Systematic review

Mandibular advancement appliances for the treatment of paediatric obstructive sleep apnea: a systematic review


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Summary

Objective: To evaluate the effectiveness of mandibular advancement appliances (MAAs) for treatment of pediatric obstructive sleep apnea (OSA).

Methods: Several electronic databases (The Cochrane Database, EMBASE, Healthstar, MEDLINE, PubMed) were systematically searched, as well as a limited grey literature (Google Scholar) and manual searches. A health sciences librarian helped with the selection of Medical Subject Headings (MeSH), key words, and combinations of key words with truncations to account for any differences in controlled terminology in the different databases. Only studies that evaluated the effects of MAAs in children with OSA were pursued.

Results: Only 4 articles satisfied all inclusion criteria. Selected studies were retrospective except one study that was a quasi-randomized clinical trial. High risk of bias (Cochrane Risk of Bias assessment) was judged in all included studies. Based on the limited available evidence use of MAAs in a POSA population may result in improvements in Apnea Hypopnea Index (AHI) scores. However complete normalization of AHI scores was not demonstrated. Heterogeneity in study designs and collected information precluded meta-analysis.

Limitations: There are significant weaknesses in the existing evidence due primarily to absence of control groups, small sample sizes, lack of randomization and short-term results. Determination of AHI scores with MAAs still in the mouth should be avoided.

Conclusions: The current limited evidence may be suggestive that MAAs result in short-term improvements in AHI scores, but it is not possible to conclude that MAAs are effective to treat pediatric OSA. Medium- and long-term assessments are still required.

Introduction

Sleep-disordered breathing (SDB) represents a continuum of respiratory disorders from snoring to obstructive sleep apnea (OSA). It is characterized by increased upper airway resistance, which temporarily interrupts pulmonary ventilation, oxygenation, and sleep quality (1). The prevalence of paediatric OSA is estimated to be between 1 and 4 per cent (2, 3).

The most common cause of paediatric OSA is adenotonsillar hypertrophy (4). Paediatric OSA has been associated with craniofacial abnormalities including mandibular retrusion, midface dysplasia, maxillary constriction, and increased vertical growth (5).

If paediatric OSA is left untreated, it can lead to problems in physical growth (6), neurocognitive abnormalities (7), and impairments in cardiovascular function (8). Currently, there is no consensus on the best method to treat paediatric OSA (9). The most common treatment
There are a number of orthodontic treatment modalities that have been suggested to reduce the symptoms of paediatric OSA, and, at the same time, improve the associated craniofacial abnormalities. These include rapid maxillary expansion (RME) (13), mandibular advancement appliances (MAAs) (12), and orthopaedic maxillary protraction (14). The success of orthodontic appliances in improving symptoms of OSA has been attributed to enlarging the airway.

MAAs can increase the lateral dimension of the velopharyngeal airway. This is accomplished as a result of forward positioning of the mandible and reduced collapsibility of the airway (15). Stimulation of upper airway dilator muscles (genioglossus) with advancement appliances has also been suggested to improve upper airway stabilization (16). From an orthodontic perspective, MAAs alter the neuromuscular forces on the craniofacial skeleton and dentition, promoting a combination of dentoalveolar changes, and skeletal growth.

A 2007 Cochrane Review investigated functional orthopaedic appliances in paediatric patients with OSA (17). This review found one article that met inclusion criteria (18) and concluded that functional orthopaedic appliances may be effective in patients with paediatric OSA; however, strong and conclusive evidence was missing. Since this systematic review, recent articles have been published on the effectiveness of MAAs in patients with paediatric OSA. Therefore, the objective of this study is to evaluate the effectiveness of MAAs in paediatric OSA and update the previous related conclusions.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement checklist was used as a template (19).

Protocol and registration

Protocol and registration were not available.

Eligibility criteria

The population, intervention, comparison, outcome, study design (PICOS) question format was used to formulate a clinical question and well-defined inclusion criteria.

Population: Children and adolescents (up to age 16) with sleep apnea.

Intervention: Treatment with a MAA.

Comparison: Treatment versus control or before and after treatment.

Outcome: Primary outcome was change in Apnea Hypopnea Index (AHI) as measured by polysomnography (PSG). Secondary outcomes of interest include oxygen desaturation, daytime and nocturnal symptoms, and dental and skeletal changes.

Study design

Randomized or non-randomized clinical trials, either prospective or retrospective.

Exclusion criteria

Patients with craniofacial syndromes, studies with concomitant interventions [i.e. continuous positive airway pressure (CPAP), surgical mandibular advancement, or adenotonsillectomy], and patients older than 16 years were excluded. Patients older than 16 years were excluded as this is the upper age limit at which growth modification appliances are usually effective in children.

Information sources and search strategy

With the assistance of a senior health sciences librarian, a systematic search of electronic databases was completed using PubMed, EMBASE (OvidSP), MEDLINE (OvidSP), Healthstar (OvidSP), Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews from their inception to the third week of August 2014. The search was conducted using Medical Subject Headings (MeSH), key words, and combinations of key words with truncations to account for any differences in controlled terminology in the different databases. The specific search strategies for each database are shown in Supplementary Table 1.

Hand searches of the reference lists of relevant articles were completed to identify other pertinent articles. Limited grey literature and Google Scholar searches were completed to identify relevant publications that may have been missed by the electronic database search. No limits were applied to any of the search strategies.

Study selection

In the first step of the review process, two reviewers independently reviewed article titles and available abstracts of the electronic search results. When an abstract was not available or inadequate information was provided in the abstract, the full text was obtained and reviewed. Any article that evaluated MAAs in paediatric OSA patients was considered for phase 1 inclusion. Discrepancies were resolved by a third reviewer. Full text articles were then obtained for those meeting phase 1 inclusion criteria. In phase 2 of the review process, the same two reviewers evaluated the full text articles independently by applying the remaining inclusion/exclusion criteria listed above. A third investigator again resolved discrepancies in the selection of articles. Reference lists of the selected articles were reviewed to identify any articles that may have been missed. Study authors were contacted if any important information was unclear following detailed review of the full article.

Data items

The data extracted from the studies that met the inclusion criteria were study design, sample size, mean age, type of MAA, treatment duration with the advancement appliance, change in AHI, and secondary outcomes of interest, if available.

Data collection process

Two reviewers extracted data independently, in duplicate. Extracted data was combined and compared for accuracy. Discrepancies were resolved by a third reviewer.

Risk of bias in individual studies

The selected studies were methodologically appraised according to The Cochrane Risk of Bias criteria (20) for assessing individual studies. Two reviewers assessed the quality of the studies independently, in duplicate. Discrepancies were resolved by a third reviewer.

Data synthesis

If the available collected information was found to be adequate, a meta-analysis was considered.

Results

Study selection

The methodological flow chart for the selection process is outlined in Figure 1. The specific reasons for exclusion of articles in phase 2 are
It has been hypothesized that appliances that mandate a therapeutic effect by enlarging the upper airway (velopharynx). In adults, the mandibular advancement device (MAD) is the most common non-CPAP appliance used to treat OSA (89). Studies in adult populations have found that a MAD has a diminished or similar effect on OSA signs and symptoms compared to a CPAP, but with improved tolerance and compliance to the device (90, 91). MADs have therefore been suggested for adult patients with mild to moderate OSA or for those patients who cannot tolerate CPAP (89). Specifically, those with mild OSA, younger age, lower body mass indices, and females have been reported to benefit from MADs (92).

In contrast, treatment of children with OSA remains a challenge. Although adenotonsillectomy is the most common treatment for patients with paediatric OSA, a study found that 47 per cent of patients still had abnormal sleep parameters (93) thereafter. This was likely due to the multifactorial nature of paediatric OSA. Compared to watchful waiting, adenotonsillectomy does appear to reduce symptoms and improve quality of life (94). Unlike adults, the use of CPAP in children who do not have severe signs and symptoms has not been advocated due to poor compliance and undesired craniofacial changes that follow its prolonged use.

The accompanying craniofacial abnormalities often seen in paediatric OSA patients are suggestive of the pertinence for interceptive orthodontic treatment, while simultaneously managing some symptoms of paediatric OSA. In patients with mandibular retrognathia, MAAs have been suggested to improve symptoms associated with OSA.

The studies included in this review used different appliances to achieve mandibular advancement. Most studies utilized a removable appliance to achieve mandibular changes (18, 21, 23). In addition to advancing the mandible, two studies incorporated a tongue retainer (to stimulate the tongue to rest directly behind upper incisors and improve habitual position of the tongue) in their appliance (18, 21) and one of those studies also included a maxillary expansion screw (21). For this study, the protocol did not specify if and how much the maxillary expansion screw was activated. The only study using a fixed MAA also incorporated a rapid palatal expander in the appliance, achieving an average expansion of 3.2 mm over 15 days (22). All of the studies reported that included patients had a BMI within the normal range.

Two studies were 6 months in length, however differed drastically in their protocol for appliance wear. One study required patients to wear the appliance full time for 1 week, then nights only (21), while the other required full-time wear except meals (18). Assuming that the nights only patients wore their appliance for 8 hours, while the full-time patients wore their appliance for 22 hours, there is a 14-hour difference in appliance wear per day between both studies. Both studies reported improved changes in AH1. The other two included studies (22, 23) were longer in duration (around 1 year) and required full-time wear of the MAA. Both these studies also demonstrated improvement in some PSG parameters following treatment.

A key factor that influences response to MAA is compliance. Only one of the studies used a fixed MAA (22), while the others required patient compliance for the MAA (18, 21, 23). While these studies indicated the protocol for wear of the MAA, none of them evaluated the level of compliance that was achieved.

If one of the goals of treatment with a MAA is to achieve permanent changes in skeletal and dental relationships, treatment duration longer than 6 months is likely required. Thus, while both of the 6-month studies reported improvement in OSA symptoms, neither reported that ideal mandibular position had been achieved (18, 21). Further, in both studies, the final PSG was done immediately.
### Table 1. Summary of study characteristics of included articles.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Sample size</th>
<th>Mean age (years)</th>
<th>Type of mandibular advancement appliance</th>
<th>Duration of advancement appliance</th>
<th>Study results</th>
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<tbody>
<tr>
<td>Zhang et al.</td>
<td>Non-randomized clinical trial</td>
<td>Treatment group: 46 (31 males, 15 females), No control group</td>
<td>9.7 years ± 1.5</td>
<td>Twin block (Mandible was advanced to the point that the lower incisors reached an edge-to-edge relationship with the upper incisors)</td>
<td>Full-time wear (except during meals) for 10.8 months Patients were seen each month for follow-up Treatment with appliance ended 1 month after mandible reached desired position</td>
<td>Average AHI index decreased from 14.08 ± 4.25 to 3.39 ± 1.86 (P &lt; 0.01) Lowest SaO$_2$ increased from 77.78 ± 3.38 to 93.63±2.66 (P &lt; 0.01) Apnea was defined as complete interruption of airflow that lasts at least two breaths. Hypopnea was defined as ≥ 50% reduction of airflow with arousal and/or &gt;3% drop in SaO$_2$. Mean SaO$_2$ did not change significantly (P &gt; 0.05) from 96.22 ± 1.11 to 96.52 ± 1.07 Cephalometric data demonstrated a significant increase in superior posterior airway space, middle airway space, SNB angle and facial convexity (P &lt; 0.01) Significant reduction in respiratory effort related arousals 7.06 ± 5.37 to 1.31 ± 1.45 (P &lt; 0.05) due to a total increase in airway volume (P &lt; 0.01). Significant reduction in respiratory disturbance index 7.3 ± 5.6 to 1.3 ± 1.8 (P &lt; 0.05) Length of the mandible (Co-Gn) increased by 6.1 mm</td>
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<td>Schutz et al</td>
<td>Non-randomized clinical trial</td>
<td>Treatment group: 16, No control group</td>
<td>12.6 years ± 11.5 months</td>
<td>Herbst appliance and maxillary expander Mandible was advanced 6mm and opened 4mm vertically. Stepwise activations were completed Rapid palatal expander was adapted to the Herbst appliance and expanded for 15 days. Mean maxillary expansion was 3.19 mm.</td>
<td>12 months (fixed herbst appliance for 24 hours/day)</td>
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<tr>
<td>Cozza et al.</td>
<td>Non-randomized clinical trial</td>
<td>Treatment group: 20 (10 males, 10 females), Control group (healthy): 20 (10 males, 10 females), Control group had no treatment</td>
<td>Treatment group: 5.91 years (range 4–8 years), Control group: 6 years (range 5–7 years)</td>
<td>Modified monobloc (full occlusal coverage with maxillary expansion screw and tongue retainer). A Tucat’s pearl on a sliding wire was used to determine the reference point for the tip of the tongue.</td>
<td>6 months Appliance worn full time for the first week then nights only</td>
<td>Significant reduction in apnoea–hypopnoea index from 7.88 to 3.66 (P = 0.0003)</td>
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<tr>
<td>Study</td>
<td>Study design</td>
<td>Sample size</td>
<td>Mean age (years)</td>
<td>Type of mandibular advancement appliance</td>
<td>Duration of advancement appliance</td>
<td>Study results</td>
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<td>Appliance placed the mandible in an edge-to-edge incisor relationship</td>
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<td>Apnoea was defined as cessation of airflow for at least 10 seconds</td>
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<td>Occlusal coverage prevented maxillary posterior teeth from erupting, however eruption of posterior mandibular teeth was encouraged by trimming acrylic from the occlusal surface</td>
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<td>Hypopnoea was defined as reduction in the amplitude of airflow or thoracoabdominal wall movement greater than 50% of baseline for more than 10 seconds (oxygen desaturation did not need to occur) or the same reduction with oxygen desaturation of at least 3% and associated with arousal</td>
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<td>Lingual arch soldered to lower primary molars was used to provide anchorage and prevent jaw opening during sleep.</td>
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<td>Daytime sleepiness and sleep quality improved in treated patients (Epworth sleepiness scale decreased from 15.2 ± 4.9 to 7.1 ± 2)</td>
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<td>Class II intermaxillary elastics were used at night from the monobloc to the lower lingual arch</td>
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<td>No significant difference in the minimum arterial oxygen saturation</td>
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<tr>
<td>Villa et al. (18)</td>
<td>Randomized clinical trial</td>
<td>Treatment group: 19 (10 males, 9 females)</td>
<td>Treatment group: 6.86 years ± 2.34 years</td>
<td>Acrylic bite plate for mandibular positioning. Each appliance had a lingual ‘target’ which was an acrylic ring to stimulate the tongue into proper position Appliance was uniquely designed to correct each patient’s mandibular malposition (Retrognathic mandibles were advanced, deep bites were raised, and cross-bites were recentred)</td>
<td>6 months</td>
<td>Significant reduction in apnoea-hypopnoea index from 7.1 ± 4.6 to 2.6 ± 2.2 (P &lt; 0.001) versus control group which did not show any reduction</td>
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<td></td>
<td></td>
<td>Control group (OSA): 13 (10 males, 3 females)</td>
<td>Control group: 7.34 years ± 3.1 years</td>
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<td>Authors considered at least a 50% reduction in the AHI as successful treatment with an oral appliance. AHI fell 50% in 9/14 treated patients (64.2%)</td>
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<td></td>
<td></td>
<td>Control group had no treatment</td>
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<td>Desaturation index decreased in treated patients but was not significant</td>
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**Table 1.** Continued
following the 6-month treatment period. Neither study indicated if there was any retention or follow-up protocol post appliance removal and if any additional interventions were needed to manage either OSA or the craniofacial anomaly. In contrast, the studies that were longer in duration indicated improvement in skeletal relationships or facial profile following treatment (22, 23). This improvement may also be attributed to the fact that both these studies evaluated patients who were at their peak growth period.

A key consideration in determining whether MAAs produce long-term effects is whether the final PSG was done with the appliance in situ. This information would clarify whether use of the MAA produced skeletal changes or merely repositioned the mandible momentarily to a more forward position when the PSG was conducted. Since positioning the mandible forward normally enlarges the oropharynx, improvement in sleep parameters may not be the result of permanent skeletal changes or improvement in craniofacial abnormalities but just the fact that the mandible was repositioned forward. The included studies varied widely in this regard. Two studies completed the post-treatment PSG without the MAA in place (22, 23), while one study completed the PSG with the appliance in situ (21). The other included study did not indicate whether the appliance was in situ for the post-treatment PSG (18).

It is of value to note that only one of the included studies indicated the pre-treatment severity of mandibular retrognathism (22). This is important in patient selection as well as patient education as it is important to know which patients will benefit most from a MAA as well as which patients may still require additional treatment for jaw disproportions.

Limitations

Although the studies reported improvement in some PSG values with the MAA, none of the respiratory variables returned to normal pediatric reference values. This is likely reflective that other aetiologic factors, not just an anatomical problem, play a role in this paediatric OSA population. Thus, even if treatment using a MAA appears successful, patients will likely still require follow-up and long-term monitoring from their physician. The multidisciplinary nature of OSA, requiring management and interaction of many members of the health care team, cannot be emphasized enough.

The included studies were found to have a high risk of potential bias. Although one study was a quasi-randomized clinical trial, the method of allocation (alphabetically by surname) was inadequate (18). In this study, the number of patients randomized was different from the number of patients analysed due to a large number of patients lost to follow-up. Other methodological problems across studies include no allocation concealment, no blinding, and failure to calculate and justify sample size. Two of the included studies did not include a control group (22, 23). While both authors indicate that a control group was purposely left out due to the fact that it would be unethical to withhold treatment in mandibular retrognathic patients during peak growth, we cannot rule out the effects of normal growth in either of these studies. Among the studies that did include a control, both control groups varied. In one study, controls were healthy patients without OSA (21), while in another study, controls had OSA (18). Neither of the control groups received any type of treatment. While it would have been ideal for all studies to include a control group, the studies without controls provide valuable information (22, 23). Both these studies demonstrated that ideal mandibular position had been achieved post-treatment. Additionally, both these studies were longer in duration and included patients who were in their pubertal growth spurt.

It is important to note that any oral appliance that repositions the mandible forward will immediately enlarge the upper airway space. Thus, a PSG while the appliance is in the mouth may result in temporarily outcomes. This does not, however, demonstrate that the aetiology of the problem has been resolved. If the aetiology of paediatric OSA is mandibular retrognathia, permanent skeletal and dental abnormalities are required. These changes require treatment of longer duration than 1 year. Thus, without long-term studies and without knowing whether the appliance was in situ for the final PSG, we cannot determine if the effects of oral appliances are short-lived.

Recent evidence sheds light on the role of maxillary transverse constriction in paediatric SDB (95). This study found that palatal crossbite involving at least three teeth was significantly higher in

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Table 2. Risk of bias assessment.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study</th>
<th>Zhang et al. (23)</th>
<th>Schutz et al. (22)</th>
<th>Cozza et al. (21)</th>
<th>Villa et al. (18)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sequence generation</strong> (selection bias)</td>
<td>High: inadequate generation of a random sequence for selection</td>
<td>High: inadequate generation of a random sequence for selection</td>
<td>High: inadequate generation of a random sequence for selection</td>
<td>High: inadequate generation of a random sequence for selection</td>
<td>Moderate: randomization assigned alphabetically by surname</td>
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<tr>
<td><strong>Allocation concealment</strong> (selection bias)</td>
<td>High: inadequate concealment of allocations</td>
<td>High: inadequate concealment of allocations</td>
<td>High: inadequate concealment of allocations</td>
<td>High: inadequate concealment of allocations</td>
<td>High: inadequate concealment of allocations</td>
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<tr>
<td><strong>Blinding of participants and personnel (performance bias)</strong></td>
<td>High: performance bias due to knowledge of the allocated intervention by patients and personnel during study</td>
<td>High: performance bias due to knowledge of the allocated intervention by patients and personnel during study</td>
<td>High: performance bias due to knowledge of the allocated intervention by patients and personnel during study</td>
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<td>High: performance bias due to knowledge of the allocated intervention by patients and personnel during study</td>
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<tr>
<td><strong>Blinding of outcome assessment (detection bias)</strong></td>
<td>Unclear: unclear if outcome assessor was blinded</td>
<td>Low: no missing outcome data</td>
<td>Low: no missing outcome data</td>
<td>Low: no missing outcome data</td>
<td>Low: no missing outcome data</td>
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<tr>
<td><strong>Incomplete outcome data (attrition bias)</strong></td>
<td>Low: pre-specified outcomes were reported</td>
<td>Low: pre-specified outcomes were reported</td>
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<td>Low: pre-specified outcomes were reported</td>
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<td><strong>Selective outcome reporting (reporting bias)</strong></td>
<td>High: no control group</td>
<td>High: no control group</td>
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<tr>
<td><strong>Other sources of bias</strong></td>
<td>Unclear</td>
<td>Unclear</td>
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<tr>
<td><strong>Overall risk of bias</strong></td>
<td>High</td>
<td>High</td>
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</table>
patients at high-risk for SDB (68%) compared to those at low-risk (23.2%). Further, treatment with RME demonstrated a 14 per cent improvement in quality of life scores in the high-risk SDB group. Thus, in the short-term, RME may be a favourable treatment modality for improvement of quality of life in children with mild SDB who are also maxillary transverse deficient.

In summary, our findings are consistent with the conclusions of a previous systematic review (17). Our review found three additional relevant articles that we considered pertinent (21–23) which show some support for the use of MAA in a selective group of paediatric OSA patients.

If treatment with a MAA does in fact demonstrate long-term stability, the showcased effects are promising. Not only will treatment have the ability to improve symptoms of paediatric OSA, it also takes advantage of the adolescent growth spurt and may produce permanent skeletal and dentoalveolar changes to improve the malocclusion. Additionally, if permanent change is demonstrated, children may not need to wear the MAA permanently thereafter as skeletal growth may have resolved one of the main contributing factors of paediatric OSA. The multifactorial aetiology of paediatric OSA has to be considered.

Conclusion

- The current limited evidence may be suggestive that MAAs result in improvements in AHI scores, but it is not possible to conclude that MMAs are effective to treat paediatric OSA.
- There are significant weaknesses in the existing evidence due primarily to absence of control groups, small sample sizes, lack of randomization and short-term results.

Supplementary material

Supplementary material is available at European Journal of Orthodontics online.

References


