies were retrospective, which might present a possible risk of selection bias. Furthermore, the variety of MAD designs might play an important role in outcomes/side effects. Also, the different timeframe assessments make it impossible to accurately compare their effects in correlation with time. However, a movement direction tendency has been found, and control groups in some of the studies[13-15,18] helped to detect actual changes due to MAD therapy excluding changes due to growth/time.

CONCLUSIONS AND IMPLICATIONS OF KEY FINDINGS

Overall, use of the oral appliance demonstrates no significant skeletal change in anteroposterior dimension. The results of this study show that the short- and long-term use of an oral appliance predominantly causes dental changes in the craniofacial morphology in patients with OSA. The general findings also accounted for posterior rotation of the mandible accompanied by an increase in vertical dimension, decrease of OB and OJ, and retroclination of upper incisors and proclination of lower incisors.

The longer the patients wear the MAD, the more pronounced the side effects. A more efficient MAD with a lower amount of forward mandible advancement (but still with positive results) is ideal for treatment of sleep apnea. Because dentoskeletal side effects after using oral appliances are inevitable, clinicians should be encouraged to follow up with their patients and make regular assessments during treatment. Clinical tracking of MAD therapy could detect craniofacial changes earlier during treatment.

ABBREVIATIONS

ALFH – Anterior lower facial height
CPAP – Continuous positive airway pressure
LPFH – Lower posterior facial height
MAD – Mandibular advancement devices
NRCT – Nonrandomized clinical trials
OB – Overbite
OJ – Overjet
OSA – Obstructive sleep apnea
RCT – Randomized clinical trials
TAFH – Total anterior facial height
TPFH – Total posterior facial height

REFERENCES

1. Li N, Li HP, Wang P, Yan YR, Li SQ, Li QY. Nocturnal mean oxygen saturation is associated with secondary polycythemia in young adults with obstructive sleep apnea, especially in men. *Nat Sci Sleep*. 2019;11:377-386.

2. Tsara V, Amfilochiou A, Papagrigorakis MJ, Georgopoulos D, Liolios E. Guidelines for diagnosis and treatment of sleep-related breathing disorders in adults and children. Definition and classification of sleep related breathing disorders in adults: different types and indications for sleep studies (Part 1). *Hippokratia*. 2009;13(3):187-191.

3. Warunek SP. Oral device therapy in sleep apnea syndromes: a review. *Semin Orthod*. 2004;10:73-89.

4. Martins AB, Tufik S, Moura SM. Síndrome da apnéia-hipopnéia obstrutiva do sono. Fisiopatologia. *Jornal Brasileiro de Pneumologia*. 2007; 33(1): 93-100. 5.

5. Spicuzza L, Caruso D, Di Maria G. Obstructive sleep apnoea syndrome and its management. *Ther Adv Chronic Dis*. 2015;6(5):273-285.

6. de Vries GE, Hoekema A, Vermeulen KM, et al. Clinical- and cost-effectiveness of a mandibular advancement device versus continuous positive airway pressure in moderate obstructive sleep apnea. *J Clin Sleep Med*. 2019;15(10):1477-1485.

7. Kushida CA, Morgenthaler TI, Littner MR, et al. American Academy of Sleep (2006) Practice parameters for the treatment of snoring and Obstructive Sleep Apnea with oral appliances: An update for 2005. *Sleep* 29: 240–243."

8. Ng A, Gotsopoulos H, Darendeliler AM, Cistulli PA. Oral appliance therapy for obstructive sleep apnea. *Treat Respir Med*. 2005;4(6):409-422.

9. White DP, Shafazand S. Mandibular advancement device vs. CPAP in the treatment of obstructive sleep apnea: are they equally effective in short term health outcomes? *J Clin Sleep Med*. 2013;9(9):971-972.

10. Sharples LD, Clutterbuck-James AL, Glover MJ, et al. Meta-analysis of randomised controlled trials of oral mandibular advancement devices and continuous positive airway pressure for obstructive sleep apnoea-hypopnoea. *Sleep Med Rev*. 2016;27:108-124.

11. Doff MH, Finnema KJ, Hoekema A, Wijkstra PJ, de Bont LG, Stegenga B. Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on dental side effects. *Clin Oral Investig*. 2013;17(2):475-482.

12. Almeida FR, Lowe AA, Sung JO, Tsuiki S, Otsuka R. Long-term sequellae of oral appliance therapy in obstructive sleep apnea patients: Part 1. Cephalometric analysis. *Am J Orthod Dentofacial Orthop*. 2006;129(2):195-204.

13. Bacon W, Tschill P, Sforza E, Krieger J. [A device for mandibular advancement in respiratory disorders of sleep. Clinical study]. *Orthod Fr*. 2000;71(4):295-302.

14. Doff MH, Hoekema A, Pruim GJ, Huddleston Slater JJ, Stegenga B. Long-term oral-appliance therapy in obstructive sleep apnea: a cephalometric study of craniofacial changes. *J Dent*. 2010;38(12):1010-1018.

15. Fransson A. A mandibular protruding device in obstructive sleep apnea and snoring. *Swed Dent J Suppl*. 2003(163):1-49.

16. Hammond RJ, Gotsopoulos H, Shen G, Petocz P, Cistulli PA, Darendeliler MA. A follow-up study of dental and skeletal changes associated with mandibular advancement splint use in obstructive sleep apnea. *Am J Orthod Dentofacial Orthop*. 2007;132(6):806-814.

17. Hou HM, Sam K, Hägg U, et al. Long-term dentofacial changes in Chinese obstructive sleep apnea patients after treatment with a mandibular advancement device. *Angle Orthod*. 2006;76(3):432-440.

18. Ringqvist M, Walker-Engström ML, Tegelberg A, Ringqvist I. Dental and skeletal changes after 4 years of obstructive sleep apnea treatment with a mandibular advancement device: a prospective, randomized study. *Am J Orthod Dentofacial Orthop*. 2003;124(1):53-60.

19. Robertson C, Herbison P, Harkness M. Dental and occlusal changes during mandibular advancement splint therapy in sleep disordered patients. Eur J Orthod. 2003;25(4):371-376.

20. Teixeira AOB, Andrade ALL, Almeida R, Almeida MAO. Side effects of intraoral devices for OSAS treatment. *Braz J Otorhinolaryngol*. 2018;84(6):772-780.

21. Wang X, Gong X, Yu Z, Gao X, Zhao Y. Follow-up study of dental and skeletal changes in patients with obstructive sleep apnea and hypopnea syndrome with long-term treatment with the Silensor appliance. *Am J Orthod Dentofacial Orthop*. 2015;147(5):559-565.

22. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health*. 1998;52(6):377-384.

23. Knappe SW, Bakke M, Svanholt P, Petersson A, Sonnesen L. Long-term side effects on the temporomandibular joints and oro-facial

function in patients with obstructive sleep apnoea treated with a mandibular advancement device. *J Oral Rehabil*. 2017;44(5):354-362.

24. Chen H, Lowe AA, de Almeida FR, Fleetham JA, Wang B. Three-dimensional computer-assisted study model analysis of long-term oral-appliance wear. Part 2. Side effects of oral appliances in obstructive sleep apnea patients. *Am J Orthod Dentofacial Orthop*. 2008;134(3):408-417.
25. Battagel JM, Kotecha B. Dental side-effects of mandibular advancement splint wear in patients who snore. *Clin Otolaryngol*. 2005;30(2):149-156.
26. Marklund M, Franklin KA, Persson M. Orthodontic side-effects of mandibular advancement devices during treatment of snoring and sleep apnoea. *Eur J Orthod*. 2001;23(2):135-144.
27. Marklund M. Predictors of long-term orthodontic side effects from mandibular advancement devices in patients with snoring and obstructive sleep apnea. *Am J Orthod Dentofacial Orthop*. 2006;129(2):214-221.
28. Martinez-Gomis J, Willaert E, Nogues L, Pascual M, Somoza M, Monasterio C. Five years of sleep apnea treatment with a mandibular advancement device. Side effects and technical complications. *Angle Orthod.* 2010;80(1):30-36.
29. Robertson CJ. Dental and skeletal changes associated with long-term mandibular advancement. *Sleep*. 2001;24(5):531-537.

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DISCLOSURE STATEMENT

The authors report no conflicts of interest.

Table 1. Quality Index of Individual Studies

		Almeida F. et al.	Bacon W. et al.	Battagel J. and Kotecha B.	Chen et al.	Doff M. et al.	Fransson A. et al.	Hammond R. et al.	Hou H. et al.	Knappe S. et al.	Marklund M. et al	Marklund M.	Martinez J. et al.	Ringqvist M. et al.	Robertson C. et al.	Teixeira A. et al.	Wang X. et al.
		2006	2000	2005	2008	2010	2003	2007	2006	2017	2001	2006	2010	2003	2003	2017	2015
		Study 1	Study 2	Study 3	Study 4	Study 5	Study 6	Study 7	Study 8	Study 9	Study 10	Study 11	Study 12	Study 13	Study 14	Study 15	Study 16
Reporting																	
Question **1**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **2**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **3**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **4**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **5**	0 no, 1 partially, 2 yes	1	0	0	1	1	0	1	0	0	0	0	1	0	0	0	0
Question **6**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **7**	0 no, 1 yes	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1
Question **8**	0 no, 1 yes	1	0	1	0	1	0	0	1	1	1	1	1	1	1	0	1
Question **9**	0 no, 1 yes	1	0	0	0	1	1	0	1	1	0	0	1	1	1	0	1
Question **10**	0 no, 1 yes	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1
External validity																	
Question **11**	0 no, 1 yes	1	1	0	0	1	1	1	0	1	0	0	1	1	1	0	1
Question **12**	0 no, 1 yes	1	1	0	0	1	1	0	0	1	0	0	0	1	1	0	1
Question **13**	0 no, 1 yes	1	0	0	0	1	1	1	0	1	0	0	1	1	0	0	1
Internal validity - bias																	
Question **14**	0 no, 1 yes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Question **15**	0 no, 1 yes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Question **16**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **17**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **18**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **19**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Question **20**	0 no, 1 yes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Internal validity - confounding																	
Question **21**	0 no, 1 yes	0	1	0	0	1	0	1	0	0	1	1	1	1	0	0	0
Question **22**	0 no, 1 yes	0	1	0	0	1	0	0	0	0	0	0	1	1	0	0	0
Question **23**	0 no, 1 yes	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Question **24**	0 no, 1 yes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Question **25**	0 no, 1 yes	1	1	0	0	1	0	0	0	0	0	0	1	1	0	0	0
Question **26**	0 no, 1 yes	0	1	1	0	1	1	0	1	1	0	0	1	1	1	0	1
Power Questions																	
Question **27**	0, 1, 2, 3, 4, 5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Total Score		**20**	**19**	**15**	14	**23**	**16**	17	**16**	**19**	15	15	22	**22**	**18**	12	**19**
Quality		good	fair	fair	poor	good	fair	fair	fair	fair	fair	fair	good	good	fair	poor	fair

Table 2. Main characteristics of the studies included in the systematic review.

Author (year)	Type/Design of MAD	Treatment time mean	SNA (˚)	SNB (˚)	ANB (˚)	Facial Height (mm)	Mandibular Plane Angle (˚)	Overjet (mm)	Overbite (mm)	Upper teeth position (˚)	Lower teeth position (˚)
Almeida F. et al. (2006)	Klearway	7.3 y	Class I subgroup, from 0.9˚ (<6 y) to -0.8˚ (>8y)	N/A	+0.5˚	TAFH: +1.8; ALFH: +1.8	SN-MP: +0.7˚; PP-MP: +1.0˚. SN-MP from -0.1˚ (<6 y) to 1.9˚ (>8y)	-2.6	-2.8	U1-SN: -3.1˚; U1-PP: -3.5˚	L1-MP: + 6.6˚
Bacon W. et al. (2000)	Twin Block type joined into single unit	2 y	N/S change	+1.7˚	N/A	TAFH: + 7.4	SN-MP: +3˚	N/A	N/A	N/A	N/A
Battagel J. and Kotecha B. (2005)	Herbst Mandibular Advancement Splint	2 y	N/A	N/A	N/A	N/A	N/A	-0.5	-0.4	N/A	N/A
Chen et al. (2008)	Klearway	7.4 y	N/A	N/A	N/A	N/A	N/A	-1.15 to -1.55	-1.25 to -1.69	N/A	N/A
Doff M. et al. (2010)	Thornton Adjustable Positioner	2 y	N/S change	-0.4˚	N/A	TAFH: +0.9; ALFH: +0.8	N/A	-1.7	-1	UI-MxP: -2˚	LI-MP: +3.7˚
Fransson A. (2003)	Heat Cured MMA Resin MAD	2 y	N/S change	-0.4˚	N/A	TAFH: + 0.7	SN-MP: + 0.4˚	-0.5	-0.8	N/A	LI-MP: + 1.5˚
Hammond R. et al. (2007)	2 Piece Acrylic Design	25 m	N/S change	N/S change	N/S change	N/S change	N/S change	-0.2	-0.3	N/S change	proclination: +0.96˚, protrusion: +0.52 (in mm)
Hou H. et al. (2006)	Harvold Monoblock Type of Functional Appliance	3 y	N/S change	N/S change	N/A	TAFH: +0.7; ALFH: +0.8; LPFH: +0.6; TPFH: +0.4	MP-SN: +0.3˚	> 3y: -0.8	-0.6	N/A	N/A
Knappe S. et al. (2017)	2 Piece Custom Made Hard Acrylic Design	3 y	N/A	N/A	N/A	N/A	N/A	N/A	-1.1	N/A	N/A
Marklund M. et al (2001)	Monoblock MAD with full occlusal coverage	2.5 y	N/A	N/A	N/A	N/A	N/A	-0.4	-0.4	N/A	N/A
Marklund M. (2006)	Monoblock MAD with full	5 y	N/A	N/A	N/A	N/A	N/A	-0.6	-0.6	N/A	N/A

	occlusal coverage										
Martinez J. et al. (2010)	2 Full Coverage Acrylic Splints	4.8 y	N/A	N/A	N/A	N/A	N/A	>14m: -0.76, >21m: -0.85, > 58m: -1.1	>14m: -0.58, >21m: -0.72, > 58m: -0.81	N/A	N/A
Ringqvist M. et al. (2003)	Monoblock MAD	4 y	N/S change (A-A')	-0.6 (B-B' in mm)	N/A	N/A	SN-MP: +0.5 ˚	N/S change	N/S change	N/S change	N/S change
Robertson C. et al. (2003)	Non-adjustable Rigid Splint	2 y	+0.32˚	N/A	+0.29˚	TAFH: + 0.76	N/A	-0.87	-0.61	-1.58˚	L1-MP: +2.71˚
Teixeira A. et al. (2017)	Twin Block	6.4 m	N/A	N/A	N/A	N/A	N/A	-0.61	-0.76	N/A	IMPA: +2.2˚
Wang X. et al. (2015)	Silensor Appliance	4 y	N/S change	N/S change	N/S change	TAFH < 3 y: +1.21, > 3 y: +1.56; ALFH < 3 y: +1.46, > 3 y: +1.52	MP-FH: < 3 y: +1.25˚, > 3 y: +1.48˚	> 4y: -1.03	<3 y: -0.59, > 4y: -1.01	U1-SN: -1.49˚; U1-NA: -1.41˚	L1-MP: +0.94 ˚; L1-NB: + 1.02˚

ALFH, anterior lower facial height; FH, Frankfort horizontal plane; LPFH, lower posterior facial height; MP, mandibular plane; MxP, maxillary plane; N/A, not applicable; N/S, not significant; OB, overbite; OJ, overjet; TAFH, total anterior facial height; TPFH, total posterior facial height.

Appendix 1. Databases and individualized truncations of words.

Database ***(Up to Jan 05, 2020)***	***Key words & search truncation***
Medline (N= 89**)** (Ovid) http://ovidsp.tx.ovid.com	Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily <1946 to January 05, 2020> Search Strategy: -- 1 mandibular advancement device.mp. (280) 2 limit 1 to humans (212) 3 sleep*.mp. (199211) 4 appliance.mp. (12795) 5 device.mp. (264716) 6 vertical*.mp. (123359) 7 4 or 5 (276566) 8 3 and 7 (4058) 9 1 or 8 (4065) 10 6 and 9 (89)
EMBASE (N= 105**)** (Ovid) http://ovidsp.tx.ovid.com	Database: Embase <1974 to January 05, 2020> Search Strategy: -- 1 mandibular advancement device.mp. (473) 2 sleep*.mp. (312611) 3 appliance.mp. (10326) 4 device.mp. (578370) 5 vertical*.mp. (130946) 6 3 or 4 (583956) 7 2 and 6 (10969) 8 1 or 7 (10978) 9 5 and 8 (121) 10 limit 9 to human (105)

PubMed (N= 426**)** http://www.ncbi.nln.nih.gov/pubmed	#1 Add Search mandibular advancement device 2816 #2 Add Search sleep 204329 #3 Add Search appliance 12851 #4 Add Search device 1600579 #5 Add Search vertical 112290 #6 Add Search (#3 or #4) 1609953 #7 Add Search (#2 and #6) 9309 #8 Add Search (#1 or #7) 11381 #9 Add Search (#8 and #5) 426
Cochrane (N= 14**)**	Search Name: Date Run: 01/05/2020 Comment: ID Search Hits #1 sleep 35138 #2 mandibular advancement 422 #3 #1 and #2 282 #4 vertical 5903 #5 #3 and #4 15
LILACS (N= 20**)** lilacs.bvsalud.org	Sleep Apnea, Obstructive/therapy, Snoring, Mandibular Advancement / instrumentation, Cephalometry, Polysomnography, Treatment Outcome, Sleep Apnea Syndromes/diagnosis Sleep Wake Disorders/diagnosis.