Comparative evaluation of Continuous positive airway pressure and mandibular advancement device in the treatment of obstructive sleep apnea: a systematic review and meta-analysis

Original Article

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ABSTRACT

BACKGROUND: The goal of this study was to review relevant randomized controlled trials in order to determine efficacy of continuous positive airway pressure (CPAP) with those mandibular advancement devices (MAD) in treatment of patients with obstructive sleep apnea (OSA).

METHODS: An electronic search was performed using appropriate keywords, in MEDLINE, PubMed, EMBASE, and Cochrane Library from 2018 to November 2021, to select randomised controlled trials (RCTs) comparing the effects of continuous positive airway pressure, mandibular advancement devices in reducing Apnea-Hypopnea Index (AHI), Epworth Sleepiness Scale score in adult OSA patients. Inclusion criteria were the diagnosis of OSA and success evaluation performed with a polysomnography, follow-up of 12 months. The processes of study search, selection, data extraction, assessment of risk of bias and evaluation of evidence quality were conducted independently by two reviewer authors. Meta-analyses were performed in Review Manager 5, Stata11.0 and Stats Direct 2.7.9.

RESULTS: Five RCTs were finally included in this review. A total 121 patients in CPAP group and 103 in the MAD group. Compared with MAD, CPAP significantly decreased AHI (WMD: 3.33, 95%CI: 0.05, 6.60). However, in Epworth sleepiness scale score after therapy between MAD group 59 patients and CPAP group 75 patients there was no significant difference seen in both groups (WMD: 0.59, 95%CI: -1.60, 2.77).

CONCLUSION: CPAP yielded better polysomnography outcomes, especially in reducing AHI, than MAD. Though, similar results from MAD and CPAP in terms of clinical and other related outcomes were found, suggesting that it would appear proper to offer MAD to patients who were intolerable to CPAP.

KEYWORDS: Continuous positive airway pressure, Mandibular advancement devices, Obstructive sleep apnea.

INTRODUCTION:

Obstructive sleep apnea (OSA) is a sleep disorder in which airflow stops or decreases significantly during breathing efforts. The prevalence of symptomatic obstructive sleep apnea in adults is estimated at 3 to 30%, with the disease being more common in men than in women.[1] OSA is a common chronic sleep breathing disorder characterized by recurrent episodes of complete and incomplete upper airway obstruction during sleep. OSA is characterized by snoring, apnea, or suffocation-induced sensations in the sleep, deteriorated sleep quality, gastro-esophageal reflux, increased nocturnal urination or enuresis, dry mouth, salivation during sleep, grinding of teeth at the time of sleep, nocturnal seizures, and morning headaches, daytime sleepiness, fatigue, memory loss and sexual dysfunction.[2]

One of the most common symptoms of obstructive sleep apnea is to experience excessive sleepiness during the day time. This can have a negative impact on work potency, quality of life and leads to increased road traffic accidents.[3] The Epworth Sleepiness Scale[4] (ESS) is the most used tool to measure daytime sleepiness and average propensity in people with obstructive sleep apnoea. It is a self-administered questionnaire that can help determine one's level of daytime sleepiness and average sleep tendency in eight typical daily scenarios. Each scenario is rated as

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either 0 (would never fall asleep), 1 (slight chance of dozing), 2 (moderate chance of dozing), or 3 (high chance of dozing). The scores are then summed to give an overall score between 0 and 24, with ESS scores of 10 being considered normal.[5] However, despite its subjective nature, the ESS remains a commonly used tool in clinical trials and daily clinical practice due to its ease of use, simplicity, and reliability.[1]

The diagnosis of OSA/hypopnea syndrome is based not only on history, self-examination, and evidence of clinical features, but also requires evidence of abnormal respiratory events with polysomnography (PSG) or home apnea testing. Although quantitative postoperative analysis using apnea-hypopnea index (AHI) reduction is the standard measure for assessing successful surgical outcomes, the value of the subjective assessment of postoperative sleepiness and quality of life derived from these surveys should not be underestimated. The total number of apnea and hypopnea events divided by the total hours of sleep observed on an electroencephalogram gives the AHI.[6]

Obstructive sleep apnea can be effectively treated with continuous positive airway pressure, which is considered the gold standard of care. Continuous positive airway pressure (CPAP) therapy can relieve patients' upper airway obstruction, effectively correct the onset of sleep apnea, relieve and correct hypoxemia and hypercapnia. However, compliance with CPAP treatment is not ideal. Mandibular Advancement Device (MAD) has been increasingly used in clinical practice in recent years and has become the first treatment choice for patients with mild to moderate OSA as well as for severe patients who cannot tolerate CPAP treatment.[7]

Many randomized trials had compared the outcomes of MAD versus CPAP in the treatment of patient with OSA, most of which indicate that MAD are less effective in reducing AHI but are preferred over CPAP however, none of this trial has been done for longer follow up period. Therefore, this systematic review along with a meta-analysis was planned to evaluate the efficacy of CPAP versus MAD at 1 year follow up for the treatment of OSA, and to provide a basis for the selection of clinical treatment.

METHODS:

This systematic review was structured according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines 2009.[8]

Search strategy:

To identify studies pertaining to the clinical results of CPAP versus MAD in the treatment of OSA, we reviewed the Cochrane library, PubMed, and Embase databases for relevant articles published through November 2021. We also reviewed the references of all identified articles to identify additional studies. Search terms were as follows: CPAP, continuous positive airway pressure, nasal continuous positive airway pressure, continuous positive airway pressure, MAD, mandibular advancement device, adjustable mandibular advancement device, mandibular advancement device treating, oral appliances, OA, obstructive sleep apnea, OSA, obstructive sleep apnea symptom, OSAS, and sleep obstructive apnea syndrome. These terms were used in combination with “AND” or “OR”. This literature review was performed independently by two investigators, with a third resolving any disputes as needed.

STUDY SELECTION:

The review process consisted of two parts. The first part aimed at primary screening of identified articles for applicability by reading their abstracts. Complete texts of those articles which were found relevant including those identified by the manual search were evaluated. Any variations in views between the investigators were assessed by a third investigator. The following set of inclusion and exclusion criteria was applied in the first review phase.

INCLUSION CRITERIA:

Included studies met the following criteria: 1) Randomized controlled trials; 2) The research subjects were patients with OSA; 3) Treatment included CPAP and MAD; 4) Studies with atleast 1 year follow up; 5) English language.

EXCLUSION CRITERIA:

Studies were excluded for meeting the following criteria: 1) Articles on pediatric subjects, 2) Treatment other than MAD and CPAP, 3) Studies with less than 1 year follow up, 4) An article other than English language, 5) Irrelevant outcomes.

DATA EXTRACTION AND META - ANALYSIS:

Title and abstract of articles and reports resulting from the search strategy were screened by two review authors. Full reports were obtained where studies met the inclusion criteria or where a clear decision were not able to made from the title or abstract. Disagreements were resolved by discussion. Reviews and systematic reviews as well as all included studies were scanned for relevant trials. Data were extracted, independently and in triplicate, using a previously prepared data extraction form, which included the characteristics of trials participants, intervention, control groups if appropriate and outcomes.

STATISTICALANALYSIS:

Meta-analysis was performed using Review Manager version 5.3 software, Copenhagen (Nordic Cochrane Centre, The Cochrane Collaboration, 2014) to create forest plots. Heterogeneity in study results was assessed using chi-squared and I^2 tests and appropriate analysis models (fixed-effects or random-effects) were determined. A chi-squared $P \leq 0.05$ and an $I2 > 50\%$ indicated high heterogeneity and the random-effects model was used in this case. A chi-squared $P > 0.05$ and an $I2 > 50\%$ indicated acceptable heterogeneity and the fixed-effects model was instead used. Continuous variables were given as mean ± standard deviation and were compared on the basis of mean difference (MD), while categorical data were given as percentages and compared based on relative risk (RR)/odds ratios (ORs). MD and 95% CI was used to analyze all the indexes.

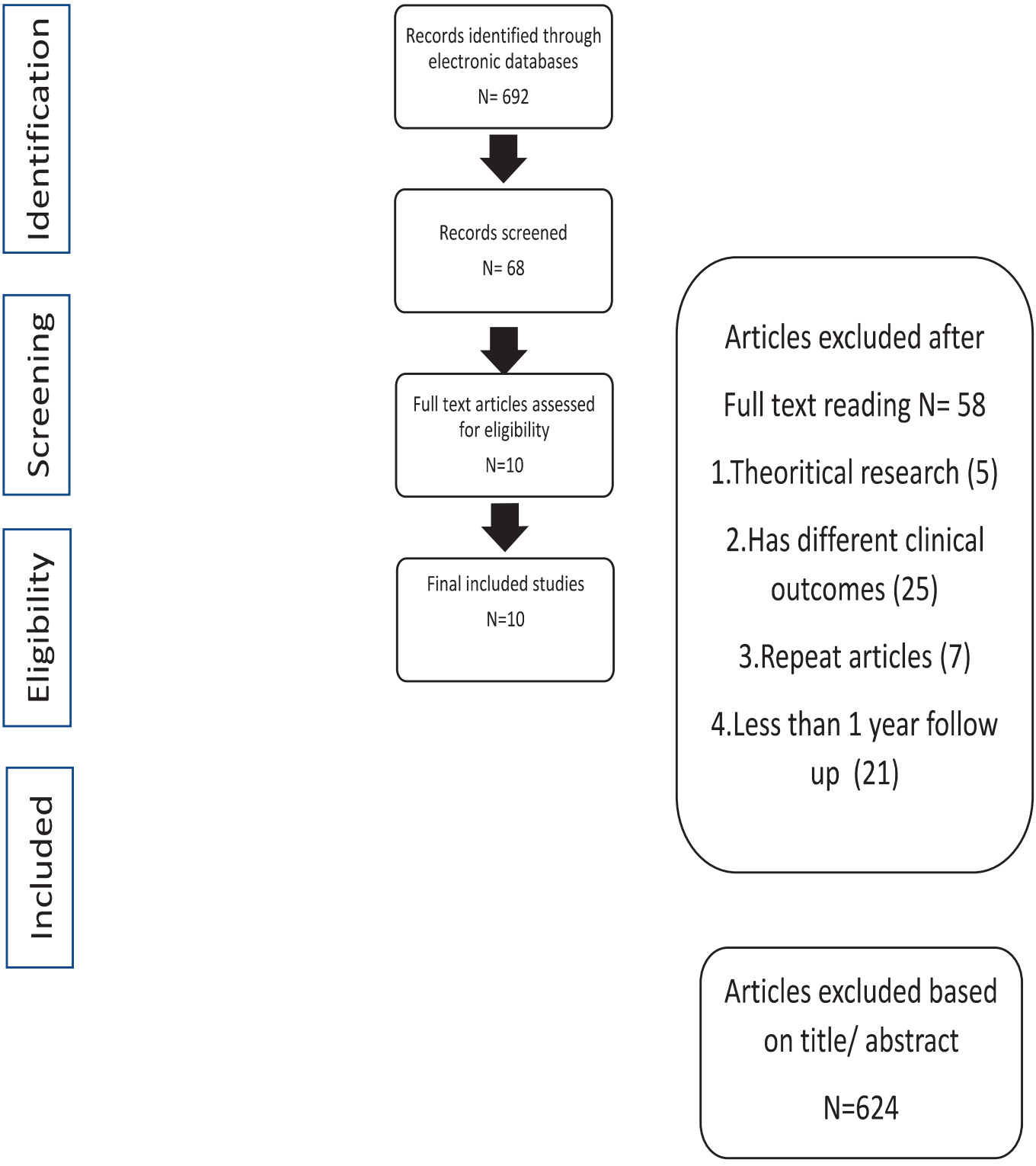
RESULTS:

Search Result:

We searched three electronic databases in November 2021 using our initial keyword search, which resulted in 692 articles, of which 624 were discarded following a title/abstract review. The remaining 68 articles were subject to a complete full-text assessment, leading to 58 articles being excluded for failing to meet the study inclusion criteria. Reasons for exclusion of these studies included: theoretical research (5), lack of clinical outcomes (25), duplicate articles (7) and mless than 1 year follow up (21). We finally identified a total of 10 studies that met the inclusion criteria for

this systematic review and meta-analysis. The PRISMA flowchart shows the study selection process which is outlined in Fig. 1.

Figure 1 flow of Study Identification, Exclusion and Inclusion



Summary of Included Studies:

Ten studies were eligible for qualitative analysis where CPAP and MAD were used as intervention and their effect on OSA patients was compared. The studies included in this systematic review were randomized controlled trials comparing CPAP and MAD. Table 1 summarizes the basic information of each study, including author names, year of publication, design, severity of OSA, the detail of therapy.

Table 1 : Summary of included studies

STUDY	DESIGN	SEVERITY OF OSA	PERIOD	MAD		CPAP	
				AHI (n)	ESS (n)	AHI (n)	ESS (n)
Grietje E et al[9]	Parallel Multicentre RCT	Moderate	1 year	9.15±5.65 (24)	7.1±5.2(29)	1.55±1.15 (30)	5.3± 3.9(37)
Grietje E et al[10]	RCT	Moderate	1 year	6.5±4(17)	5.8±(3.7(17)	0.9±0.7(23)	4.6± 4.1(23)
Aarab et al[11]	RCT	Moderate	1 year	15.0±10.5 (15)	4.7±4.5(15)	20.2±8.6(13)	5.2±5.6(13)
Michiel et al[12]	RCT	Severe	1 year	7.5±5.5(33)	5.5±(2.5(33)	6.5±0.1(37)	5.5± 3.5(37)
Julia AM et al[13]	RCT	Severe	1 year	1.3±1.9(37)	6.5±6.6(17)	1.7±3.4(17)	6.5± 6.6(17)
Togeiro et al[14]	RCT	Mild	1 year	3.8±12.6(25)		1.7±14.2(31)	
Luciana et al[15]	RCT	Mild	1 year	3.8±12.6(19)		1.7±14.2(15)	
Thais Maro et al[16]	RCT	Mild	1 year	2.4±9.4(24)		2.6±8.7(17)	
Julia Anne et al[17]	RCT	Severe	1 year	2.7±3.2		0.47±1.1	
Haichun et al[18]	RCT	Severe	1 year		5.21±0.86 (19)		5.37±1.50 (19)

(n) Number of OSA patient

CLINICAL OUTCOME:

AHI:

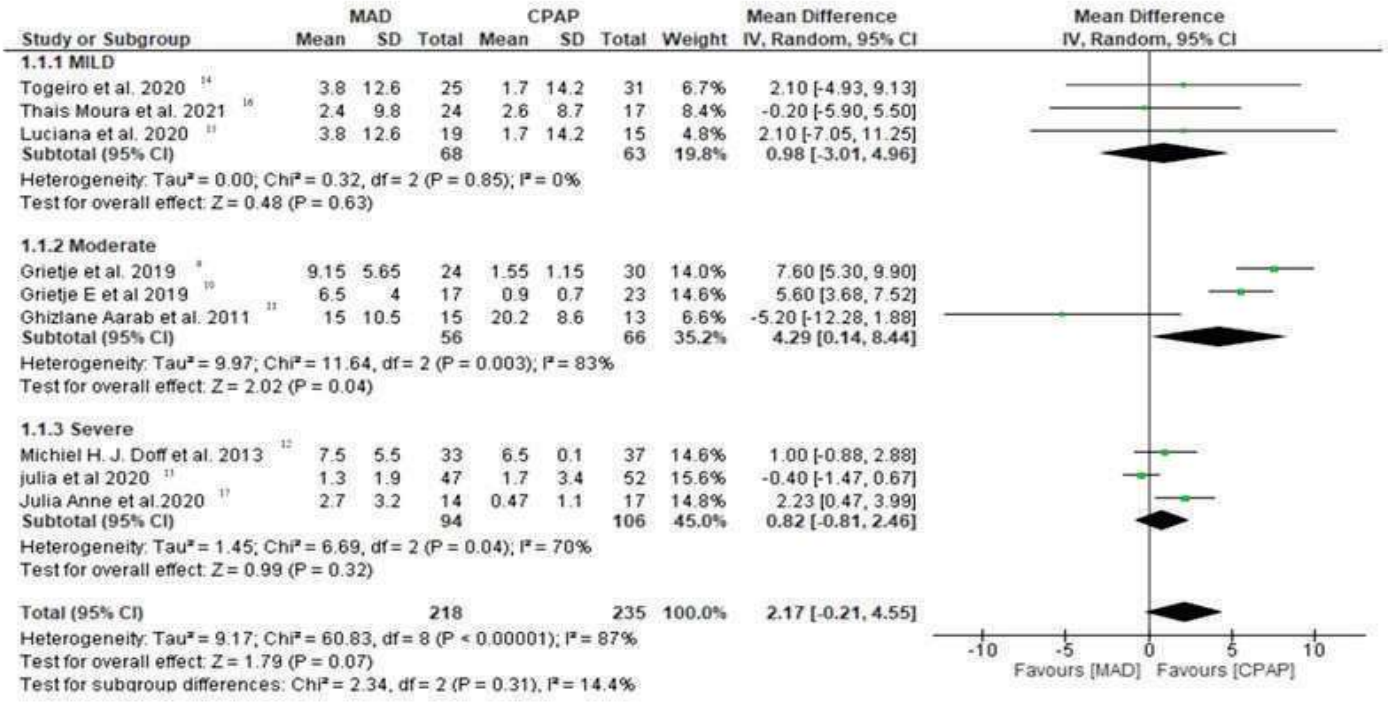
In total 9 studies including 218 patients with MAD and 235 patients with CPAP reported the results of AHI. In mild group 68 patients for MAD and 63 patients for CPAP group, based on chi- square P = 0.85 and an I^2 = 0% the random effect model was chosen to analyse the AHI. There is no significant difference between CPAP group and MAD group.

In moderate group 56 patients for MAD and 66 patients for CPAP group, based on chi- square P = 0.003 and an I^2= 83% the random effect model was chosen to analyse the AHI. Compared with MAD, CPAP significantly decreased AHI.

In severe group 94 patients for MAD and 106 patients for CPAP group, based on chi- square P = 0.04 and an I^2 = 70% the random effect model was chosen to analyse the AHI. There is no significant difference between CPAP group and MAD group.

Overall comparison of mild, moderate and severe revealed no significant difference between OSA treatment. Test for sub-group difference shows P=0.31 and I^2 =14.4%.

Figure : 2 Meta analysis for comparison of apnea-hypopnea index (AHI) in continuous positive airway pressure and mandibular advancement device



ESS:

In total 6 studies including 145 patients in MAD and 161 in CPAP group reported the result of ESS.

In mild group no studies were found in this group so results are not estimated.

While in moderate group 61 patients for MAD and 73 patients for CPAP group, based on chi- square P = 0.54 and an I^2= 0% the random effect model was chosen to analyse the AHI. There is no significant difference between CPAP group and MAD group.

In severe group 84 patients for MAD and 88 patients for CPAP group, based on chi- square P = 0.46 and an I^2 = 0% the random effect model was chosen to analyse the AHI. There is no significant difference between CPAP group and MAD group.

Overall comparison of moderate and severe revealed no significant difference between OSA treatment. test for sub-group difference shows P=0.11 and I^2 =60.1%

Figure : 3 Meta analysis for comparison of Epworth sleepiness scale in continuous positive airway pressure and mandibular advancement device

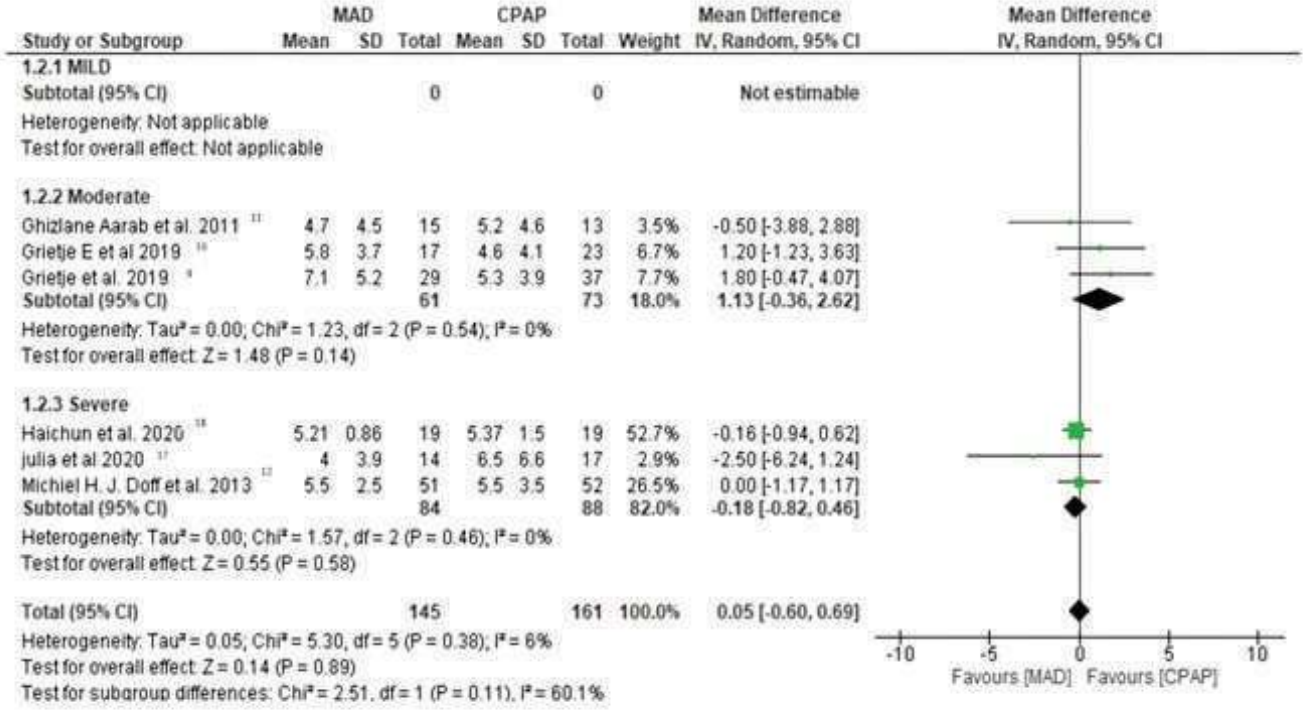
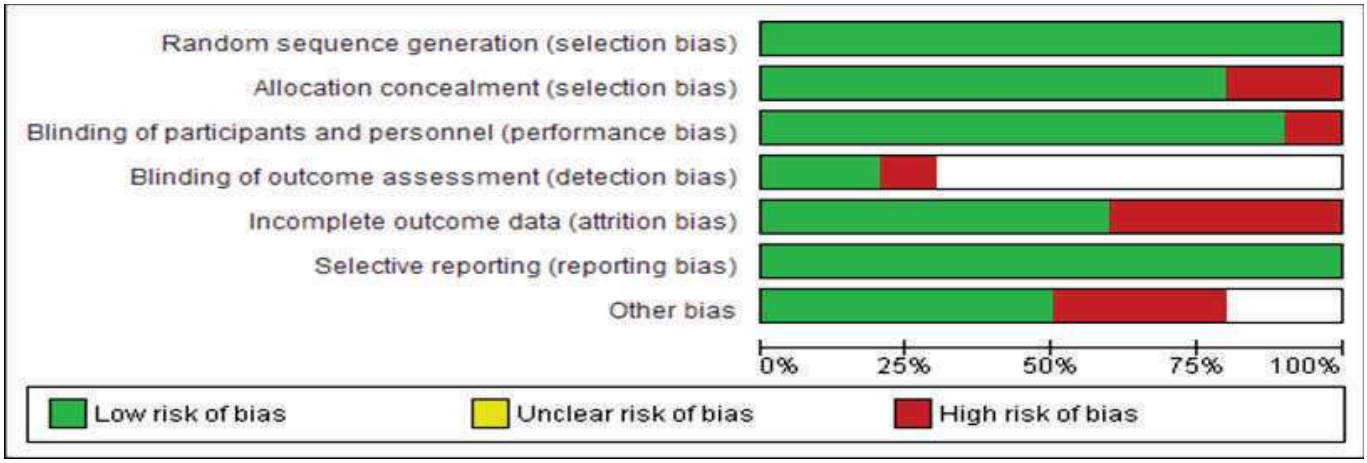
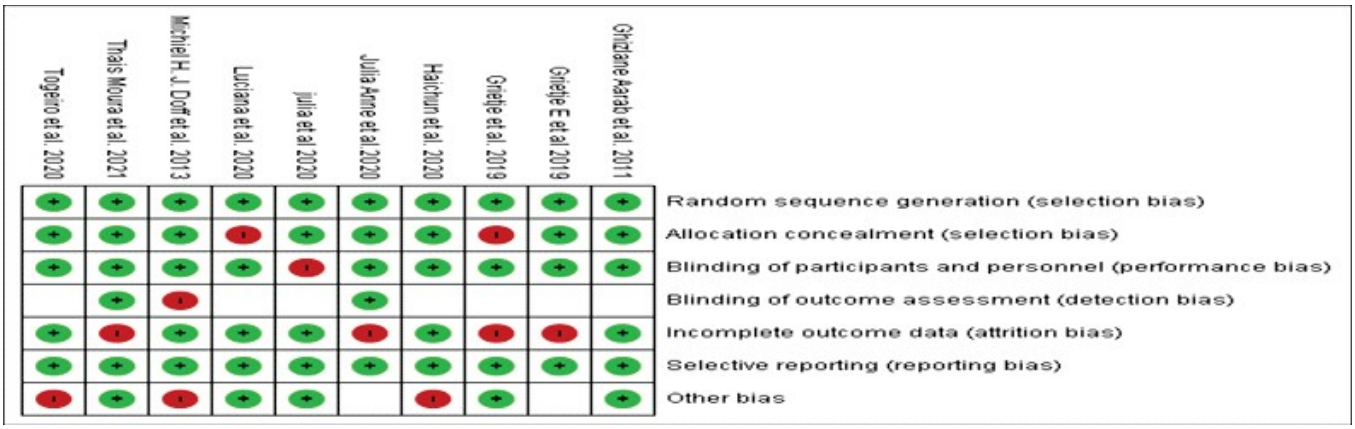


Figure : 4 Risk of bias





DISCUSSION:

OSA refers to the frequent occurrence of apnea and hypoventilation during sleep. Clinically, it can be manifested as snoring which is not regular, and patients consciously suffocated breath, and even have repeated episodes of respiratory suppression leading to patient waking up (often accompanied by increased nocturia, morning headache, dizziness and dry mouth and pharynx and a series of symptoms). At present, OSA is generally considered to be a systemic disease and is an one of the cause of sudden death and road accidents, so it is a serious social problem.

Treatment for OSA includes one side sleep, CPAP, orthodontics, surgery, and medication. Among them, CPAP is the preferred and initial treatment for adult OSA patients. The commonly used non-invasive auxiliary ventilation in clinical practice includes general fixed pressure CPAP. Indications of CPAP: (1) moderate to severe OSA patients (AHI>15); (2) patients with mild OSA (AHI 5 to 15), but with obvious symptoms (such as daytime sleepiness, cognitive impairment, depression, etc.), combined or complicated with cardiovascular disease and diabetes, etc; (3) OSA still persists after other treatment; (4) OSA combined with COPD, that is, "overlap syndrome"; and (5) Perioperative treatment of OSA patients.

Although many randomized trials and systematic reviews have supported the evidence that CPAP is more advantageous than MAD in reducing OSA. Another most preferred treatment of choice is MAD which is applicable to patients with simple snoring and mild to moderate OSA, especially those with mandibular retraction. For patients who cannot tolerate CPAP, cannot undergo surgery or have poor surgical results, it can be used as a supplement or alternative to CPAP treatment.

This systematic review included only RCTs comparing CPAP with MAD based on both subjective and objective outcomes of OSA patient in 1 year follow up period. These outcomes were mainly measured with polysomnography (objective outcomes) and questionnaires (subjective outcomes) before and at the end of each treatment. The patient's severity of OSA ranged from mild to severe.

This systematic review of the evidence has shown that both MAD and CPAP has improved AHI but CPAP was statistically significantly more efficacious, which agrees with previous review articles of Li W et al.[19]

Although Doff et al.[12] showed that CPAP had showed more impact in lowering the AHI than MAD in a group of mild to severe OSA patients, they found insignificant differences in both treatments. A recent meta-analysis reviewed that CPAP is more efficacious in lowering AHI than MAD in moderate-to-severe OSA patients. Further, a recent crossover study by Phillips et al.[20] showed that major health outcomes were similar after 1 month of optimal MAD and CPAP treatment in patients with moderate-to-severe OSA. Thus, the outcomes of this study are in line with previous findings wherein both MAD and CPAP show comparable treatment results in a group of mild-to-moderate OSA patients.

There has insignificant difference in ESS after therapy between CPAP and MAD group which agrees with previous review articles of Li P et al.[21] Some degree of clinical heterogeneity was found in terms of numerous factors.

Nevertheless, the present systematic review and

meta-analysis still had several potential limitations. One potential limitation was that the degree of mandibular advancement by the OAs. Different types of CPAP and MAD designs were utilized with varied characteristics and titration procedures were variable among the included trials, which caused uncertainty regarding comparisons between these studies. A second limitation was the fact that most of the included studies had high risk of bias, which may be due to 3 or more unclear or inadequate methodological components.

Moreover, a few of the included crossover trials had a high risk of a carryover effect, due to the absence of a wash-out period between treatments. A third limitation was the small sample sizes of all the included trials and the small number of studies. A funnel plot for pooled estimates to assess the potential publication bias was not performed, and unpublished studies with negative results could not be identified, so there might be publication bias as well, which could result in overestimation of the effectiveness of the interventions.

CONCLUSION

CPAP and MAD therapy both yielded a positive treatment outcome in terms of subjective and objective improvement in long follow up periods. CPAP is the most clinically effective treatment at reducing AHI in moderate to severe OSA. Both CPAP and MAD reduce subjective sleepiness to a similar extent in OSA. Based on this evidence it would appear proper to offer MAD to patients who are unable or unwilling to persist with CPAP.

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