Sleep Medicine Reviews 72 (2023) 101855

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

Orthodontic appliances for the treatment of pediatric obstructive sleep apnea: A systematic review and network meta-analysis

Min Yu [a,b,c], Yanyan Ma [d], Ying Xu [a,b,c], Jingxuan Bai [a,b,c], Yujia Lu [a,b,c], Fang Han [e,**,1], Xuemei Gao [a,b,c,*,1]

[a] Department of Orthodontics, Peking University School and Hospital of Stomatology, No. 22 Zhongguancun South Avenue, Haidian District, Beijing, 100081, PR China
[b] Center for Oral Therapy of Sleep Apnea, Peking University Hospital of Stomatology, No. 22 Zhongguancun South Avenue, Haidian District, Beijing, 100081, PR China
[c] National Center for Stomatology, No. 22 Zhongguancun South Avenue, Haidian District, Beijing, 100081, PR China
[d] Department of Stomatology, Beijing Chao-Yang Hospital, Capital Medical University, No. 8 Gongren Tiyuchang Nanlu, Chaoyang District, Beijing, 100020, PR China
[e] Sleep Division, Peking University People's Hospital, No. 11 Xizhimen South Street, Xicheng District, Beijing, 100044, PR China

A R T I C L E I N F O

Handling Editor: M Vitello

Keywords:
Sleep related breathing disorder
Children
Orthodontic appliance
AHI
Effect

A B S T R A C T

This systematic review and network meta-analysis aims to preliminarily investigate the efficacy of different orthodontic appliances for the treatment of pediatric obstructive sleep apnea (OSA). Electronic databases were systematically searched. Randomized and non-randomized controlled trials with patients <18 y treated with either mandibular advancement appliance (MAA), rapid maxillary expansion (RME), or myofunctional therapy (MFT) were included. A network meta-analysis using multivariate random effects was conducted to estimate pooled differences using the apnea-hypopnea index (AHI) as the main outcome. Eleven studies (595 patients) were included in the analysis. Compared with control, MAA was associated with significant reductions in AHI of −2.18/h (95%CI -3.48 to −0.89, $p = 0.001$). Combined treatment of RME + adenotonsillectomy (AT) and RME + MAA showed a significant decrease in AHI, with −5.13/h (95%CI -7.50 to −2.76, $p < 0.0001$) and −3.79 (95% CI -5.21 to −2.37, $p < 0.0001$), respectively. MFT was associated with a −2.45/h (95%CI -4.76 to −0.14, $p = 0.038$) decrease in AHI. However, RME alone was not associated with significant AHI reduction (0.02, 95%CI -1.72 to 1.75, $p = 0.985$). The heterogeneity of the network meta-analysis was $I^2 = 32.6\%$. Limited evidence indicated that MAA (alone or combined with RME) and RME + AT were associated with benefits for pediatric patients with OSA. This study could not find convincing evidence of a significant benefit of other orthodontic appliances over control.

1. Introduction

Pediatric obstructive sleep apnea is a sleep-related breathing disorder in children and adolescents, characterized by repetitive partial (hypopnea) or complete (apnea) obstruction of the upper airway during sleep [1]. The reported prevalence of OSA is 1.2%–5.8% in the general pediatric population [2,3]; however, OSA is often underdiagnosed in children when the primary complaint is behavioral problems. The predisposing factors for pediatric OSA include adenotonsillar hypertrophy, obesity, and underdeveloped maxilla and/or mandible [4]. If left untreated, OSA could lead to dramatic impacts on systemic health and development, and even aggressive behavior, attention deficit, emotional problems, and unfavorable craniofacial changes [5,6].

There are a few proven treatments currently available for pediatric OSA, including adenoidectomy and/or tonsillectomy, positive airway pressure (PAP), medication, and orthodontic treatments [7–9]. Orthodontic treatments, such as mandibular advancement appliances (MAA), rapid maxillary expansions (RME), and myofunctional therapy (MFT), could correct craniofacial structures during growth in favor of snoring and OSA [10]. Preliminary studies have suggested inconsistent efficacy of various orthodontic modalities [11], with different patients' characteristics, treatment combinations, and treatment duration. In previous

* Corresponding author. Department of Orthodontics, Peking University School and Hospital of Stomatology, No. 22 Zhongguancun South Avenue, Haidian District, Beijing, 100081, PR China.
** Corresponding author.
E-mail addresses: hanfang1@hotmail.com (F. Han), xmgao@263.net (X. Gao).
[1] Fang Han and Xuemei Gao contributed equally to the manuscript.

https://doi.org/10.1016/j.smrv.2023.101855
Received 7 August 2023; Received in revised form 12 September 2023; Accepted 19 September 2023
Available online 28 September 2023
1087-0792/

meta-analyses, the efficacy of each treatment modality has been analyzed [4,12]. However, the treatment efficacy among different orthodontic appliances is lacking. Network meta-analysis could be used for comparing multiple treatments that combine direct and indirect evidence in a single analysis [13]. Thus, the aim of this systematic review and network meta-analysis was to preliminarily investigate the efficacy of different orthodontic appliances for the treatment of pediatric OSA to provide evidence-based decisions in clinical practice.

2. Material and methods

The Preferred reporting items for systematic reviews and meta-analyses for network meta-analyses (PRISMA-NMA) were followed in the study [14].

2.1. Eligibility criteria

The population, intervention, comparison, outcomes, and study (PICOS) design of the eligibility criteria were as follows:

Population: participants aged <18 years with a diagnosis of OSA (defined by obstructive AHI ≥1 event/h).

Interventions: at least one of the following treatments [1]: mandibular advancement appliances (MAA) [2]; rapid maxillary expansion (RME) [3]; myofunctional therapy (MFT); and [4] other orthodontics treatment.

Comparisons: non-treatment, sham treatment, or other treatment modalities of OSA.

Outcomes: apnea-hypopnea index (AHI) at baseline and a follow-up visit, and other measured subjective or objective parameters.

Study design: randomized controlled trials (RCTs) or non-randomized controlled trials (NRCTs).

2.2. Identification of trials

The systematic literature search was conducted in electronic databases on July 5, 2023 using pre-specified search terms, including PubMed (MEDLINE), EMBASE, and Cochrane Library, with keywords such as ('breathing, sleep disordered' OR 'obstructive sleep apnea') and ('mandibular advancement' OR 'rapid maxillary expansion' OR 'myofunctional therapy' OR 'orthodontic device') and ('pediatric' OR 'children' OR 'adolescent'). Manual searches of the reference lists were completed for relevant studies. Literature searches were performed independently by two authors (M.Y. and Y·Y.M.). References of all eligible trials were also screened for relevant trials.

2.3. Study selection and data extraction

Eligibility of studies was performed separately by two authors (M.Y. and Y·Y.M.). Data were extracted by these two authors and then checked independently by one other author (X.M.G.). Characteristics of trials were recorded, including author, year, study design, sample size, treatment and control, and follow-up time. The characteristics of included participants were also recorded, including age, sex, body mass index (BMI), and relevant past medical history. The main outcome of interest was the change in the AHI. Secondary outcomes, including oxygen desaturation index (ODI), the lowest oxygen saturation ($LSpO_2$), and respiratory disturbance index (RDI), were also extracted.

2.4. Risk of bias assessment

Two authors (M.Y. and Y·Y.M.) independently evaluated the risk of bias of RCTs and NRCTs using the Cochrane collaboration tool for assessing the risk of bias [15] and the risk of bias assessment tool for non-randomized studies (RoBANS) [16], respectively, and consulted with a third reviewer (X.M.G.) if there was a discrepancy. Studies were rated on selection bias, detection bias, performance bias, attribution bias, and reporting bias with low, unclear, or high risk.

2.5. Data synthesis

First, separate meta-analyses of direct evidence were conducted for each of the treatment comparisons using Review Manager 5.4 (The Cochrane Collaboration). The heterogeneity among studies was represented by the I^2 index and the χ^2 test. This study used random-effects models to be consistent with the network meta-analysis. Second, due to the fact that there are relatively few trials directly comparing different orthodontic devices on the treatment of OSA, a network meta-analysis was performed using R 4.3.0 (The R Foundation) to compare all the treatment options indirectly [17].

3. Results

3.1. Search and study selection

Fig. 1 illustrates the flowchart of the study selection process. A total of 271 articles were identified, 173 in PubMed, 54 in Embase, 43 in Cochrane Library, and one by manual search. There were 217 articles remaining after duplications were removed. Irrelevant articles were excluded after reading the title and abstract, and 25 articles were assessed with full text. One article was excluded due to no full text. Six articles were excluded due to the lack of sleep-related parameters, and 7 trials were excluded due to incomplete results. A total of 11 articles were included in the systematic review and 10 in the network meta-analysis. The characteristics of the included studies are presented in Table 1 and Table 2.

Overall, the patients' characteristics, severity, and treatment modalities varied greatly across studies. The included RCTs mainly focused on the efficacy of MAA [18–20], and RME (combined with adenotonsillectomy) [21,22]. The included NRCTs mainly focused on the efficacy of RME [23,24] and MFT [25,26], and Remy et al.'s study investigated the efficacy of RME combined with MAA [27].

The designs of MAA included self-designed acrylic resin oral bite plates [18], MAAs consisted of two separate acrylic plates [19], and Twin-blocks [20]. The design of RME was similar across studies, but the speed of maxillary expansion was different [21–24]. The myofunctional therapy used in Villa et al.'s study included labial seal, lip tone exercises, and tongue posture exercises [28], whereas Chuang et al.'s study employed a built-in tongue bead for tongue position exercises [25]. The study by Huang et al. compared the efficacy of MFT and passive MFT [26], without other treatment modalities or sham groups as control, therefore, was excluded from the network meta-analysis.

The network graphs of the included RCTs and NRCTs are illustrated in Fig. 2a and b. Of the 11 studies included in the analysis (595 patients), three compared MAA with control [18–20], two compared RME with adenotonsillectomy (AT) [21,24], two compared RME with control [22,23], two compared MFT (+AT) with control [25,28], one compared different MFT modalities [26], and one compared RME + MAA with control [27]. As Fig. 2a shows, the geometry of the treatment network in RCTs was unequally spaced, with only two-arm studies, without direct comparisons between MFT and control. When NRCTs were considered, the treatment distribution was relatively equal, without direct comparisons between MFT + AT or RME + AT with control (Fig. 2b).

3.2. Quality assessment

The results of the quality analysis of included RCTs and NRCTs are shown in Fig. 3a and b. All the RCTs used no treatment instead of sham treatment as control, therefore, were rated high risk in blinding of participants. In NRCTs, the selection of participants was rated high risk in retrospective studies, and confounding variables were rated high risk due to the unbalanced sex or age composition. Chuang et al.'s study compared two modalities of myofunctional therapy, without a control

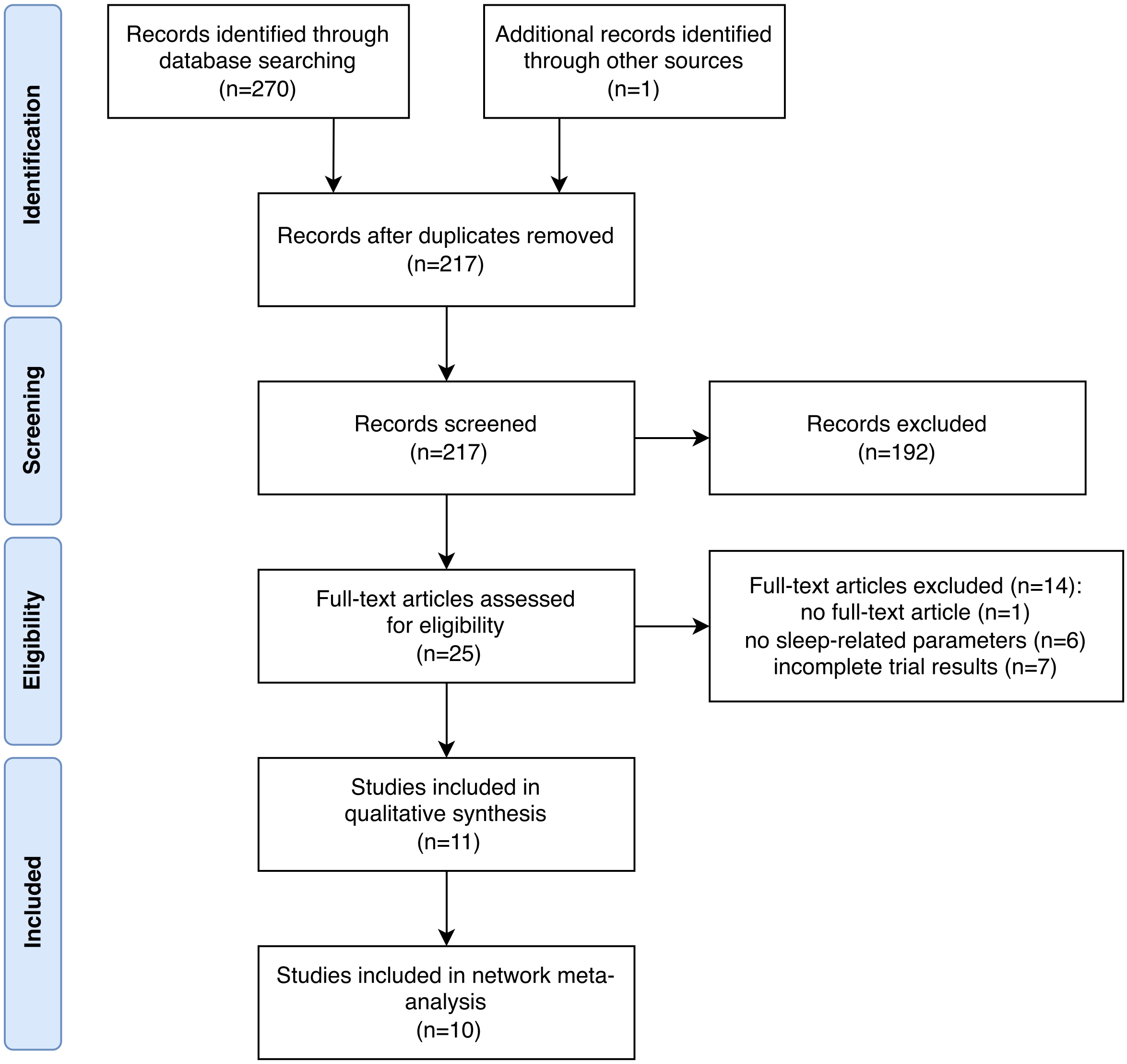

Fig. 1. The flowchart of the study selection process.

group [25], therefore, was rated high risk in other bias, and excluded in data synthesis.

3.3. Results of individual studies

The synthesized result of MAA is shown in Fig. 4a, which included 3 RCTs. There was a significant effect in favor of MAA treatment in AHI, which decreased by −2.06/h (95%CI -3.11 to −1.01/h, $p = 0.0001$, $I^2 = 25\%$). The change of AHI with MAA treatment was consistent across these studies, despite the heterogenous patients' age, BMI, and OSA severity.

The pooled analysis of one RCT and one NRCT generated a heterogenous and insignificant result in AHI with the treatment of RME ($p = 0.13$, $I^2 = 56\%$, Fig. 4b). These two studies both had participants with an average age of approximately 6.5 y, however, the initial severity of Miano et al.'s study had a wide range (AHI 17.4 ± 21.0 events/h).

The efficacy of RME + MAA based on 3 age subgroups (6–9 years) from one NRCT showed a significant decrease in AHI (−3.71/h, 95%CI -4.90 to −2.51/h, $p < 0.00001$, $I^2 = 20\%$, Fig. 4c). Chuang et al.'s study compared the efficacy between MFT and control, and AHI decreased by −1.59 ± 2.81/h in the treatment group and 0.86 ± 2.43/h in the control group ($p = 0.014$).

3.4. Secondary outcomes

Idris et al.'s study reported the $LSpO_2$ and ODI after MAA treatment [20], which increased from 85.4 ± 11.3% to 90.6 ± 5.2%, and decreased from 2.3 ± 2.2 to 1.7 ± 1.4 events/h, respectively. The $LSpO_2$ with RME was synthesized by two studies [21,22], with an increase of 3.10% (95%CI 1.81–4.39%, $p < 0.00001$, $I^2 = 34\%$). Guilleminault et al. found RME could decrease RDI from 19.5 ± 1.0 to 7.9 ± 0.5 events/h [21], whereas Hoxha found that the ODI did not change with RME from 2.07 ± 1.82 to 2.07 ± 1.54 events/h [22].

3.5. Network meta-analysis

The results of the network meta-analysis are shown in Fig. 5. Compared with inactive control, MAA and MFT were associated with significant reductions in AHI of −2.18/h (95% CI -3.48 to −0.89, $p = 0.001$) and −2.45/h (95% CI -4.76 to −0.14, $p = 0.038$), respectively. However, RME alone was not associated with significant AHI reduction (0.02, 95% CI -1.72 to 1.75, $p = 0.985$). Combined treatment modalities of RME + AT and RME + MAA showed a significant decrease in AHI, with −5.13/h (95% CI -7.50 to −2.76, $p < 0.0001$) and −3.79/h (95% CI -5.21 to −2.37, $p < 0.0001$), respectively. The treatment effect of MFT + AT was not beneficial based on indirect comparisons in the included

Table 1
Characteristics of included randomized controlled trials.

Study, year	Design	N (M/F)		Treatment	Age (y)	BMI (kg/m²)	Severity	Maxillofacial characteristics	Treatment duration	Drop out	Exminations
		Treat-ment	Control								
Guilleminault, 2011 [21]	Parallel	31 (14/17)		RME + AT	6.5 ± 0.2	–	AHI 11.8 ± 1.0[a]	Narrow maxilla, a high and narrow hard palate; tonsils scored 2+ or 3+	–	–	PSG, questionnaire
Hoxha, 2018 [22]	Parallel	15 (8/7)	15 (8/7)	Semi-RME vs. no treatment	11.87 ± 2.00	–	–	Maxillary transverse deficiency, malocclusion; no adenoid or tonsillar hypertrophy	5 months	–	HSAT, lateral cephalogram, serum and urine biomarkers
Idris, 2018 [20]	Cross-over	18 (14/4)		MAA vs. no treatment	9.8 ± 1.1	20.4 ± 5.2	AHI 2.8 ± 3.0	Class I (n = 12) and Class II (n = 4) jaw relationship	–	–	HSAT
Machado-Junior, 2016 [19]	Parallel	8 (2/6)	6 (3/3)	MAA vs. no treatment	8.14 ± 0.75[a]	–	AHI 1.58 ± 0.40	Mandibular retrusion	12 months	–	PSG
Villa, 2002 [18]	Parallel	19 (10/9)	13 (10/3)	MAA vs. no treatment	7.1 ± 2.6	17.9 ± 5.2	AHI 7.1 ± 4.6	Deep or retrusive bite or both	6 months	9	PSG, questionnaire, physical examinations
Villa, 2015 [28]	Parallel	14	13	AT + MFT vs. AT + control	5.59 ± 1.35	Centile 67.52 ± 29.58	AHI 4.72 ± 3.04	–	2 months	12	PSG, questionnaire, morphofunctional eveluation

BMI: body mass index; MAA: mandibular advancement appliance; AHI: apnea-hypopnea index; PSG: polysomnography; RME: rapid maxillary expansion; AT: adenotonsillectomy; HSAT: home sleep apnea test; MFT: myofunctional therapy.
[a] Calculated from the original study.

Table 2
Characteristics of included non-randomized controlled trials.

Study, year	Design	N (M/F)		Treatment	Age (y)	BMI (kg/m²)	Severity	Maxillofacial characteristics	Treatment duration	Drop-out	Exminations
		Treatment	Control								
Chuang, 2019 [25]	Pro-spective	40 (31/9)	17 (13/4)	Passive MFT vs. control	7.86 ± 3.09	18.09 ± 3.84	AHI 3.56 ± 2.50	–	12 months	–	PSG, questionnaire, lateral cephalogram
Huang, 2019 [26]	Pro-spective	54 (27/27)	56 (36/20)	MFT vs. passive MFT	7.66 ± 2.91[a]	16.58 ± 2.77[a]	AHI 4.86 ± 6.20[a]	–	6 months	35	PSG, lateral cephalogram
Miano, 2009 [23]	Pro-spective	9 (6/3)	13	RME vs. control	6.4 ± 1.97	–	AHI 17.4 ± 21.0	High narrow palate, occlusal anomalies; mild and severe tonsillar hypertrophy	12 months	–	PSG
Remy, 2022 [27]	Retro-spective	94	113	RME + MAA vs. control	Around 6 to 9	–	AHI around 4 to 6	Class II malocclusion	9 months	–	PSG
Villa, 2014 [24]	Pro-spective	47 (34/13)	AT vs. RME		5.03 ± 2.03	17.15 ± 3.07	AHI 11.9 ± 12.3	High-arched palate and/or malocclusions	12 months	–	PSG

BMI: body mass index; RME: rapid maxillary expansion; AHI: apnea-hypopnea index; PSG: polysomnography; AT: adenotonsillectomy; MFT: myofunctional therapy; MAA: mandibular advancement appliance.
[a] Calculated from the original study.

studies. The heterogeneity of the network meta-analysis was $I^2 = 32.6\%$.

The rankograms for each treatment modality are shown in Fig. 6a and b. Fig. 6a illustrates the ranking probabilities of RCTs. RME + AT seemed to have the best efficacy, which was consistent when NRCTs were included (Fig. 6b). The efficacy of MAA also ranked high, whether alone or combined with RME. The efficacy of MFT or RME versus control seemed to be inconsistent based on the limited comparisons of the current study.

4. Discussion

In this study, a network meta-analysis was conducted to compare different orthodontic appliances in the treatment of pediatric OSA. Limited evidence of direct and indirect comparisons showed that both RME + AT and MAA (alone or combined with RME) were associated with a decrease in AHI compared with no treatment. The present study was unable to verify the positive effectiveness of RME or MFT.

This study found that compared with controls, RME + AT seemed to be the most effective treatment modality, with AHI decreased by −5.13 (95% CI -7.50 to −2.76) events/h in the network meta-analysis. However, the effect of RME alone on AHI was not statistically different compared with no treatment in the current meta-analysis (0.02, 95% CI -1.72 to 1.75) events/h. It should be noted that the synthesized result of RME was based on patients with inconsistent OSA severity. RME, an orthopedic treatment used to alleviate maxillary transverse constriction and/or posterior crossbite in children, was found to be effective in the

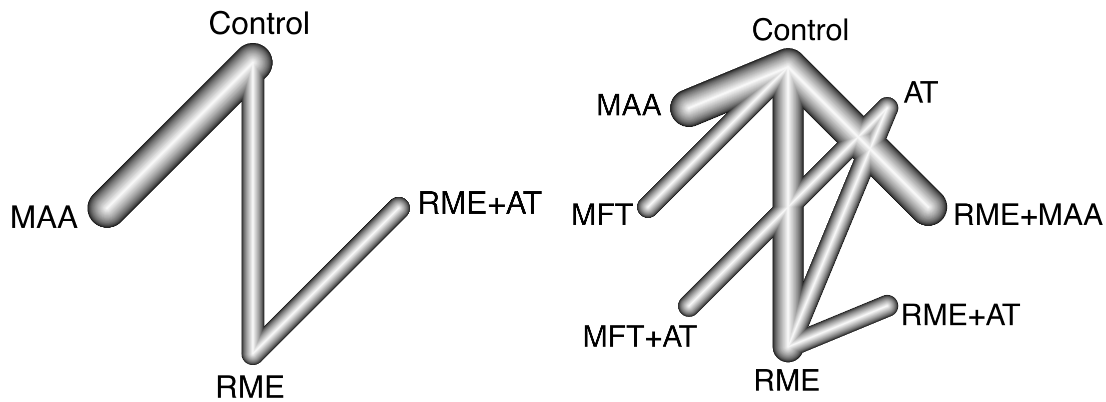

Fig. 2. The network graph of included RCTs (a) and RCTs + NRCTs (b).
RCT: randomized controlled trial; NRCT: non-randomized controlled trial; MAA: mandibular advancement appliance; RME: rapid maxillary expansion; AT: adenotonsillectomy; MFT: myofunctional therapy. In the network graph, the nodes represent the interventions in the network, and lines show the available direct comparisons between pairs of interventions, with the thickness of the lines reflecting the number of patients included in each direct comparison.

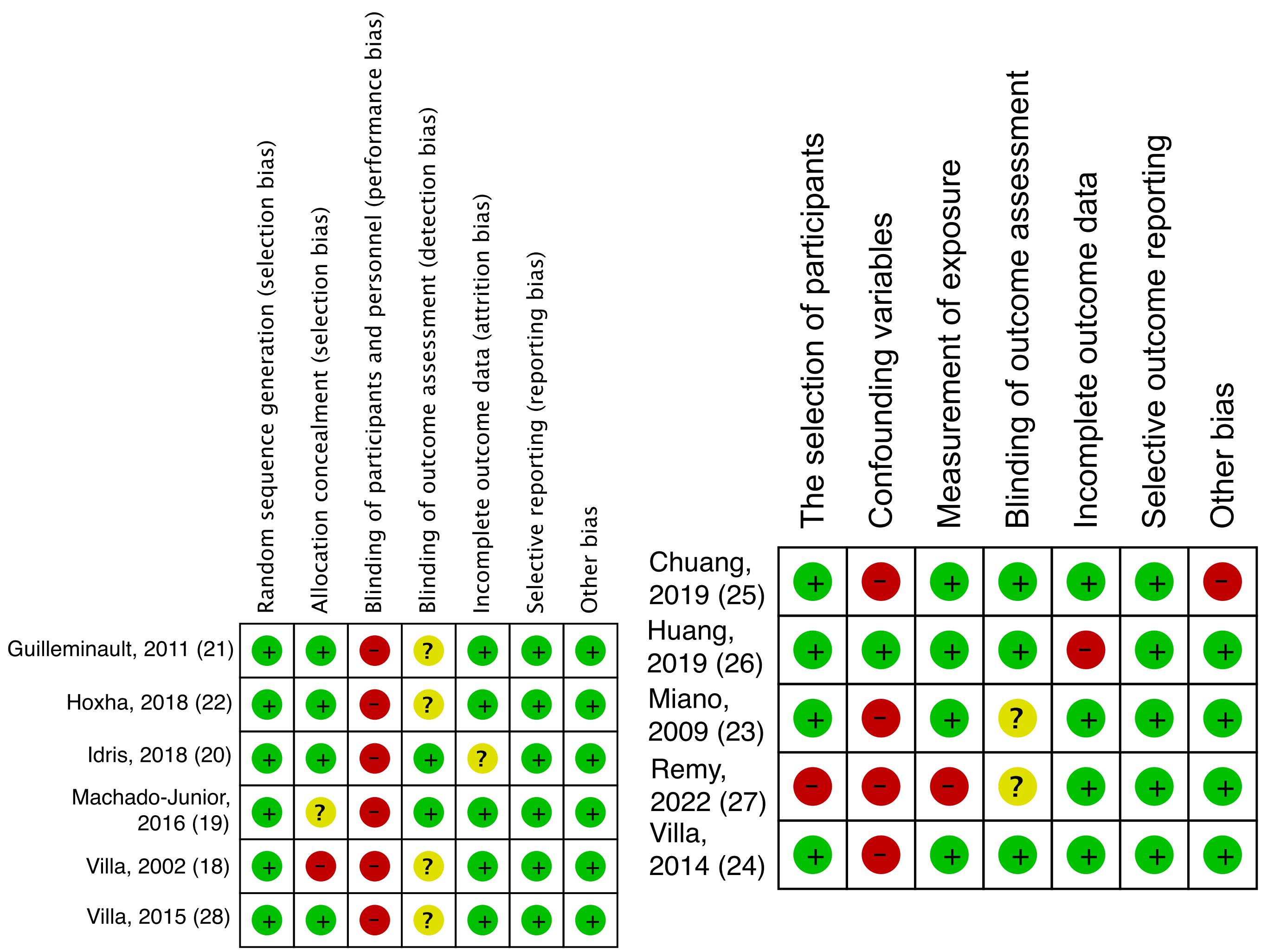

Fig. 3. The risk of bias graph of included RCTs (a) and NRCTs (b).
RCT: randomized controlled trials; NRCT: non-randomized controlled trials.

alleviation of AHI and improvement of quality of life in children [29]. The current study has observed that treatment of RME could increase $LSpO_2$ by 3.10% (95%CI 1.81–4.39%). Furthermore, previous meta-analyses have compared the efficacy of RME using one-arm studies, and the findings indicated that AHI was enhanced after RME among children with OSA [30]. Camacho et al. found that the pre- and post-RME AHI decreased from 8.9 ± 7.0/h to 2.7 ± 3.3/h (70% reduction). The study also observed that AHI improved more in children with previous AT or small tonsils (73–95% reduction) than in children with large tonsils (61% reduction) [31], which was consistent with the

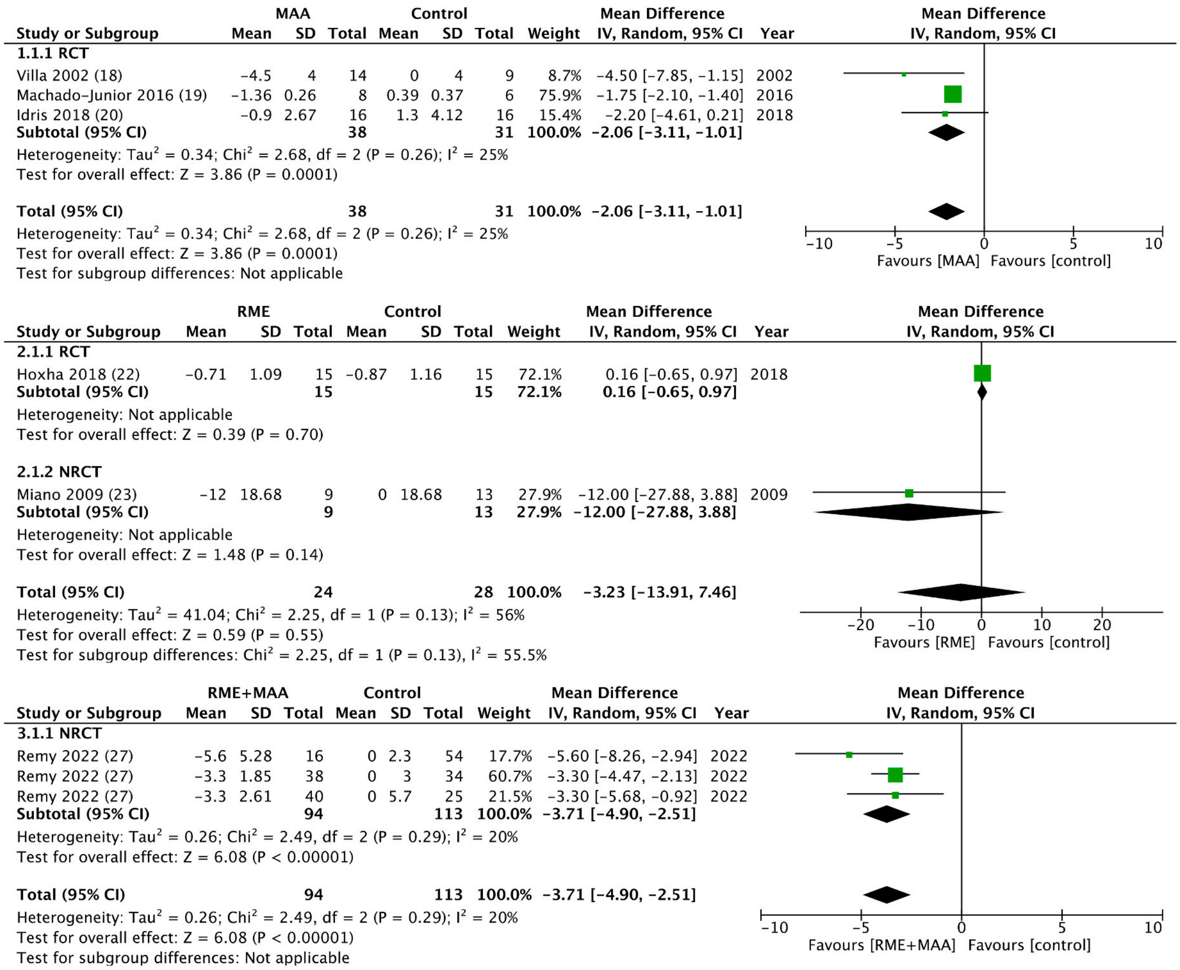

Fig. 4. Treatment effect for change in the apnea-hypopnea index (AHI) with each orthodontic treatment.
(a) MAA: mandibular advancement appliance; (b): RME: rapid maxillary expansion; (c) RME + MAA.

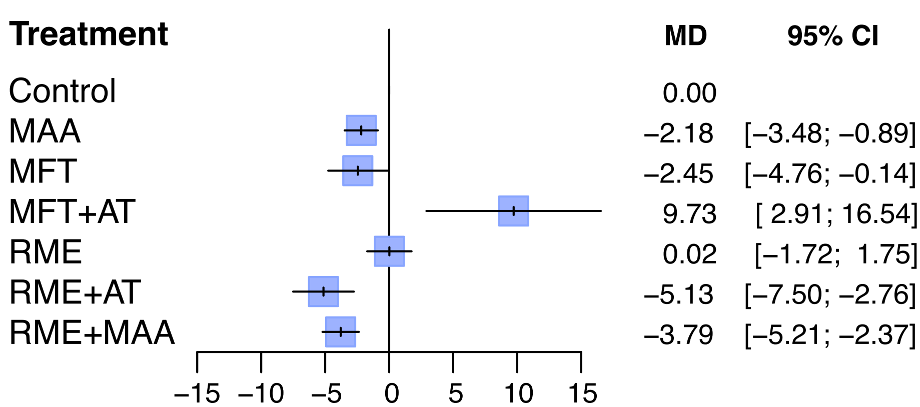

Fig. 5. Treatment effect of AHI in different orthodontic appliances (network meta-analysis, random effect model).
AHI: apnea-hypopnea index; MAA: mandibular advancement appliance; MFT: myofunctional therapy; AT: adenotonsillectomy; RME: rapid maxillary expansion.

current study. However, similar to the findings of the current study, some demonstrated that there was little convincing evidence of the benefit of RME over watchful waiting [32], because the spontaneous resolution of OSA might happen due to growth. It is suggested that pediatric patients with OSA have adenoids and tonsils examined before RME treatment. The efficacy of RME and control needs future investigations.

This study confirmed the efficacy of MAA on pediatric OSA, with synthesized AHI decreased by −2.18 (95% CI -3.48 to −0.89) events/h in the network meta-analysis, independent of patients' age, OSA severity, and BMI. MAA is an orthodontic device designed to treat mandibular deficiency, which is a predisposing factor for pediatric OSA. A Cochrane review published in 2016 investigated oral appliances for OSA in children and found insufficient evidence [33]. Ma et al. conducted a meta-analysis with two high-quality RCTs and found that the mean difference in AHI change for MAA compared with control was −1.75 (95% CI -2.07 to −1.44) events/h [12], which was consistent with the current study. Furthermore, the study also suggested efficacy could

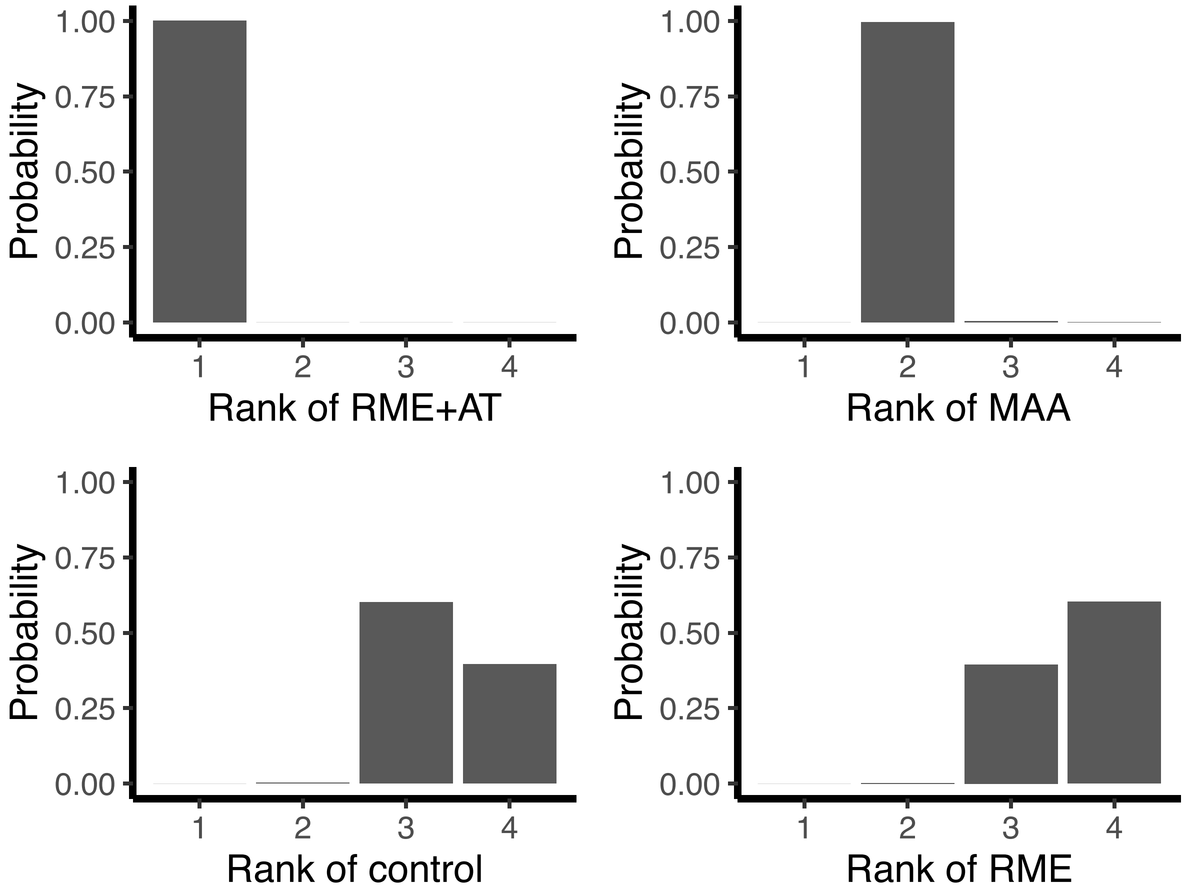

Fig. 6. Rankograms of orthodontic treatment modalities in pediatric obstructive sleep apnea.
(a) randomized controlled trials; (b) randomized and non-randomized controlled trials. OSA: obstructive sleep apnea; MAA: mandibular advancement appliance; MFT: myofunctional therapy; AT: adenotonsillectomy; RME: rapid maxillary expansion. Rankograms can show the relative ranking of interventions and the probability distribution of each intervention's rank.

be achieved in different severity subgroups based on one-arm studies. MAA seemed to be a stable modality for the treatment of pediatric OSA. This study has also observed the beneficial effect of MAA on other sleep-related parameters, including $LSpO_2$ [20]. Besides, with MAA treatment, the number of respiratory effort-related arousals reduced [34], daytime and nighttime symptoms relieved [18], and the Epworth sleepiness score (ESS) and Pediatric sleep questionnaire (PSQ) score improved [20,35]. Although not all of the benefits of MAA have been validated in trials designed with a control group, the findings of the current study might confirm the efficacy of MAA on respiratory events in the treatment of pediatric OSA. However, the efficacy of MAA combined with other treatment modalities, such as AT or RME, needs to be verified with well-designed studies in the future.

This study has observed a positive effect of MFT on pediatric OSA with −2.45 (95% CI -4.76 to −0.14) events/h decrease of AHI in the network meta-analysis combining RCTs and NRCTs. The results of the RCT indicated that after patients underwent AT, MFT could reduce AHI from 4.87 ± 3.20 to 1.84 ± 1.55 events/h [28]. In another RCT, Villa et al. used ODI to assess the efficacy of MFT, and found that ODI decreased from 5.9 ± 2.3 to 3.6 ± 1.8 events/h. Besides, MFT could also modify tongue tone and oral breathing symptoms [36]. MFT is a treatment method that involves isotonic and isometric exercises targeted at the muscles of the tongue, lip, soft palate, and lateral pharyngeal wall [36,37]. The MFT training exercises varied across studies included in the current meta-analysis, requiring clinical practice to adjust accordingly. Hsu et al. conducted a meta-analysis to evaluate the effects of MFT on both adult and pediatric OSA and found a weighted average AHI improvement of 39.5% versus baselines. Furthermore, in adult patients, MFT yielded an improvement in AHI of −7.6 events/h (95% CI -11.7 to −3.5) [38]. Nevertheless, the objective efficacy of MFT over no treatment control on pediatric OSA needs future investigation.

The current study did not find any positive impact of MFT + AT on AHI. While various exercises and devices have been utilized for MFT, only one RCT with objective sleep-related parameters was available for the current study [28]. Therefore, the network meta-analysis between MFT + AT and control had to rely heavily on indirect comparisons. It is important to note that this does not necessarily imply that MFT + AT is an ineffective treatment method. Rather, the network meta-analysis suggested that the decrease in AHI observed in the MFT + AT group was not as significant as in all control groups combined, including control groups from other treatment modalities. Further research is needed as the inference may change with more data on MFT + AT.

Based on the limited number of included studies with heterogenous study designs, this network meta-analysis could demonstrate a positive effect of MAA, with consistent efficacy in direct and indirect comparisons. The efficacy of RME + AT over control might be better than that of MAA, but the evidence is limited with only indirect comparisons and needs verification in the future. The efficacy of other orthodontic appliances cannot be extrapolated and generalized from this systematic review and network meta-analysis.

There are some limitations of this study. First, the paucity in quantity and in quality of studies evaluating the objective efficacy of orthodontic treatments for the management of pediatric OSA limited the study results. Second, a lack of comparable secondary outcomes prevented the

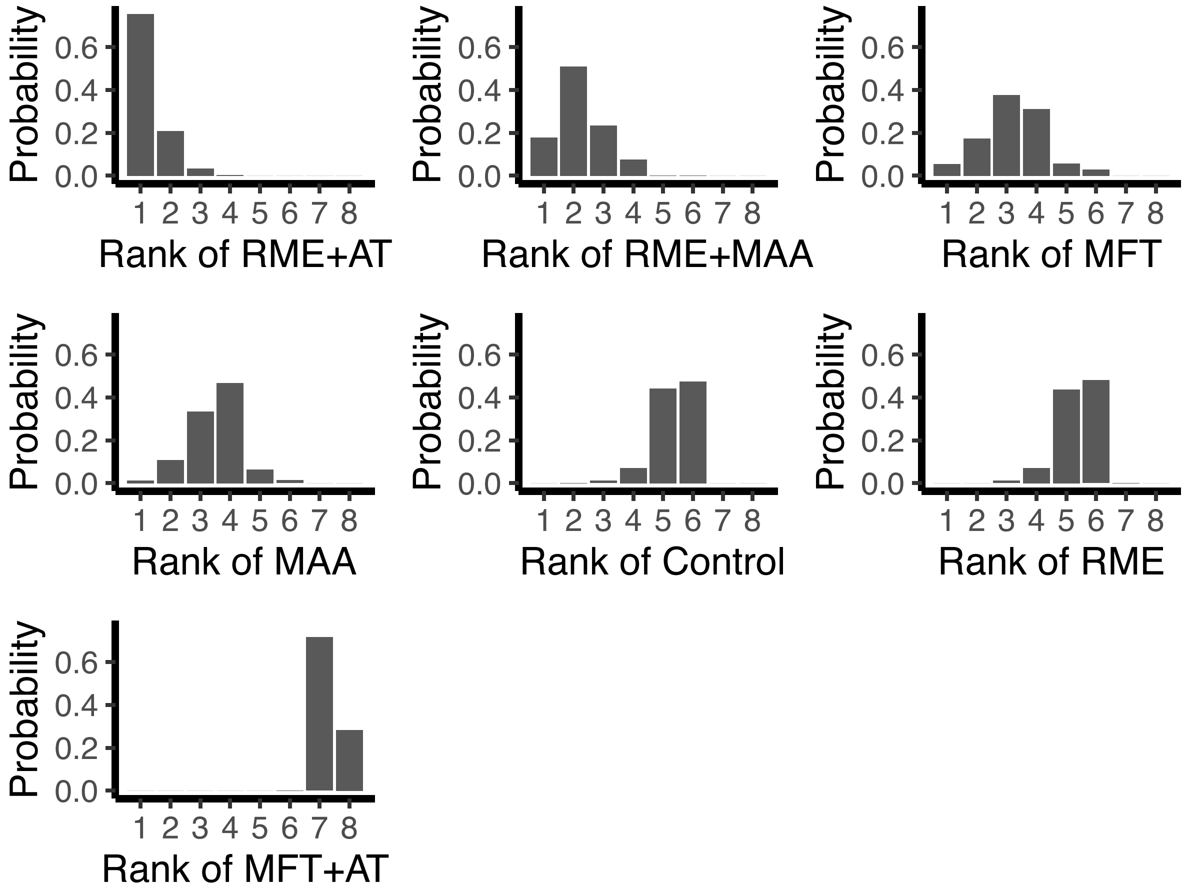

Fig. 6. (*continued*).

meta-analysis of other sleep-related parameters to assess efficacy. Other important health outcomes related to OSA, such as quality of life, neurocognitive function, and cardiovascular health, have not yet been systematically addressed in the current study. In the future, more RCTs with larger sample sizes and more specific inclusion and exclusion criteria should be conducted.

5. Conclusion

Limited evidence indicated that MAA (alone or combined with RME) and RME + AT might be associated with benefits for pediatric patients with OSA. This study could not find convincing evidence of a significant benefit of other orthodontic appliances over control. Future RCTs should be conducted for high-quality evidence of orthodontic appliances in the treatment of pediatric OSA.

6. Practice point

- Orthodontic appliances could be used as treatment modalities for pediatric obstructive sleep apnea by correcting craniofacial abnormalities.
- Mandibular advancement appliances alone or combined with rapid maxillary expansion could reduce the apnea-hypopnea index of pediatric patients with obstructive sleep apnea.
- RME combined with adenotonsillectomy might be associated with benefits for pediatric obstructive sleep apnea, while the efficacy of other orthodontic appliances over control needs future study.

7. Research agenda

- More randomized controlled trials with larger sample sizes and more specific inclusion and exclusion criteria should be conducted in the future.
- The role of adenotonsillectomy on the effect of orthodontic treatment on patients with pediatric obstructive sleep apnea needs well-designed studies.
- It could be worthwhile to investigate the effect of combining various orthodontic treatments.

Funding

This study was supported by the Clinical Research Foundation of Peking University School and Hospital of Stomatology (PKUSS-2023CRF106).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors thank all investigators and supporters involved in the study.

Abbreviations

AHI apnea-hypopnea index
AT adenotonsillectomy
BMI body mass index
ESS Epworth sleepiness scale
$LSpO_2$ the lowest oxygen saturation
MAA mandibular advancement appliance
MFT myofunctional therapy
NRCT non-randomized controlled trials
ODI oxygen desaturation index
OSA obstructive sleep apnea
PAP positive airway pressure
PICOS population, intervention, comparison, outcomes and study
PRISMA-NMA the Preferred reporting items for systematic reviews and meta-analyses for network meta-analyses
PSQ Pediatric sleep questionnaire
RCT randomized controlled trials
RME rapid maxillary expansion

References

[1] Berry RB, Brooks R, Gamaldo CE, Harding SM, Marcus CL, Vaughn BV for the American Academy of Sleep Medicine. The AASM coding manual for the scoring of sleep and associated events: rules, terminology and technical specifications, version 2.0. Wwwaasmnetorg. Darien, Illinois: American Academy of Sleep Medicine; 2012.
[2] Li AM, So HK, Au CT, Ho C, Lau J, Ng SK, et al. Epidemiology of obstructive sleep apnoea syndrome in Chinese children: a two-phase community study. Thorax 2010; 65(11):991–7.
[3] Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc 2008;5(2):242–52.
[4] Huynh NT, Desplats E, Almeida FR. Orthodontics treatments for managing obstructive sleep apnea syndrome in children: a systematic review and meta-analysis. Sleep Med Rev 2016;25:84–94.
[5] Uema SF, Vidal MV, Fujita R, Moreira G, Pignatari SS. Behavioral evaluation in children with obstructive sleep disorders. Braz. J. Otorhinolaryngol. 2006;72(1): 120–2.
[6] Gozal D. Obstructive sleep apnea in children: implications for the developing central nervous system. Semin Pediatr Neurol 2008;15(2):100–6.
[7] Leclere JC, Marianowski R, Monteyrol PJ, Akkari M, Chalumeau F, Fayoux P, et al. Guidelines of the French Society of Otorhinolaryngology. Role of the ENT specialist in the diagnosis of childhood obstructive sleep apnea-hypopnea syndrome (OSAHS). Part 1: interview and physical examination. Eur. Annals of Otorhinolaryngol. Head and Neck Disease 2019;136(4):301–5.
[8] Working group of Chinese guidelines for the diagnosis and treatment of childhood OSA. Chinese guideline for the diagnosis and treatment of childhood obstructive sleep apnea (2020). World J. Otorhinolaryngol. Head Neck Surg. 2021;7(3): 201–20.
[9] Gozal D, Tan HL, Kheirandish-Gozal L. Treatment of obstructive sleep apnea in children: handling the unknown with precision. J Clin Med 2020;9(3).
[10] Guilleminault C, Huang YS. From oral facial dysfunction to dysmorphism and the onset of pediatric OSA. Sleep Med Rev 2018;40:203–14.
[11] Pirelli P, Saponara M, De Rosa C, Fanucci E. Orthodontics and obstructive sleep apnea in children. Med Clin 2010;94(3):517–29.
[12] Yanyan M, Min Y, Xuemei G. Mandibular advancement appliances for the treatment of obstructive sleep apnea in children: a systematic review and meta-analysis. Sleep Med 2019;60:145–51.
[13] Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. BMJ 2005;331(7521): 897–900.
[14] Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med 2015;162(11):777–84.
[15] Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
[16] Kim SY, Park JE, Lee YJ, Seo HJ, Sheen SS, Hahn S, et al. Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity. J Clin Epidemiol 2013;66(4):408–14.
[17] R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2023.
[18] Villa MP, Bernkopf E, Pagani J, Broia V, Montesano M, Ronchetti R. Randomized controlled study of an oral jaw-positioning appliance for the treatment of obstructive sleep apnea in children with malocclusion. Am J Respir Crit Care Med 2002;165(1):123–7.
[19] Machado-Junior AJ, Signorelli LG, Zancanella E, Crespo AN. Randomized controlled study of a mandibular advancement appliance for the treatment of obstructive sleep apnea in children: a pilot study. Med Oral Patol Oral Cir Bucal 2016;21(4):e403–7.
[20] Idris G, Galland B, Robertson CJ, Gray A, Farella M. Mandibular advancement appliances for sleep-disordered breathing in children: a randomized crossover clinical trial. J Dent 2018;71:9–17.
[21] Guilleminault C, Monteyrol PJ, Huynh NT, Pirelli P, Quo S, Li K. Adeno-tonsillectomy and rapid maxillary distraction in pre-pubertal children, a pilot study. Sleep Breath 2011;15(2):173–7.
[22] Hoxha S, Kaya-Sezginer E, Bakar-Ates F, Kokturk O, Toygar-Memikoglu U. Effect of semi-rapid maxillary expansion in children with obstructive sleep apnea syndrome: 5-month follow-up study. Sleep Breath 2018;22(4):1053–61.
[23] Miano S, Rizzoli A, Evangelisti M, Bruni O, Ferri R, Pagani J, et al. NREM sleep instability changes following rapid maxillary expansion in children with obstructive apnea sleep syndrome. Sleep Med 2009;10(4):471–8.
[24] Villa MP, Castaldo R, Miano S, Paolino MC, Vitelli O, Tabarrini A, et al. Adenotonsillectomy and orthodontic therapy in pediatric obstructive sleep apnea. Sleep Breath 2014;18(3):533–9.
[25] Chuang LC, Hwang YJ, Lian YC, Hervy-Auboiron M, Pirelli P, Huang YS, et al. Changes in craniofacial and airway morphology as well as quality of life after passive myofunctional therapy in children with obstructive sleep apnea: a comparative cohort study. Sleep Breath 2019;23(4):1359–69.
[26] Huang YS, Chuang LC, Hervy-Auboiron M, Paiva T, Lin CH, Guilleminault C. Neutral supporting mandibular advancement device with tongue bead for passive myofunctional therapy: a long term follow-up study. Sleep Med 2019;60:69–74.
[27] Remy F, Boyer E, Daniel C, Rousval E, Moisdon P, Burgart P, et al. Management of the pediatric OSAS: what about simultaneously expand the maxilla and advance the mandible? A retrospective non-randomized controlled cohort study. Sleep Med 2022;90. 135-41.
[28] Villa MP, Brasili L, Ferretti A, Vitelli O, Rabasco J, Mazzotta AR, et al. Oropharyngeal exercises to reduce symptoms of OSA after AT. Sleep Breath 2015; 19(1):281–9.
[29] Machado-Júnior AJ, Zancanella E, Crespo AN. Rapid maxillary expansion and obstructive sleep apnea: a review and meta-analysis. Med Oral Patol Oral Cir Bucal 2016;21(4):e465–9.
[30] Bahammam SA. Rapid maxillary expansion for obstructive sleep apnea among children - systematic review and meta-analysis. Sleep Sci. 2020;13(1):70–7.
[31] Camacho M, Chang ET, Song SA, Abdullatif J, Zaghi S, Pirelli P, et al. Rapid maxillary expansion for pediatric obstructive sleep apnea: a systematic review and meta-analysis. Laryngoscope 2017;127(7):1712–9.
[32] Fernandez-Barriales M, Lafuente-Ibanez de Mendoza I, Alonso-Fernandez Pacheco JJ, Aguirre-Urizar JM. Rapid maxillary expansion versus watchful waiting in pediatric OSA: a systematic review. Sleep Med Rev 2022;62:101609.
[33] Carvalho FR, Lentini-Oliveira DA, Prado LB, Prado GF, Carvalho LB. Oral appliances and functional orthopaedic appliances for obstructive sleep apnoea in children. Cochrane Database Syst Rev 2016;10(10):Cd005520.
[34] Schütz TC, Dominguez GC, Hallinan MP, Cunha TC, Tufik S. Class II correction improves nocturnal breathing in adolescents. Angle Orthod 2011;81(2):222–8.
[35] Cozza P, Gatto R, Ballanti F, Prete L. Management of obstructive sleep apnoea in children with modified monobloc appliances. Eur J Paediatr Dent 2004;5(1):24–9.
[36] Villa MP, Evangelisti M, Martella S, Barreto M, Del Pozzo M. Can myofunctional therapy increase tongue tone and reduce symptoms in children with sleep-disordered breathing? Sleep Breath 2017;21(4):1025–32.
[37] Camacho M, Certal V, Abdullatif J, Zaghi S, Ruoff CM, Capasso R, et al. Myofunctional therapy to treat obstructive sleep apnea: a systematic review and meta-analysis. Sleep 2015;38(5):669–75.
[38] Hsu B, Emperumal CP, Grbach VX, Padilla M, Enciso R. Effects of respiratory muscle therapy on obstructive sleep apnea: a systematic review and meta-analysis. J Clin Sleep Med 2020;16(5):785–801.