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Mandibular Advancement Devices for Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis

Keywords

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ABSTRACT

Background: This systematic review and meta-analysis aimed to evaluate the effectiveness of mandibular advancement devices (MADs) in treating Obstructive Sleep Apnea (OSA), focusing on the impact of age and body mass index (BMI) on the apnea-hypopnea index (AHI) and minimum oxygen saturation (min SpO_2). Methods: A literature search was conducted in PubMed and Google Scholar for studies published from January 2013 to January 2023. Two independent authors screened the studies, assessed and evaluated risk of bias. Disagreements were resolved by consensus or consultation with a third reviewer and senior experts. The initial search yielded 1110 references, with 13 selected for inclusion. Results: MADs significantly reduced AHI and increased min SpO_2 in OSA patients. The mean difference in AHI was 15.75 (95% CI 13.19–18.30, p <0.00001). Minimum SpO_2 improved post-treatment (-3.70, 95% CI-5.52 to-1.88, p < 0.00001, Z = 3.98). Conclusion: This meta-analysis demonstrated that MADs effectively reduced AHI severity and increased min SpO_2 in OSA patients. While BMI had no significant effect, age had a notable impact on treatment outcomes.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by repeated episodes of complete or partial upper airway obstruction during sleep, followed by decreased arterial blood oxygen saturation and/or arousal.[1,2]. It affects 9%-38% of adults and 2% -5 % of children worldwide.[3] Symptoms of OSA include snoring, shortness of breath during sleep, waking up tired in the morning, headache, daytime sleepiness, and attention problems, which may lead to traffic accidents, heart problems, hypertension, gastroesophageal reflux, and sexual reluctance.[4,5] Although the etiology of OSA is multifactorial, it is associated with age, gender, weight, pathological and anatomical factors of the upper airways, and sleeping positions.[6]

OSA patients are diagnosed with overnight polysomnography (PSG), split-night PSG, or home sleep apnea testing (HSAT). An attended overnight PSG is considered the gold-standard diagnostic test for OSA.[7] According to the American Academy of Sleep Medicine (AASM) and American Academy of Dental Sleep Medicine (ADSM) Clinical Practice Guideline (2015), AHI severity is determined in three categories:[8-10] Mild OSA (AHI 5.0-14.9 events/h), moderate OSA (AHI 15.0-29.9 events/h), and severe OSA (AHI ≥30.0 events/h), respectively.

Treatment options for OSA include continuous positive airway pressure (CPAP), lifestyle changes, mandibular advancement devices (MAD), and surgery.[11-13] Even though CPAP is accepted as the gold standard method in the treatment of OSA, adherence to CPAP is challenging due to mask problems, difficulties in receiving the device, and cost.[11,14] Lifestyle changes include losing weight and avoiding alcohol and sedatives. Surgical treatments include upper airway interventions for nasal pathologies, tonsillectomy, and uvulopalatopharyngoplasty (UPPP), but the success rate is not high. MADs have now been preferred more and more by patients, particularly the ones who cannot tolerate CPAP therapy.[15] MAD comprises one- or two-piece plates attached to the upper and lower jaws. The working mechanism involves moving the lower jaw, tongue, and soft palate forward, thereby preventing the soft tissues at the back of the throat from collapsing during sleep.[16]

The effects of age and BMI on OSA are known. When previous systematic reviews and meta-analyses were examined, no study was found that simultaneously investigated the impact of age and BMI on MAD treatment.

Two studies investigated characteristic phenotypes among non-responders.[17,18] Imran H. Iftikhar *et al*., analyzed the relative effectiveness of MADs in treating sleep apnea. Four investigations compared the efficacy of CPAP and MAD in managing OSA.[19]

Research by Linda D. Sharples *et al*., revealed that although CPAP was generally more effective, MAD was particularly suitable for patients with mild OSA or those who could not tolerate CPAP.[20] Meanwhile, Martha Schwartz *et al*. reported that, while CPAP significantly reduced AHI, there was no notable difference between CPAP and MAD regarding quality of life and cognitive or functional outcomes—likely due to lower patient compliance with CPAP.[21]

The Epworth Sleepiness Scale (ESS) is a self-assessment tool designed to assess your likelihood of falling asleep during the day. It includes eight questions based on common situations that might make you feel drowsy, with responses rated on a scale from 0 (never doze off) to 3 (high chance of dozing off).

The analysis by Pattipati M. *et al*., observed that both MAD and CPAP decreased AHI and improved nadir oxygen saturation in OSA patients. However, no significant difference in ESS was found before and after treatment.[22] The study by Grietje E. de Vries *et al*. systematically reviewed the effects of oral appliance therapy (OAT) on a wide range of cardiovascular outcomes.[23] The study by Vimal Jyotsna *et al*. examined twenty-one randomized controlled trials to compare the efficacy of non-surgical treatment modalities for OSA, specifically CPAP, MAD, and sham.[24] ALQarni *et al*., assessed the effectiveness of vibrotactile positional therapy (PT) devices in positional OSA patients and found these devices to be effective in treating POSA.[25] In their meta-analysis and systematic review, Krishnamurthy P. *et al*. explored the impact of complete dentures and mandibular enhancement devices in treating edentulous OSA patients.[26] A meta-analysis by Hasthi U Dissanayake *et al*. examined the effect of OSA treatment on cardiovascular autonomic function.[27] Research by Christian Calvo-Henríquez *et al*. evaluated, through Rhinomanometry (RMM) analysis, the effect of the supine position on nasal airway resistance by comparing measurements taken before and after assuming the supine position and found that lying down increases nasal resistance while reducing nasal airflow.[28] In their study, You-Ning Gao *et al*. compared recommended treatments for OSA in adults, reporting that MAD ranked second to PAP in reducing the severity of AHI, exercise was most effective in reducing ESS, and overall, PAP, MAD, and positional therapy proved superior in reducing AHI and ESS—with lifestyle change being the least effective treatment option.[29] The evaluation by Madeline J. L. Ravesloot *et al*. determined that PT effectively improved sleep study variables and reduced sleepiness, providing evidence that new-generation PT devices significantly reduced AHI in short-term follow-up.[30] The analysis by Anna Alessandri-Bonetti *et al*. examined the relationship between MAD use and TMD symptoms, finding that pre-existing symptoms increased.[31] Research by Maria Lavinia Bartolucci *et al*. investigated the effectiveness of different Research by Maria Lavinia Bartolucci *et al*. investigated the efficacy of different MAD designs (monoblock and duo-block) in reducing AHI and improving oxygen saturation in OSA patients. While the monoblock design was associated with improved minimum oxygen saturation compared to the duo-block, the evidence suggesting that monoblock MADs were more effective in reducing AHI and enhancing minimum oxygen saturation was of very low quality, as rated by the study.[20] An investigation by Takafumi Araie *et al*. evaluated changes in dental and skeletal structures following long-term use of oral appliances in OSA patients, observing dental alterations. In contrast, skeletal structures remained unchanged.[32]

Existing literature has explored the effects of MADs on the treatment of obstructive sleep apnea, but a comprehensive evaluation of how age and body mass index influence the apnea-hypopnea index and minimum oxygen saturation in pre-treatment and post-treatment polysomnography evaluations is still lacking. This gap in research motivated this systematic literature review and meta-analysis, which aims to evaluate the efficacy of MADs in treating OSA by determining the impact of age and BMI on AHI and min SpO_2 in pre-treatment and post-treatment PSG evaluations.

METHODS

SCIENTIFIC DATABASES AND STUDY IDENTIFICATION

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations to identify relevant articles published over the last 10 years. Two independent authors (E.G. and H.K.) selected studies by screening titles and full abstracts, followed by a full-text analysis of the identified articles. Any disagreements were resolved by consensus or consultation with a third reviewer (H.B.), and senior experts (M. Ö. and V. C.) gave the final evaluation and approval of the review. For each article, data extracted included the authors, the year of publication, and the PICO items. Our study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (registration number CRD42023445707).

A comprehensive literature search was performed in PubMed and Google Scholar to identify all relevant studies published between January 2013 and January 2023. A unified search strategy was employed across both databases using the following search string: ("obstructive sleep apnea" OR "OSA" OR "positional sleep apnea") AND ("apnea-hypopnea index" OR "AHI decrease" OR "AHI improvement") AND ("mandibular advancement device" OR "MAD" OR "oral appliance"). Filters were applied to restrict results to articles published in English. Additionally, the reference lists of all included studies were manually screened to identify further relevant articles. This approach ensured that our review captured all studies meeting the predefined inclusion criteria.

STUDY SELECTION

The authors searched all papers from English-language articles with publication dates within the last 10 years (January 2023-2013). The search used a combination of the following key terms: 'Positional OSA or ahi decrease or mad or mas.'

DATA INCLUSION CRITERIA

Primary clinical outcomes relevant to this analysis included AHI and min SpO_2.

- English-language articles published between January 2013 and January 2023.
- Human studies with adult participants (age ≥18 years).
- Accepted designs included randomized controlled trials (RCTs), non-randomized controlled trials, controlled clinical trials, and observational studies (both prospective and retrospective) that provided sufficient quantitative data for analysis.
- Studies diagnosing OSA using objective methods (e.g., polysomnography).
- Studies utilizing MAD treatment as the sole intervention.
- Studies reporting pre-treatment and post-treatment data for AHI and min SpO_2, including standard deviations.
- Studies providing demographic data such as age and BMI.

DATA EXTRACTION CRITERIA

- Non-human studies.
- Studies on children or adolescents (age <18 years).
- Studies involving edentulous patients.
- Studies that combined MAD treatment with other interventions (e.g., CPAP, orthodontics, or surgery).
- Studies with missing critical data (e.g., lacking the number of participants or measures of variability necessary for quantitative synthesis).

QUALITY ASSESSMENT

One author evaluated the quality of the studies included in the meta-analysis using the NIH (National Institute of Health) Quality Assessment Tool (2014).[23]

RISK OF BIAS ASSESSMENT

Our study assessed the overall risk of bias using the ROBIS (Risk of Bias In Systematic Reviews) tool. Following ROBIS guidelines, our review process was structured into key domains, including study eligibility criteria, study identification and selection, data collection and appraisal, and synthesis of findings. Two independent reviewers conducted study selection and data extraction, and any disagreements were resolved by consensus or consultation with a third reviewer. By adhering to these procedures, we minimized the risk of bias in our review and ensured that our findings were robust and reliable.

Subsequently, publication bias among reviews was investigated. Publication bias refers to the selective publication of research findings based on their statistical significance or the direction and magnitude of their results. It occurs when studies with statistically significant or positive results are more likely to be published. In contrast, studies with non-significant or negative results are suppressed or less likely to be published. More generally, publication bias is an error system that occurs in inference from studies that are conditioned by the state of publication (Begg & Berlin, 1988). Standard distribution plots and Funnel Plots, the Begg Mazumdar Rank Correlation test, and the Egger Regression Test are graphical methods to detect publication bias in meta-analysis results.

STATISTICAL ANALYSIS

This study synthesized mean and standard deviation (Body Mass Index (BMI), age, AHI, min SpO_2). Our meta-analysis reported all the outcomes using the random-effects model (Der Simonian-Laird method) to account for interstudy variability. We evaluated heterogeneity between the studies of the Cochran Q test and the inconsistency index (I^2), each of which has been proposed to quantify the degree of heterogeneity between studies.

The usual way of assessing true heterogeneity in the meta-analysis that Cochran (1954) described was Q statistics.

The Q test statistics,

$$Q = \sum_{i=1}^{k} w_i y_i^2 - \frac{\left(\sum_{i=1}^{k} w_i y_i\right)^2}{\sum_{i=1}^{k} w_i} \qquad Q = \sum_{i=1}^{k} w_i (y_i - \overline{y})^2$$

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is obtained with this formula. The Q statistic is calculated by summing the squared deviation from the overall effect estimate, weighting the contribution of each study via inverse variance. The I^2 index, also known as the I-squared statistic, is a measure of true heterogeneity separating the Q test result from the difference in degrees of freedom (k - 1) from the Q value and is multiplied by 100. Thus, its index is similar to the within-class correlation in the cluster sample.

A multivariate meta-regression analysis was performed to explore heterogeneity. Meta-regression is an extension of the standard meta-analysis that examines the extent to which statistical heterogeneity among the results of multiple studies may be related to one or more characteristics of the studies. We assessed publication bias by using the Egger regression method and funnel graph. We performed statistical analyses by using Open Meta-Analyst (CEBM @ Brown), Jamovi, Review Manager 5.3 (RevMan) program, developed by the Cochrane Collaboration, and SPSS 25.0 (SPSS, Chicago). We considered a P value $\leq$ .05 as significant. Since this study is heterogeneous, a random effects model was used to model between-group variation.

RESULTS

A total of 1110 studies were identified. Non-full text and non-English articles were excluded. After screening titles and abstracts, 619 articles were excluded for lack of relevant data, inappropriate study design, or not meeting the inclusion criteria. Of the remaining 491 articles, 13 studies ultimately met all inclusion criteria and were included in the analysis.[33-45] The PRISMA flow diagram in Figure 1 summarizes the selection process. A full report on all these articles according to the PICO criteria is available in Table 1.

First, the descriptive statistics of the studies were calculated, the histogram graph was drawn, and the AHI and SpO_2 values in the pre-and post-groups were compared *(Table 2, Figure 2)*.

- The mean age was 50.61 ± 4.083 years.
- The mean BMI value was 27.32 ± 2.65 kg/m².
- The AHI value before and after treatment was 27.82 ± 8.67; 11.45 ± 4.55 events/hour.
- The minimum SpO_2 value was 81.47 ± 3.37%; 85.36 ± 2.32%.

THE EFFECT OF MANDIBULAR ADVANCEMENT DEVICES ON APNEA-HYPOPNEA INDEX

In this study, the results of the Q test statistic (45.90) and the I^2 statistic (74%) (P <0.00001) in determining the heterogeneity between studies are presented in Figure 3.

A meta-analysis of 13 studies (pre-treatment and post-treatment AHI reduction) was performed to evaluate the effect of the method *(Table 3)*. Four studies assessed a total of 651 people with OSA who were referred to MMA, showing a significant difference in favor of treatment. When comparing the pre-treatment and post-treatment AHI, the mean difference was 15.75 (DM = 15.75), 95% CL 13.19 to 18.30, p < 0.00001)

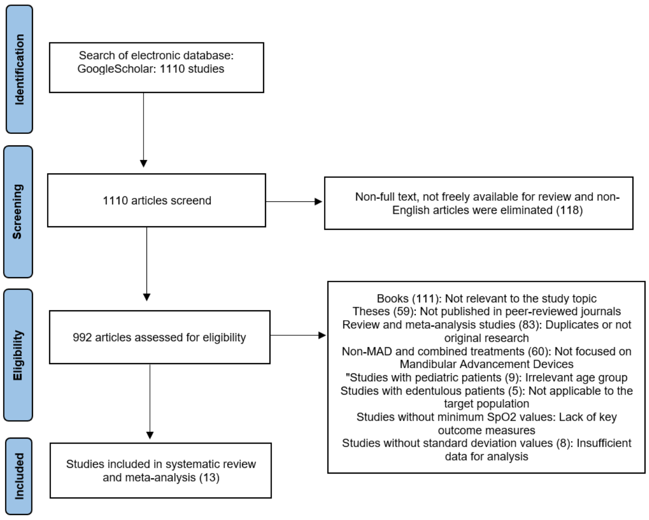

Figure 1: A PRISMA flow diagram shows the articles identified at each search stage.

(Figure 3). The fact that the total diamond-shaped effect size does not touch the 0 (zero) line shows that the relationship is significant (Graph 1). If the confidence interval of the effect size does not include zero, it indicates that the relationship is statistically significant. In summary, it has been observed that the treatment makes a difference.

Funnel plots were drawn in the study. The funnel chart traditionally has a function of effect size on the horizontal axis and standard error on the vertical axis. Estimates of the extensive review graph are accurately determined at the top and close to average effect sizes. The results of the meta-analysis of publication bias in the studies included in the meta-analysis under the random effect model are given below. Funnel plot *(Figure 4)*, Egger regression test Begg, and Mazumdar Rank Correlation test results are available *(Table 3)*.

The Egger regression test result (p=0.256) and the funnel plot are symmetrical in the 95% confidence region with no publication bias. As a result of the meta-regression analysis, it is observed that the variable that affects heterogeneity is age (P=0.019).

THE EFFECT OF MANDIBULAR ADVANCEMENT DEVICE ON MINIMUM OXYGEN SATURATION (SPO_2)

To evaluate the effect of the method on min SpO_2, 13 studies (pre-min SpO_2 – post-min-SpO_2) *(Figure 5)* were assessed. The mean difference (pre-min SpO_2-post min-SpO_2) was calculated. In summary, it was observed that the treatment made a difference (-3.70, 95% CL -5.52 to -1.88, p < 0.00001, Z=3.98). The min SpO_2 values increased after the treatment *(Figure 5)*.

Subsequently, publication bias among studies was investigated. The funnel graph was drawn in the study *(Figure 6)*. The results of the meta-analysis conducted in the JAMOVI program of publication bias under the random effect model of the studies included in the meta-analysis are given below. Below are the Funnel graph, Egger regression test, and Begg and Mazumdar Rank Correlation test results. According to these results, it can be said that there is no publication bias at the confidence level (p>0.05).

Table 1. PICO components of relevant studies, showing the patient population, intervention applied, comparison group, and results obtained for each publication.

Author, Year	P (Population)	I (Intervention)	C (Comparison)	O (Outcome)
Phillips et al., 2013	Adult patients with moderate-to-severe OSA diagnosed by polysomnography	Continuous Positive Airway Pressure (CPAP) treatment	Oral appliance (mandibular advancement device) treatment	Improvement in health outcomes (AHI reduction, enhanced sleep quality, decreased daytime sleepiness, improved quality of life)
Banhiran et al., 2014	Adult OSA patients	Adjustable thermoplastic MAD	Pre-treatment vs. post-treatment evaluation (single-arm design)	Reduction in AHI, improved oxygen saturation, and assessment of device practicability and patient compliance
Lin et al., 2015	Adult OSA patients	Oral appliance (MAD) treatment	Pre-treatment vs. post-treatment comparison	Improvement in endothelial function (e.g., enhanced Flow-Mediated Dilation)
Durán-Cantolla et al., 2015	Adult OSA patients	Mandibular advancement device (MAD) treatment	Randomized controlled crossover design (MAD period vs. control/sham period)	Efficacy in reducing AHI and enhancing sleep parameters
Takaesu et al., 2016	Patients with positional OSA	MAD treatment	Nasal CPAP treatment	Comparable efficacy in AHI reduction and oxygenation improvement
Lee et al., 2016	Adult OSA patients receiving non-CPAP treatment	Oral appliance / other non-CPAP interventions	Comparison of different success definitions (using cardiopulmonary coupling criteria)	Determination of treatment success through improved cardiopulmonary coupling and related sleep indices
Kim et al., 2018	Adult OSA patients	MAD treatment	Pre-treatment vs. post-treatment cephalometric analysis	Soft palate morphological changes associated with polysomnographic improvement (e.g., AHI reduction)
Marco Pitarch et al., 2018	Adult OSA patients	MAD treatment	Pre-treatment vs. post-treatment evaluation	Reduction in AHI and overall improvement in sleep parameters
Wee et al., 2018	Adult OSA patients undergoing MAD treatment	MAD treatment	Comparison based on different success criteria (long-term symptom resolution vs. new-onset hypertension)	Long-term symptom improvement and evaluation of hypertension incidence
Uniken Venema et al., 2020	Adult OSA patients	MAD treatment (with CPAP as comparator)	Long-term follow-up comparing MAD vs. CPAP	Assessment of long-term outcomes, including AHI improvement, treatment compliance, and overall health over 10 years
Lee et al., 2020	Adult OSA patients	Sleep surgery	MAD treatment	Comparison of effects on nocturnal cardiac autonomic activity
Rocha et al., 2021	Public transport drivers with OSA	MAD treatment	Pre-treatment vs. post-treatment evaluation	Reduction in daytime sleepiness, improved quality of life, and enhanced polysomnographic profile
Chiaro et al., 2021	Adults with mild to moderate OSA	New mandibular oral device (MAD)	Pre-treatment vs. post-treatment comparison	Improvement in polysomnographic parameters (e.g., AHI reduction, better oxygen saturation)

Table 2. Descriptive statistics of study parameters.

	Minimum	Maximum	Mean	Std. Deviation
Age	45.54	61.00	50.618	4.08332
BMI	24.10	32.40	27.3238	2.64671
Pre-min SpO_2 mean	75.40	87.10	81.4723	3.37159
Post-min SpO_2 mean	83.00	90.40	85.3654	2.32444
Pre-AHI mean	15.30	44.00	27.8238	8.67207
Post-AHI mean	4.80	21.30	11.4469	4.55435

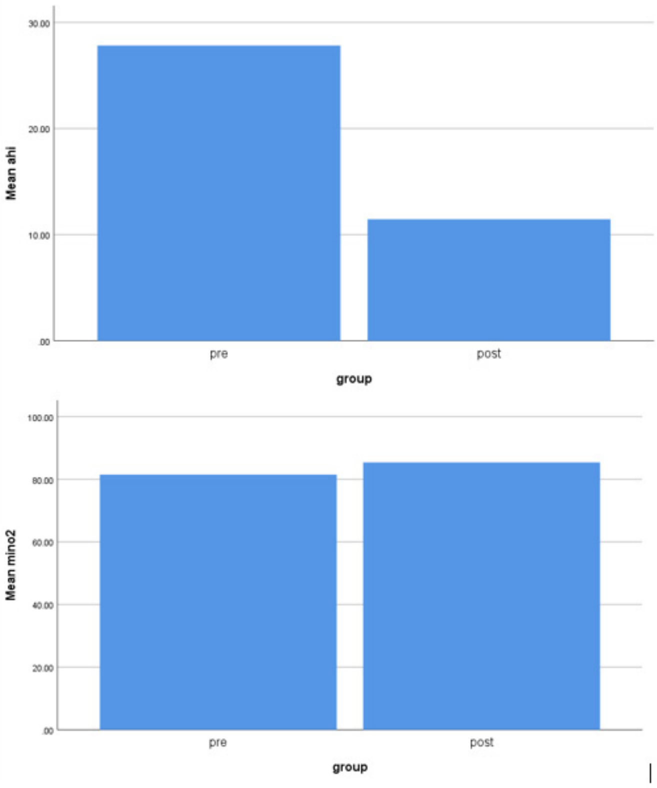

Figure 2: Distribution of pre- and post-AHI (left) and SpO_2 (right).

In the meta-regression analysis, the variable year significantly affected heterogeneity (p = 0.048 < 0.05). This result suggests that the distribution of studies over time may have influenced the heterogeneity in the meta-analysis. In other words, factors or methodological differences that varied across the years of the studies could have contributed to increased variability (heterogeneity) in the overall effect size.

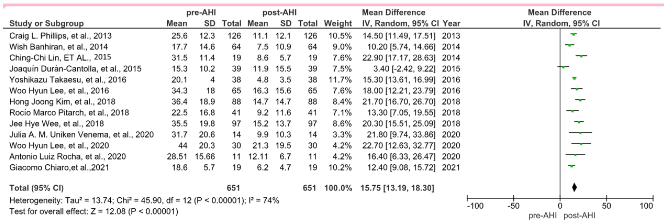

Figure 3: Meta-analysis: comparison of AHI pre- and post-treatment.

Table 3. Descriptive statistics of study parameters.

Publication Bias Assessment

Test Name	Value	P
Fail-Safe N	2732.000	<0.001
Begg and Mazumdar Rank Correlation	0.128	0.590
Egger's Regression	1.136	0.256
Trim and Fill Number of Studies	3.000	.

Note. Fail-safe N calculation using the Rosenthal approach

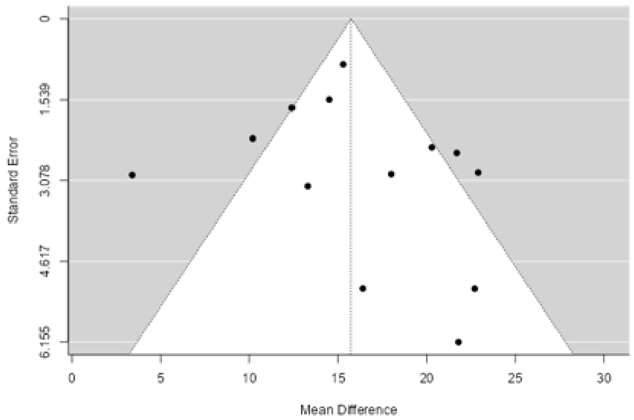

Figure 4: Funnel plot for AHI.

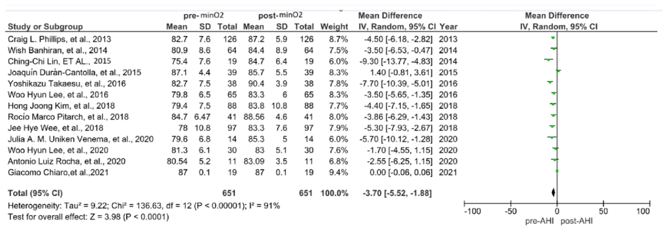

Figure 5: Comparison of min SpO_2 pre-treatment and post-treatment.

According to the results of the meta-analysis, it was concluded that MADs were effective in treating OSA, reduced AHI in 651 individuals in the sample, and increased min SpO_2.

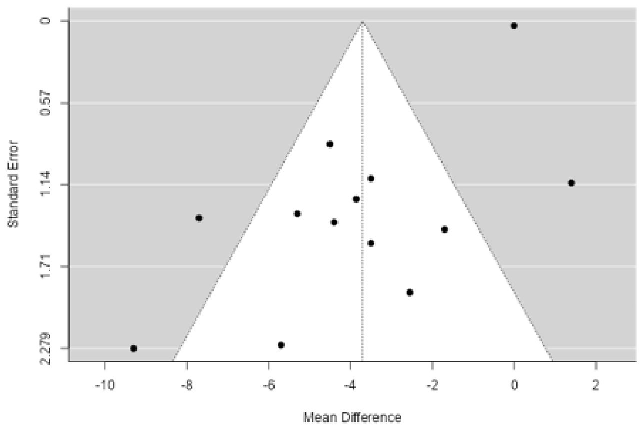

Figure 6: Funnel graph of minimum SpO_2.

DISCUSSION

This updated meta-analysis, including 651 participants, confirms the efficacy of mandibular advancement devices (MADs) in treating obstructive sleep apnea (OSA). Our results demonstrate a significant reduction in the apnea-hypopnea index (AHI) and an improvement in minimum oxygen saturation (min SpO_2) following MAD treatment, consistent with previous studies.

The present study shows that MAD treatment substantially decreases AHI and increases min SpO_2 in OSA patients. These improvements alleviate the severity of OSA symptoms and improve overall sleep quality.

Prior research indicates that the mechanical design of MADs can influence treatment outcomes. For instance, Iftikhar *et al.*[19] reported that devices with attached midline traction and unattached bilateral interlocking yielded the highest performance scores for AHI reduction and improved sleep parameters such as ESS and min SaO_2. Similarly, although the supporting evidence is limited, Bartolucci *et al.*[20] found that monoblock designs might improve oxygen saturation more effectively than duo-block designs.

Several studies have compared MADs with continuous positive airway pressure (CPAP) therapy. While CPAP often achieves more significant reductions in AHI, its effectiveness is sometimes offset by lower patient compliance. Meta-analyses by Schwartz *et al.*[21] and Pattipati *et al.*[22] suggest that despite CPAP's superior efficacy in specific measures, both modalities yield comparable outcomes regarding quality of life, cognitive performance, and overall patient satisfaction, particularly in cases of mild to moderate OSA.

In addition to MADs and CPAP, alternative non-surgical treatments have been investigated. Vibrotactile positional therapy (PT) devices, as described by ALQarni *et al.*,[25] have been shown to be effective in reducing AHI and the time spent in the supine position. In edentulous patients, complete dentures have also been used; however, the effectiveness of dentures as an oral appliance does not appear as robust as that of MADs.[26]

Meta-analytical findings indicate that specific clinical characteristics such as younger age, female gender, lower BMI, smaller neck circumference, and less severe baseline AHI predict a more favorable response to MAD treatment.[17] Identifying these predictors can aid in selecting patients who are likely to benefit most from this therapy.

Despite their benefits, MADs may lead to side effects. Increased temporomandibular joint symptoms have been reported,[31] and long-term use can result in dental and skeletal changes, such as alterations in overjet and overbite.[32] Clinicians should consider these potential drawbacks when recommending MAD therapy.

Beyond improvements in respiratory parameters, MAD treatment appears to influence autonomic function favorably. Dissanayake *et al.*[27] observed a reduction in sympathetic activity after OSA treatment. Meanwhile, de Vries *et al.*[23] noted that oral appliance therapy is comparable to CPAP in lowering blood pressure and improving other cardiovascular outcomes.

Increased nasal airway resistance associated with the recumbent position can affect treatment efficacy. Findings by Calvo-Henríquez *et al.*[28] suggest that nasal resistance increases and airflow decreases when patients lie down, an aspect that may be relevant in optimizing both CPAP and MAD therapies.

A key observation from this meta-analysis is that age plays a significant role in treatment outcomes—older patients tend to show more pronounced improvements, likely due to age-related decreases in upper airway muscle tone. In contrast, BMI did not significantly influence the efficacy of MAD treatment, indicating that factors other than adiposity may be more critical in determining therapeutic success.

CONCLUSION

Mandibular advancement device significantly reduces AHI and increases min SpO_2 in obstructive sleep apnea patients. BMI had no significant effect when BMI and age were evaluated to improve obstructive sleep apnea, where age was found to be essential data. Further research is needed to examine the effects of BMI and age on MAD treatment in OSA patients.

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