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APARELHOS ORTOPÉDICOS INTRAORAIS DE AVANÇO MANDIBULAR NA APNEIA OBSTRUTIVA DO SONO PEDIÁTRICA: REVISÃO GUARDA-CHUVA

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Tese apresentada à Faculdade de Ciências Médicas da Universidade Estadual de Campinas como parte dos requisitos exigidos para obtenção do título de Doutora em Ciências.

Orientador: Prof. Dr. Almiro José Machado Júnior

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RESUMO

Introdução: A apneia obstrutiva do sono (AOS) em crianças é definida pela interrupção total ou parcial do fluxo aéreo de modo intermitente, devido ao colabamento da via aérea superior durante o sono.[1] É condição frequente na infância com prevalência entre 1,2% a 5,7% [2], e que pode afetar diferentes aspectos da vida da criança como cognitivo, função metabólica e cardiovascular, entre outros. Existem algumas opções de tratamento como adenotonsilectomia, terapia miofuncional, aparelhos de avanço mandibular (AAM), expansão rápida da maxila e dispositivos de pressão aérea positiva, mas ainda há dúvidas sobre qual método é mais adequado para o tratamento da AOS em crianças. *Objetivo:* Analisar a eficácia dos aparelhos de avanço mandibular na síndrome da apneia obstrutiva do sono em crianças. *Métodos:* A pesquisa foi realizada em agosto de 2021 e utilizou diversas bases de dados como: PubMed, EBSCO (Dentistry & Oral Sciences Source), LILACS, Ovid, SciELO Web of Science, EMBASE BIREME, BBO BIREME e Biblioteca Cochrane. *Resultados:* Somente três revisões sistemáticas e duas metanálises foram incluídas no estudo. Todos os estudos mostraram alguma melhora, não somente no aumento do espaço de via aérea, mas também na redução do índice de apneia e hipopneia, que foi aproximadamente de 50% de seu valor inicial, devido ao uso dos aparelhos de avanço mandibular no tratamento da apneia obstrutiva do sono em crianças. *Conclusão:* Apesar de haver a necessidade de mais estudos randomizados, com maior número de pacientes e critérios específicos de inclusão e exclusão para o estabelecimento adequado de protocolos de tratamento, os aparelhos de avanço mandibular podem ser considerados como parte do tratamento multidisciplinar da apneia obstrutiva do sono na infância.

Palavras-chaves: avanço mandibular; apneia obstrutiva do sono; crianças.

ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is defined as intermittent partial or complete collapse of the upper airway during sleep.[1] It's a common condition in childhood, with a prevalence ranging from 1,2% to 5,7% [2], and it can harm several aspects of children's life such as cognitive, metabolic and cardiovascular functions, among others. There are treatment options, such as adenotonsillectomy, myofunctional therapy, mandibular advancement appliances (MAAs), rapid maxillary expansion, and positive airway pressure devices, but there is still doubt about which method is more suitable for the treatment of OSA in children. *Objective:* To analyze the effectiveness of MAAs in the treatment of OSA in children. *Methods:* The search was conducted in August 2021 in different electronic databases, such as PubMed, EBSCO (Dentistry & Oral Sciences Source), LILACS, Ovid, SciELO Web of Science, EMBASE BIREME, BBO BIREME, and the Cochrane Library. *Results:* Only three systematic reviews and two meta-analyses were included in the present study. All studies showed improvement in the score on the apnea-hypopnea index, with a reduction around 50%, after using MAAs in the treatment of pediatric OSA. *Conclusion:* Although more randomized studies are needed, MAAs can be considered part of the multidisciplinary treatment for pediatric OSA.

Keywords: mandibular advancement; obstructive sleep apnea; children.

SUMÁRIO

1 INTRODUÇÃO

A apneia obstrutiva do sono (AOS) em crianças é definida pela interrupção total ou parcial do fluxo aéreo de modo intermitente, devido ao colabamento da via aérea superior durante o sono.[1] Trata-se de condição frequente na infância com prevalência entre 1,2% a 5,7% [2] e que pode trazer diversas consequências como redução da atenção e concentração, atrasos de aprendizagem, prejuízo na consolidação da memória, comportamento agressivo [3,4], alterações metabólicas, problemas pondero-estaturais, distúrbios cardiovasculares, enurese noturna, entre outras [2].

Os principais fatores de risco associados são: sexo masculino, raça negra, história familiar positiva para AOS, prematuridade, obesidade, rinite alérgica, asma, doenças neurológicas, doenças neuromusculares e alterações do esqueleto facial, como a micrognatia e a hipoplasia do terço médio da face [5].

Diferente dos adultos a AOS pediátrica encontra-se, na maioria das vezes, relacionada `a hipertrofia de tonsilas palatinas e faríngea, que ocasiona o estreitamento da via aérea superior. A obesidade infantil também está entre as principais causas da apneia obstrutiva na infância, porém a complexidade da AOS pode ser exemplificada por outros fatores relacionados como o esqueleto facial e tônus neuromuscular.[6]

O diagnóstico deve seguir alguns critérios como ronco habitual (≥3 vezes/semana), presença de esforço/obstrução respiratória ou sintomas diurnos como sonolência excessiva ou hiperatividade (relacionados à fragmentação do sono), além dos achados polissonográficos de um ou mais eventos obstrutivos por hora de sono, ou PCO_2 acima de 50mmHg por mais de 25% do tempo de sono, associado a roncos, movimentos toracoabdominais paradoxais, ou redução da amplitude da onda de pressão do fluxo nasal [7].

A AOS pediátrica é classificada de acordo com o valor do índice de apneia e hipopneia (IAH) registrado no exame de polissonografia, sendo considerada leve com IAH > 1 ≤ 5/hora, moderada com IAH > 5 ≤ 10/hora e grave com IAH >10/hora [5].

A escolha do tratamento da AOS em crianças considera: idade, gravidade dos sintomas, achados clínicos, presença comorbidades e achados polissonográficos[8]. Existem diversos tratamentos disponíveis atualmente para a AOS, como a terapia miofuncional, a adenotonsilectomia, o CPAP (*continuous positive airway pressure*) aparelho de pressão aérea positiva contínua, e o uso de aparelhos ortodônticos/ortopédicos de avanço mandibular e/ou expansão rápida da maxila. Entretanto, nem todos possuem a mesma eficácia e tolerância.

A cirurgia de adenotonsilectomia é o tratamento mais comum da AOS na população pediátrica e tem se mostrado bastante efetiva ao longo dos anos em crianças não-obesas,

inclusive com melhora da oximetria[9]. Porém, alguns estudos apontam a adenotonsilectomia como curativa em cerca de 25-75% dos pacientes.[10-12]

O CPAP (*continuous positive airway pressure*), aparelho de pressão aérea positiva contínua, é considerado um tratamento de primeira linha na AOS em crianças sem hipertrofia adenotonsilar, porém com pouca tolerância (25-50%)[13-15] e risco de sequelas craniofaciais após uso prolongado do aparelho.[16-17]

A terapia miofuncional colabora no reposicionamento da língua, melhora a respiração nasal e aumenta o tônus muscular, prevenindo apneia residual pós-adenotonsilectomia e contribuindo na adesão ao CPAP.[18]

Outro recurso terapêutico, são os aparelhos ortodônticos/ortopédicos de avanço mandibular. O avanço mandibular é um tratamento bem estabelecido no controle da AOS em adultos.

Em crianças e adolescentes, tem-se como objetivo corrigir a retrognatia mandibular redirecionando e estimulando o crescimento ósseo mandibular anteriormente, de modo passivo ou ativo. Isso pode ser alcançado por meio do uso de diferentes aparelhos funcionais, como Herbst, Frankel II, bloco duplo (*twin-block*), entre outros[19].

Aparelhos ortopédicos funcionais têm sido utilizados para o tratamento da retrognatia mandibular em crianças e adolescentes, e recentemente, para o tratamento da AOS. Esses aparelhos são capazes de aumentar o espaço de via aérea superior, reduzir a colapsabilidade da via aérea e melhorar o tônus muscular[20,21,22,23], eliminando, assim, um dos fatores de risco para a AOS no adulto.

2 OBJETIVOS

O objetivo desta revisão guarda-chuva é fazer uma síntese de revisões sistemáticas e metanálises sobre a eficácia dos aparelhos intraorais ortodônticos/ortopédicos de avanço mandibular no tratamento da apneia obstrutiva do sono em crianças com retrognatia, utilizando como parâmetro principal a variação do índice de apneia e hipopneia (IAH).

3 METODOLOGIA

Os Principais Itens para Relatar Revisões sistemáticas e Metanálises (PRISMA) foram considerados na revisão guarda-chuva a seguir. A mesma foi registrada no sistema PROSPERO sob identificação CRD42021285521.

3.1 Critérios de inclusão:

- População: pediátrica e adolescentes (18 anos de idade ou menos) diagnosticados com AOS na ausência de síndromes craniofaciais;
- Intervenção: aparelhos de avanço mandibular;
- Comparativo: com ou sem grupo controle;
- Resultados: resultado primário foi o Índice de Apneia e Hipopneia (IAH); resultados secundários foram saturação de oxigênio, qualidade do sono e espaço em via aérea superior;
- Tipo de estudo: revisões sistemáticas e metanálises.

3.2 Métodos de busca:

Para a realização da revisão guarda-chuva foram selecionados artigos de revisão sistemática e metanálises das seguintes bases de dados: PubMed, EBSCO (Dentistry & Oral Sciences Source), LILACS, Ovid, SciELO Web of Science, EMBASE BIREME, BBO BIREME e a Biblioteca Cochrane, de 2015 até agosto de 2021. As palavras-chave consideradas foram: “apneia do sono”, “obstrutiva”, “SAOS”, “resistência de via aérea superior”, “distúrbio respiratório do sono”, “avanço mandibular”, “aparelhos intraorais”, “protator mandibular”, “tratamento ortodôntico”, “crianças” e “pediátrica”.

3.3 Seleção dos estudos:

A seleção das revisões sistemáticas e metanálises foi realizada por dois revisores (C.C.M., F.R.A.) de modo independente, e as divergências foram solucionadas por um terceiro revisor (A.J.M.Jr.). Somente foram incluídos estudos com texto completo disponível.

3.4 Análise de dados:

As revisões sistemáticas e metanálises elegíveis para o estudo foram avaliadas pela ferramenta ROBIS (*Risk Of Bias In Systematic Reviews*) da Universidade de Bristol.

Tanto nos critérios para elegibilidade dos estudos, quanto nos métodos realizados para identificar e/ou selecionar estudos, os artigos incluídos nesta revisão guarda-chuva foram

considerados como de baixo potencial de viés. Já no critério de síntese e resultados, apenas um artigo foi classificado como de risco de viés incerto.

Na avaliação de risco de viés geral, os artigos foram classificados como de baixo risco.

Quadro 1. Análise de risco de viés (ferramenta ROBIS).

Autor/ano	Elegibilidade	Identificação e seleção	Coleta de dados e avaliação	Síntese e resultados	Risco de viés geral
Yanyan et al., 2019[17]	S/S/S/S/PS Baixo	PS/SI/S/S/S Baixo	S/PS/S/S/S Baixo	S/S/S/PS/PN/PS Baixo	Baixo
Bariani et al., 2021[18]	S/PS/S/S/PS Baixo	PS/SI/S/S/S Baixo	S/S/S/SI/SI Baixo	S/N/PS/S/PN/N Incerto	Baixo
Nazarali et al., 2015[19]	S/S/S/S/PS Baixo	PS/SI/S/S/S Baixo	S/S/PS/S/PS Baixo	S/S/PS/S/PS/PS Baixo	Baixo
Carvalho et al., 2016[20]	S/S/S/S/PS Baixo	PS/SI/S/PS/S Baixo	S/S/S/S/S Baixo	S/S/S/S/S/S Baixo	Baixo
Huynh et al., 2015[21]	S/S/S/S/PS Baixo	PS/S/S/S/S Baixo	S/PS//PS/S/PS Baixo	S/S/PS/S/PS/S Baixo	Baixo

S = sim; PS = provavelmente sim; SI = sem informações; PN = provavelmente não; N = não.

4 RESULTADOS

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468 Review Article

Mandibular Advancement Appliances in Pediatric Obstructive Sleep Apnea: An Umbrella Review

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Abstract

Introduction Obstructive sleep apnea (OSA) is defined as intermittent partial or complete collapse of the upper airway during sleep. It is a common condition in childhood, with an incidence ranging from 1.2% to 5.7%, and it can harm several aspects of children's life, such as cognitive, metabolic and cardiovascular functions, among others.

There are treatment options, such as adenotonsillectomy, myofunctional therapy, mandibular advancement appliances (MAAs), rapid maxillary expansion, and positive airway pressure devices, but there is still doubt about which method is more suitable for the treatment of OSA in children.

Objective To analyze the effectiveness of MAAs in the treatment of pediatric OSA.

Materials and Methods The search was conducted in August 2021 in different electronic databases, such as PubMed, EBSCO (Dentistry & Oral Sciences Source), LILACS, Ovid, SciELO, Web of Science, EMBASE BIREME, BBO BIREME, and the Cochrane Library.

Results Only three systematic reviews and two meta-analyses were included in the present study. All studies showed improvement in the score on the apnea-hypopnea index after using MAAs in the treatment of pediatric OSA.

Conclusion Although more randomized studies are needed, based on the present umbrella review, MAAs must be considered part of the multidisciplinary treatment for pediatric OSA.

Keywords

- mandibular advancement
- obstructive sleep apnea
- children

Introduction

Obstructive sleep apnea (OSA) is defined as intermittent partial or complete collapse of the upper airway during sleep.[1] It is a common condition in childhood, with an incidence ranging from 1.2% to 5.7%,[2] and it can harm several aspects of children's life, resulting in attention deficit, learning delay, memory consolidation impairment, aggressive

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behavior,[3,4] metabolic disorders, cardiovascular disease, and nocturnal enuresis, for example.

Unlike the cases in adults, pediatric OSA is most related to adenotonsillar hypertrophy, which narrows the upper airway. Obesity is also among the main causes of pediatric OSA, but its complexity can also be explained by other factors, such as craniofacial type and neuromuscular tone.[5]

The choice of treatment for pediatric OSA considers age, severity of symptoms, clinical findings, presence of comorbidities and polysomnographic results.[6] Nowadays, there are many treatment options, such as adenotonsillectomy, myofunctional therapy, mandibular advancement appliances (MAAs), rapid maxillary expansion (RME), and positive airway pressure, but not all of them have the same efficacy and tolerance.

Adenotonsillectomy is still the most performed treatment in cases of pediatric OSA, and it has been highly effective throughout the years in non-obese children, even resulting in an improvement in oximetry results.[7] However, some studies[8–10] have reported that adenotonsillectomy is curative in 25% to 75% of the patients.

Continuous positive airway pressure (CPAP) is considered the first-line treatment in pediatric OSA without adenotonsillar hypertrophy, although with low tolerance (25% to 50%) [11–13] and risk of craniofacial sequels after long-term use.[14,15] Myofunctional therapy helps tongue repositioning, improves nasal breathing, and increases muscle tone, preventing residual apnea after adenotonsillectomy and increasing CPAP adherence.[16]

Another therapeutic resource can be found in MAAs: mandibular advancement is well established in adult OSA treatment; in children, the aim is to correct mandibular retrognathia through redirection and stimulation of anterior mandibular growth, in a passive or active manner, which can be achieved through different appliances, such as the Herbst, Frankell II, twin-block, and others.[17]

Functional orthopedic appliances have been used to treat mandibular retrognathia in children and teenagers and, recently, to treat OSA. They are able to increase upper airway space, reduce airway collapsibility, and improve muscle tone.[18,20] Thus one risk factor for adult OSA may have been solved.

The main goal of the present umbrella review was to analyze the effectiveness of MAAs in the treatment of pediatric OSA by means of apnea-hypopnea index (AHI) variability.

Materials and Methods

The present umbrella review followed the checklist of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Inclusion Criteria

- Population: children and adolescents (age $\leq$ 18 years) diagnosed with OSA without craniofacial syndromes.
- Intervention: MAAs.
- Comparison: with and without a control group.
- Outcome: AHI.
- Study design: systematic review and e meta-analysis.

Search Strategy

A systematic search was conducted until August 2021 in the following electronic databases: PubMed, EBSCO (Dentistry & Oral Sciences Source), LILACS, Ovid, SciELO, Web of Science, EMBASE BIREME, BBO BIREME, and the Cochrane Library. The search terms were *sleep apnea*, *obstructive*, *OSA*, *sleep disordered breathing*, *mandibular advancement*, *oral appliances*, *mandibular protractor*, *orthodontic treatment*, *children*, and *pediatric*.

Study Selection

Two reviewers (CCM and FRA) independently selected the articles, and only full-text articles were included.

Data Collection

The following data were extracted from each study included: author, year of publication, study design, age of the sample, treatment, and AHI before and after MAAs.

Risk of Bias in Individual Studies

To evaluate the risk of bias in individual studies, the University of Bristol's Risk of Bias in Systematic Reviews (ROBIS) tool was used. Two reviewers (CCM and FRA) independently evaluated the quality of the studies.

Both in terms of the criteria for the eligibility of studies and the methods, the articles included were considered to have low potential for bias. In the synthesis and results criterion, only one article was classified as presenting an unclear risk of bias. In the overall risk of bias assessment, the articles were classified as low risk, as they considered the heterogeneity of the data (►**Table 1**).

Results

The flow chart of the selection process is illustrated in ►**Figure 1**. A total of 36 articles were identified: 4 in EBSCO, 8 in PubMed, 8 in LILACS, 9 in EMBASE BIREME and BBO BOREME, 6 in the Cochrane Library, and 1 through other sources; 32 articles remained after duplicates were removed. Then, 27 articles were excluded after screening the titles, abstracts, study designs, and full text availability. Five articles remained: three systematic reviews and two meta-analyses.

The results of the present umbrella review are organized in ►**Table 2**, followed by the studies included in each systematic review and meta-analysis, in ►**Table 3**. The selected articles were published between 2015 and 2021. The sample sizes ranged from 32 to 269 individuals aged between 3.5 and 14 years.

Several types of MAAs were used, such as single acrylic plate, twin-block, two acrylic plates (Planas), Herbst + RME, Bioadjusta X, modified monoblock, Myobrace/MyOSA, Andresen activator, Frankel II, and a thermoplastic intraoral appliance.

Table 1 Risk of bias in the included studies according to the ROBIS tool.

Author/year	Eligibility	Identification and selection	Data collection	Synthesis and results	Risk of bias
Yanyan et al., 2019[17]	Y/Y/Y/Y/PY Low	PY/NI/Y/Y/Y Low	Y/PY/Y/Y/Y Low	Y/Y/Y/PY/PN/PY Low	Low
Bariani et al., 2021[18]	Y/PY/Y/Y/PY Low	PY/NI/Y/Y/Y Low	Y/Y/Y/NI/NI Low	Y/N/PY/Y/PN/N Unclear	Low
Nazarali et al., 2015[19]	Y/Y/Y/Y/PY Low	PY/NI/Y/Y/Y Low	Y/Y/PY/Y/PY Low	Y/Y/PY/Y/PY/PY Low	Low
Carvalho et al., 2016[20]	Y/Y/Y/Y/PY Low	PY/NI/Y/PY/Y Low	Y/Y/Y/Y/Y Low	Y/Y/Y/Y/Y/Y Low	Low
Huynh et al., 2015[21]	Y/Y/Y/Y/PY Low	PS/S/S/S/S Low	Y/PY/PY/Y/PY Low	Y/Y/PY/Y/PY/Y Low	Low

Abbreviations: N. no; NI, no information; PN, probably no; PY, probably yes; ROBIS, Risk of Bias in Systematic Reviews; Y, yes.

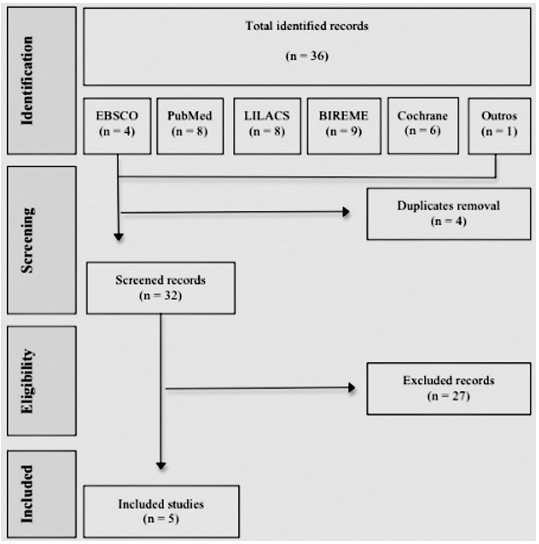

Fig. 1 Flow chart of the selection process of studies.

In addition, different protocols regarding the period of use were established, ranging from 3 weeks to 20 months. In most studies, the MAAs treatment had a minimum duration of 6 months, with the exception of a subgroup treated for 3 weeks in the study by Yanyan et al.[17] Long-term treatment (6 to 12 months) was more effective than short-term treatment. In general, MAAs were well tolerated in the pediatric population, with only 14 treatment dropouts (6 controls and 8 patients treated with MAAs), in the included studies.

All studies presented a reduction in the AHI after treatment with MAAs, except those in the study by Rădescu et al.[31] In two studies,[18,19] although there was a reduction in the AHI, it could not be statistically analyzed due to the considerable heterogeneity of the data. In the other 3 studies,[17,20,21] a reduction of at least 50% in the AHI was observed, which was considered as therapeutic success, even if the scores were not within the normal range.

Discussion

In the last decade, several studies[19,21] have reported that multidisciplinary (including orthodontic) treatments for pediatric OSA can really improve not only snoring, but also apnea through growth balance correction.

Mandibular advancement combined with RME is an alternative treatment method for pediatric patients with sleep respiratory disturbances.[17,21]

In 1860, RME was reported for the first time as an orthodontic treatment for the correction of maxillary constriction. However, RME was linked to OSA treatment, since it was able to reduce, in children, nocturnal enuresis, a common OSA symptom. Nowadays, RME is often performed through a fixed intraoral orthodontic appliance, gradually adjusted throughout the treatment.[21]

According Yanyan et al.,[17] high-quality meta-analyses support mandibular advancement in OSA patients, even in severe cases, as long as the treatment is established before pubertal peak. Long-term treatment (of at least 6 months) is superior to the short-term treatment. Mandibular advancement appliances improve the AHI and increase posterior airway space, reducing airway collapsibility. From the orthodontic perspective, MAAs also promote dentoalveolar changes and bone growth.[17]

Several factors contribute to OSA occurrence, such as obesity and adenotonsillar hypertrophy, conditions that narrow the superior airway. Other conditions are abnormalities in craniofacial growth, such as atresic maxilla, mandibular retrognathia, increased vertical growth, and neuromuscular disorders.[18,20]

A significant number of children do not respond to adenotonsillectomy, which is still the primary treatment for OSA, and most of them do not tolerate CPAP therapy. Therefore, functional orthopedic appliances, if correctly prescribed, are well tolerated and are able to increase airway space during sleep, reduce airway collapsibility, and improve muscle tone.[18,20]

As the functional appliance brings the jaw forward, an increase in the superior airway space occurs. Therefore, the

Table 2 Characteristics of the meta-analyses and systematic reviews included in the present study.

Study	Study design	Age	Treatment duration	ΔAHI	AHI reduction (%)	Conclusion
Yanyan et al., 2019[17]	Meta-analysis	No significant subgroup difference ($I^2 = 0\%$; $p = 0.59$)	Difference in treatment duration was observed: 3 weeks, 6 months, 10-12 months ($I^2 = 65.9\%$; $p = 0.05$); long-term treatment (6 months, 10-12 months) may be more effective	-1.75 events/h (95% confidence interval: -2.07–1.44; $p = 0.00001$)	50% for mild (1.72/3.5), 57% for moderate (4.27/7.5), and 76% for severe (10.69/14.08) cases	MAAs can be effective for mild to severe OSA before the end of pubertal peak; long-term treatment (of at least 6 months) may be more effective
Bariani et al., 2021[18]	Systematic review	7.61 ± 1.99 years	7.71 ± 5.13 months	12 studies reported reduced AHI after treatment (could not be statistically analyzed due to the considerable heterogeneity of pooled data)	Could not be statistically analyzed due to the considerable heterogeneity of pooled data	FOA can be considered a potential additional treatment in children with OSA
Nazarali et al., 2015[19]	Systematic review	8.71 ± 1.67 years	9.6 ± 2.89 months	Could not be statistically analyzed due to heterogeneity of pooled data	≥ 50% (1 study used RDI)	MAAs may improve AHI scores
Carvalho et al., 2016[20]	Systematic review	7.1 ± 2.6 years	6 months	-4.5 events/h ($p < 0.001$)	50% in 9 of the 14 subjects	64.2% of success
Huynh et al., 2015[21]	Meta-analysis	6.37 ± 1.72 years	6 months	-4.5 events/h; $p < 0.001$ (Villa et al.[15]); -4.22 events/h; $p = 0.0003$ (Cozza et al.[32])	≥ 50%	MAAs can help in the management of pediatric snoring and OSA

Abbreviations: AHI, apnea-hypopnea index; FOA, functional orthodontic appliance; MAAs, mandibular advancement appliances; OSA, obstructive sleep apnea; RDI, respiratory disturbance index.

Table 3 Characteristics of the studies included in the meta-analyses and systematic reviews selected for the present study.

Study	Study design	Subjects	Age	Interventions	Wearing time	Drop- out	Outcomes
Villa et al. 2002[22]	Randomized controlled trial	MAAs: 19; control: 13	6.86 ± 2.34 years; 7.34 ± 3.10 years	An acrylic plate; no treatment	6 months (24h) –	5 4	MAAs: AHI from 7.1 to 2.6; control: unchanged
Nunes and Francesco-Mion, 2009[23]	Randomized controlled trial	MAAs: 24; control: 16	6-9 years	Bioajusta X appliance; no treatment	6 months –	0 0	MAAs: improvements in breathing and snoring (questionnaire), airway space volumetric gain; control: airway space reduction
Machado- Júnior et al., 2016[24]	Randomized controlled trial	MAAs: 8; control: 8	8.13 ± 0.99 years; 8.39 ± 1.31 years	Two acrylic plates; no treatment	12 months (24h)	0 2	MAAs: AHI from 1.66 to 0.30; control: AHI from 1.58 to 1.97
Idris G. et al., 2018[25]	Crossover-Randomized controlled trial	MAAs: 9; control: 9	9.8 ± 1.1 years	Twin-block; sham MAAs	3 weeks overnight	3 0	MAAs: AHI from 2.8 to 1.9; control: AHI from 2.4 to 3.7
Cozza et al., 2004[26]	Non-randomized controlled trial (prospective)	20	5.91 ± 1.14 years	Modified monobloc	6 months overnight	0	AHI from 7.88 to 3.66
Schütz et al., 2011[27]	Non-randomized controlled trial (prospective)	16	12.6 years ± 11.5 months	Herbst + RME	12 months (24h)	0	AHI from 4.8 to 1.3 and airway space improvement
Zhang et al., 2013[28]	Non-randomized controlled trial (prospective)	46	9.7 ± 1.5 years	Twin-block	10.8 months (24h)	0	AHI from 14.08 to 3.39 and airway space improvement
Levrini et al., 2018[29]	Non-randomized controlled trial (prospective)	9	4-8 years	Myobrace/MyOSA	3 months	0	AHI reduction was statistically significant ($p = 0.0425$)
Maspero et al., 2015[30]	Non-randomized controlled trial (prospective)	MAAs: 40; control: 10	9-14 years; 9-14 years	Andresen activator	16 months	0	AHI and airway space improvements
Rădescu et al., 2017[31]	Case report	1	8 years	Twin-block	12 months	0	AHI increased from 2.6 to 10.2
Rose and Schessl, 2006[32]	Case report	1girl and 1 boy	8 years and 6.5 years	Frankel II	20 Months and 9 months	0	Girl: AHI normalized; boy: less apnea and oxygen desaturation
Schessl et al., 2006[33]	Case report	1	3.5 years	Frankel II	14 months	0	RDI from 66 to 2
Modesti- Vedolin et al., 2018[25]	Pilot study	18	8.3 ± 2.3 years	Thermoplastic intraoral device (superior and inferior)	2 months	0	RDI from 10 to 4.5

Abbreviations: AHI, apnea-hypopnea index; MAAs, mandibular advancement appliances; RDI, respiratory disturbance index; RME, rapid maxillary expansion.

AHI will be improved, as long as the patient is wearing the appliance. Yet, if the etiology of the problem is retrognathia or maxillary constriction, skeletal and dentoalveolar correction must be achieved to complete correction of the malocclusion and stability of results.

If these changes are accomplished permanently, pediatric patients no longer need to wear the MAAS, since the skeletal growth is complete and this important OSA predisposing factor will be solved.[19]

Obstructive sleep apnea is related to many diseases and social problems. Many adults begin snoring and experiencing other respiratory disturbances, such as OSA, in childhood; hence, the relevance of early diagnosis and treatment to prevent long-term complications in adult life. These measures also contribute to reduce costs to the healthcare system and improve quality of life.[20]

The diagnosis of OSA is based on anamnesis, physical examination, and laboratory tests, and, to date, polysomnography is the gold-standard examination. Although adenotonsillectomy is widely performed to treat pediatric OSA around the world, recurrence is very common, particularly in children with skeletal deformities, such as mandibular retrognathia, maxillary constriction, or both.[20]

All studies included in the present review showed AHI reduction, except for Rădescu et al.,[31] who observed an AHI increase. An early orthodontic treatment with a functional appliance appeared to be an accurate device to correct the molar relationship and reduce overjet in children with retrognathic mandible, but, in this study,[31] the results were lower than expected, and the authors highlighted that pharyngeal surgery should be considered after anti-inflammatory therapies, and consultation with an otolaryngologist should be mandatory before the orthodontic treatment.[31] Nevertheless, we should emphasize that Rădescu et al.,[31] report a single case in their study.

Studies[17–21] were carried out with children who had not undergone adenotonsillar surgery. Zhang et al.[28] and Rose and Schessl[32] excluded children with adenotonsillar hypertrophy. Modesti-Vedolin et al,[34] treated children in the Otolaryngology Service who were in the waiting list for amygdalectomy, and they observed a reduction in the respiratory disturbance index from 10 to 4.5/h. Villa et al[22] included children with adenotonsillar hypertrophy and they still observed an improvement in the AHI, from 7.1 to 2.6/h, as well as a reduction in adenotonsillar hypertrophy after 6 months.[22]

Pediatric OSA often has a multifactorial etiology, which could justify cases of residual apnea in patients only submitted to one treatment modality, such as adenotonsillectomy. Nowadays, there are many treatment options, such as myofunctional therapy, adenotonsillectomy, CPAP, MAAs, and/or RME.

To establish an adequate treatment plan for pediatric OSA, the factors involved in airway obstruction must be identified, such as obesity, adenotonsillar hypertrophy, facial skeleton abnormalities etc.[35] According to what is found, it may be necessary to combine therapies to achieve cure.

Mandibular advancement appliances are well tolerated, even in treatments longer than 6 months, according to the results of previous studies.[28,30] The Herbst appliance, for example, has intermaxillary anchorage; therefore, as it advances the mandible, it causes a contrary reaction of equal intensity in the upper dental arch. Since it is partially fixed to the teeth, it can work 24 hours a day and eliminate the chances of poor adherence to treatment. The two acrylic plates (Planas) consist of indirect tracks supported by metallic arches joining the upper and lower parts, which ensures the preservation of mandibular posture.

On the other hand, the twin-block consists of two (upper and lower) bite blocks with inclined planes, which are designed to fit together so that the mandible adopts an anterior position. The Frankel II appliance, unlike the Andresen activator, was not designed to move teeth by exerting pressure, but by controlling muscle pressures, thus inducing therapeutic changes.

Some possible side-effects related to the MAAs are more likely to happen in patients with Angle class-I and III malocclusion, because the mandibular advancement can lead class-I patients to class III, and, in the condition of class-III patients can be worsened by the mandibular advancement.[36] Mandibular advancement appliances may cause posterior dental disocclusion, orofacial and temporomandibular joint pain, and tooth breakage during mastication. All these undesirable effects are most common in the long-term treatment (of at least 5 years),[36] which exceeds the treatment period of the studies included in the present umbrella review.

Another aspect that should be considered is that MAAs may decrease the intraoral space for the tongue, which can be displaced backwards, leading to a collapse of the tongue base. Machado-Júnior et al.,[24] for example, took this aspect into account in their study, so their appliance, despite being based on the Planas device, was modified to minimize this possible undesirable effect. Occlusion between the plates and, consequently, mandibular advancement was achieved by means of two tracks built on the occlusal part of the apparatus, not on the lingual part, as recommended by Planas. Union between the two upper half arches was achieved not by means of an expansion screw as recommended by Planas, but by means of a Cofen spring.[24]

As a rule, functional orthopedics aims to guide the natural growth of the craniofacial skeleton, using the devices as translators of the forces of the muscles against the basal bones and the alveolar process.

The herein data obtained show that MAAs are a viable and complementary therapeutic resource for the treatment of OSA in children and adolescents with craniofacial disorders, such as those with Angle class-II malocclusion, maxillary narrowing, and mandibular retrognathia, which are very frequent alterations in mouth breathers. This emphasizes the importance of multidisciplinary treatment involving Otorhinolaryngology and Dentistry.

Although none of the studies included reported a cure for OSA (AHI $<$ 1 event/h) after the use of MAAS, the reduction of at least 50% in respiratory events in children who had not undergone adenotonsillar surgery, associated with adherence, shows its effectiveness. However, the few studies

analyzed had small samples, except for the one by Bariani et al.,[18] in which the sample was larger, but the statistical analysis was not possible due to the heterogeneity of the data. Therefore, the results must be analyzed carefully. This is a relatively new field within sleep medicine, with many questions to be explained.

Conclusion

Although more randomized studies are needed, based on the present umbrella review, MAAs must be considered part of a multidisciplinary treatment for children with OSA.

Highlights

- Pediatric OSA often has a multifactorial etiology.
- It may be necessary to combine therapies to achieve cure.
- Mandibular advancement appliances are well tolerated and result in a reduction of at least 50% in respiratory events.
- Long-term treatment (from 6 to 12 months) is more effective.
- There is a lack of statistically significant data in this field.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Tsara V, Amfilochiou A, Papagrigorakis JM, et al. Guidelines for diagnosing and treating sleep related breathing disorders in adults and children (Part 3: obstructive sleep apnea in children, diagnosis and treatment). Hippokratia 2010;14(01): 57–62
2 Marcus CL, Brooks LJ, Draper KA, et al; American Academy of Pediatrics. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130(03):e714–e755. Doi: 10.1542/peds.2012-1672
3 Lewin DS, Rosen RC, England SJ, Dahl RE. Preliminary evidence of behavioral and cognitive sequelae of obstructive sleep apnea in children. Sleep Med 2002;3(01):5–13. Doi: 10.1016/s1389-9457(01)00070-3
4 O'Brien LM, Mervis CB, Holbrook CR, et al. Neurobehavioral implications of habitual snoring in children. Pediatrics 2004; 114(01):44–49. Doi: 10.1542/peds.114.1.44
5 Behrents RG, Shelgikar AV, Conley RS, et al. Obstructive sleep apnea and orthodontics: An American Association of Orthodontists White Paper. Am J Orthod Dentofacial Orthop 2019;156(01): 13–28.e1. Doi: 10.1016/j.ajodo.2019.04.009
6 American Academy of Sleep Medicine. International classification of sleep disorders. 3rd ed. Darien, IL: American Academy of Sleep Medicine;; 2014
7 Mitchell RB, Kelly J. Outcome of adenotonsillectomy for obstructive sleep apnea in obese and normal-weight children. Otolaryngol Head Neck Surg 2007;137(01):43–48. Doi: 10.1016/j.otohns.2007.03.028
8 Brietzke SE, Gallagher D. The effectiveness of tonsillectomy and adenoidectomy in the treatment of pediatric obstructive sleep apnea/hypopnea syndrome: a meta-analysis. Otolaryngol Head Neck Surg 2006;134(06):979–984. Doi: 10.1016/j.otohns.2006.02.033
9 Friedman M, Wilson M, Lin HC, Chang HW. Updated systematic review of tonsillectomy and adenoidectomy for treatment of pediatric obstructive sleep apnea/hypopnea syndrome. Otolaryngol Head Neck Surg 2009;140(06):800–808. Doi: 10.1016/j.otohns.2009.01.043
10 Tauman R, Gulliver TE, Krishna J, et al. Persistence of obstructive sleep apnea syndrome in children after adenotonsillectomy. J Pediatr 2006;149(06):803–808. Doi: 10.1016/j.jpeds.2006.08.067
11 Roberts SD, Kapadia H, Greenlee G, Chen ML. Midfacial and Dental Changes Associated with Nasal Positive Airway Pressure in Children with Obstructive Sleep Apnea and Craniofacial Conditions. J Clin Sleep Med 2016;12(04):469–475. Doi: 10.5664/jcsm.5668
12 Hawkins SM, Jensen EL, Simon SL, Friedman NR. Correlates of Pediatric CPAP Adherence. J Clin Sleep Med 2016;12(06): 879–884. Doi: 10.5664/jcsm.5892
13 Xanthopoulos MS, Kim JY, Blechner M, et al. Self-Efficacy and Short-Term Adherence to Continuous Positive Airway Pressure Treatment in Children. Sleep 2017;40(07):. Doi: 10.1093/sleep/zsx096
14 Tsuda H, Almeida FR, Tsuda T, Moritsuchi Y, Lowe AA. Craniofacial changes after 2 years of nasal continuous positive airway pressure use in patients with obstructive sleep apnea. Chest 2010;138(04): 870–874. Doi: 10.1378/chest.10-0678
15 Villa MP, Pagani J, Ambrosio R, Ronchetti R, Bernkopf E. Mid-face hypoplasia after long-term nasal ventilation. Am J Respir Crit Care Med 2002;166(08):1142–1143. Doi: 10.1164/ajrccm.166.8.257c
16 Koka V, De Vito A, Roisman G, et al. Orofacial Myofunctional Therapy in Obstructive Sleep Apnea Syndrome: A Pathophysiological Perspective. Medicina (Kaunas) 2021;57(04):323. Doi: 10.3390/medicina57040323
17 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; 60:145–151. Doi: 10.1016/j.sleep.2018.12.022
18 Bariani RCB, Bigliazzi R, Cappellette Junior M, Moreira G, Fujita RR. Effectiveness of functional orthodontic appliances in obstructive sleep apnea treatment in children: literature review. Rev Bras Otorrinolaringol (Engl Ed) 2022;88(02):263–278. Doi: 10.1016/j.bjorl.2021.02.010
19 Nazarali N, Altalibi M, Nazarali S, Major MP, Flores-Mir C, Major PW. Mandibular advancement appliances for the treatment of paediatric obstructive sleep apnea: a systematic review. Eur J Orthod 2015 Dec;37(06):618–626. Doi: 10.1093/ejo/cju101. Epub 2015 Feb 12. PMID: 25681125
20 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 Oct 5;10(10):CD005520. Doi: 10.1002/14651858.CD005520.pub3. PMID:27701747;PMCID: PMC6458031
21 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 Feb;25:84–94. Doi: 10.1016/j.smrv.2015.02.002. Epub 2015 Feb 17. PMID: 26164371
22 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 Jan 1;165(01): 123–127. Doi: 10.1164/ajrccm.165.1.2011031. PMID: 11779741
23 Nunes WR, Francesco-Mion RCD. Early treatment and preventive strategies for obstructive sleep apnea and hypopnea with the bioajusta x orthodontic- orthopedic treatment. Sleep Med 2009; 10:541–542
24 Machado-Júnior 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 Jul 1;21(04):e403–e407. Doi: 10.4317/medoral.21072. PMID: 26946208; PMCID: PMC4920451
25 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

Apr;71:9–17. Doi: 10.1016/j.jdent.2018.01.006. Epub 2018 Jan 31. PMID: 29357293

26 Cozza P, Polimeni A, Ballanti F. A modified monoblock for the treatment of obstructive sleep apnoea in paediatric patients. Eur J Orthod 2004 Oct;26(05):523–530. Doi: 10.1093/ejo/26.5.523. PMID: 15536841

27 Schütz TC, Dominguez GC, Hallinan MP, Cunha TC, Tufik S. Class II correction improves nocturnal breathing in adolescents. Angle Orthod 2011 Mar;81(02):222–228. Doi: 10.2319/052710-233.1. PMID: 21208073

28 Zhang C, He H, Ngan P. Effects of twin block appliance on obstructive sleep apnea in children: a preliminary study. Sleep Breath 2013 Dec;17(04):1309–1314. Doi: 10.1007/s11325-013-0840-5. Epub 2013 Apr 6. PMID: 23558604

29 Levrini L, Salone GS, Ramirez-Yanez GO. Efficacy of a Pre-Fabricated Myofunctional Appliance for the Treatment of Mild to Moderate Pediatric Obstructive Sleep Apnea: A Preliminary Report. J Clin Pediatr Dent 2018;42(06):475–477. Doi: 10.17796/1053-4625-42.6.14. Epub 2018 Aug 7. PMID: 30085867

30 Maspero C, Giannini L, Galbiati G, Kairyte L, Farronato G. Upper airway obstruction in class II patients. Effects of Andresen activator on the anatomy of pharyngeal airway passage. Cone beam evaluation. Stomatologija 2015;17(04):124–130. PMID: 27189498

31 Rãdescu OD, Albu S, Baciut M, Bran S, Coman AC, Bechir ES, et al. Results in the treatment with twin block polymeric appliance of the retrognathic mandible in sleep apnea patients. Rev Mater Plast 2017;54:473–476

32 Rose E, Schessl J. Orthodontic procedures in the treatment of obstructive sleep apnea in children. J Orofac Orthop 2006 Jan;67 (01):58–67. English, German. . Doi: 10.1007/s00056-006-0534-8. PMID: 16447025

33 Schessl J, Rose E, Korinthenberg R, Henschen M. Severe obstructive sleep apnea alleviated by oral appliance in a three-year-old boy. Respiration 2008;76(01):112–116. Doi: 10.1159/000098407. Epub 2007 Jan 5. PMID: 17202808

34 Modesti-Vedolin G, Chies C, Chaves-Fagondes S, Piza-Pelizzer E, Lima-Grossi M. Efficacy of a mandibular advancement intraoral appliance (MOA) for the treatment of obstructive sleep apnea syndrome (OSAS) in pediatric patients: A pilot-study. Med Oral Patol Oral Cir Bucal 2018 Nov 1;23(06):e656–e663. Doi: 10.4317/medoral.22580. PMID: 30341264; PMCID: PMC6260994

35 Kaditis A, Kheirandish-Gozal L, Gozal DAlgorithm for the diagnosis and treatment of pediatric OSA: a proposal of two pediatric sleep centersSleep Med 2012 Mar;13(03):217–227. Doi: 10.1016/j.sleep.2011.09.009. Epub 2012 Feb 1. PMID: 22300748

36 Karadeniz C, Lee KWC, Lindsay D, Karadeniz EI, Flores-Mir C. Oral appliance -generated malocclusion traits during the long-term management of obstructive sleep apnea in adults: A systematic review and meta- analysis. 316.1

5 CONCLUSÃO

Apesar de haver a necessidade de mais estudos randomizados, os aparelhos de avanço mandibular podem ser considerados como parte do tratamento multidisciplinar da AOS na infância e adolescência.

6 REFERÊNCIAS DA TESE

1. Tsara V, Amfilochiou A, Papagrigorakis JM, Georgopoulos D, Liolios E, Kadiths A, et al. Guidelines for diagnosing and treating sleep related breathing disorders in adults and children (Part 3: obstructive sleep apnea in children, diagnosis and treatment). Hippokratia. 2010 Jan;14(1):57-62. PMID: 20411064; PMCID: PMC2843575.
2. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, et al; American Academy of Pediatrics. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2012 Sep;130(3):e714-55. doi: 10.1542/peds.2012-1672. Epub 2012 Aug 27. PMID: 22926176.
3. Lewin DS, Rosen RC, England SJ, Dahl RE. Preliminary evidence of behavioral and cognitive sequelae of obstructive sleep apnea in children. Sleep Med. 2002 Jan;3(1):5-13. doi: 10.1016/s1389-9457(01)00070-3. PMID: 14592247.
4. O'Brien LM, Mervis CB, Holbrook CR, Bruner JL, Klaus CJ, Rutherford J, Raffield TJ, Gozal D. Neurobehavioral implications of habitual snoring in children. Pediatrics. 2004 Jul;114(1):44-9. doi: 10.1542/peds.114.1.44. PMID: 15231906.
5. Grime C, Tan HL. Sleep Disordered Breathing in Children. Indian J Pediatr. 2015; 82(10):945-55.
6. Behrents RG, Shelgikar AV, Conley RS, Flores-Mir C, Hans M, Levine M, et al. Obstructive sleep apnea and orthodontics: An American Association of Orthodontists White Paper. Am J Orthod Dentofacial Orthop. 2019 Jul;156(1):13-28.e1. doi: 10.1016/j.ajodo.2019.04.009. PMID: 31256826.
7. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014; 146(5):1387-94.
8. American Academy of Sleep Medicine. International classification of sleep disorders. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
9. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for obstructive sleep apnea in obese and normal-weight children. Otolaryngol Head Neck Surg. 2007 Jul;137(1):43-8. doi: 10.1016/j.otohns.2007.03.028. PMID: 17599563.
10. Brietzke SE, Gallagher D. The effectiveness of tonsillectomy and adenoidectomy in the treatment of pediatric obstructive sleep apnea/hypopnea syndrome: a meta-analysis. Otolaryngol Head Neck Surg. 2006 Jun;134(6):979-84. doi: 10.1016/j.otohns.2006.02.033. PMID: 16730542.

11. Friedman M, Wilson M, Lin HC, Chang HW. Updated systematic review of tonsillectomy and adenoidectomy for treatment of pediatric obstructive sleep apnea/hypopnea syndrome. Otolaryngol Head Neck Surg. 2009 Jun;140(6):800-8. doi: 10.1016/j.otohns.2009.01.043. PMID: 19467393.
12. Tauman R, Gulliver TE, Krishna J, Montgomery-Downs HE, O'Brien LM, Ivanenko A, Gozal D. Persistence of obstructive sleep apnea syndrome in children after adenotonsillectomy. J Pediatr. 2006 Dec;149(6):803-8. doi: 10.1016/j.jpeds.2006.08.067. PMID: 17137896.
13. Roberts SD, Kapadia H, Greenlee G, Chen ML. Midfacial and Dental Changes Associated with Nasal Positive Airway Pressure in Children with Obstructive Sleep Apnea and Craniofacial Conditions. J Clin Sleep Med. 2016 Apr 15;12(4):469-75. doi: 10.5664/jcsm.5668. PMID: 26715402; PMCID: PMC4795272.
14. Hawkins SM, Jensen EL, Simon SL, Friedman NR. Correlates of Pediatric CPAP Adherence. J Clin Sleep Med. 2016 Jun 15;12(6):879-84. doi: 10.5664/jcsm.5892. PMID: 27092702; PMCID: PMC4877321.
15. Xanthopoulos MS, Kim JY, Blechner M, Chang MY, Menello MK, Brown C, et al. Self-Efficacy and Short-Term Adherence to Continuous Positive Airway Pressure Treatment in Children. Sleep. 2017 Jul 1;40(7). doi: 10.1093/sleep/zsx096. PMID: 28541508.
16. Tsuda H, Almeida FR, Tsuda T, Moritsuchi Y, Lowe AA. Craniofacial changes after 2 years of nasal continuous positive airway pressure use in patients with obstructive sleep apnea. Chest. 2010 Oct;138(4):870-4. doi: 10.1378/chest.10-0678. Epub 2010 Jul 8. PMID: 20616213.
17. Villa MP, Pagani J, Ambrosio R, Ronchetti R, Bernkopf E. Mid-face hypoplasia after long-term nasal ventilation. Am J Respir Crit Care Med. 2002 Oct 15;166(8):1142-3. doi: 10.1164/ajrccm.166.8.257c. PMID: 12379564.
18. Koka V, De Vito A, Roisman G, Petitjean M, Filograna Pignatelli GR, Padovani D, et al. Orofacial Myofunctional Therapy in Obstructive Sleep Apnea Syndrome: A Pathophysiological Perspective. Medicina (Kaunas). 2021 Apr 1;57(4):323. doi: 10.3390/medicina57040323. PMID: 33915707; PMCID: PMC8066493.
19. 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 Aug;60:145-151. doi: 10.1016/j.sleep.2018.12.022. Epub 2019 Jan 29. PMID: 31182328.

20. Bariani RCB, Bigliazzi R, Cappellette Junior M, Moreira G, Fujita RR. Effectiveness of functional orthodontic appliances in obstructive sleep apnea treatment in children: literature review. Braz J Otorhinolaryngol. 2021 Mar 14:S1808-8694(21)00055-0. doi: 10.1016/j.bjorl.2021.02.010. Epub ahead of print. PMID: 33757756.
21. Nazarali N, Altalibi M, Nazarali S, Major MP, Flores-Mir C, Major PW. Mandibular advancement appliances for the treatment of paediatric obstructive sleep apnea: a systematic review. Eur J Orthod. 2015 Dec;37(6):618-26. doi: 10.1093/ejo/cju101. Epub 2015 Feb 12. PMID: 25681125.
22. 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 Oct 5;10(10):CD005520. doi: 10.1002/14651858.CD005520.pub3. PMID:27701747;PMCID: PMC6458031.
23. Bernardes R, Di Bisceglie Ferreira LM, Machado Júnior AJ, Jones MH. Effectiveness of functional orthopedic appliances as an alternative treatment among children and adolescents with obstructive sleep apnea: Systematic review and meta-analysis. Sleep Med. 2023 May;105:88-102. doi: 10.1016/j.sleep.2023.03.008. Epub 2023 Mar 15. PMID: 37004341.

7 ANEXOS

Anexo A. Dispensa do Comitê de Ética.

OF. CEP nº 94/202

UNICAMP

CEPUNICAMP
comitê de ética em pesquisa

PRP
pró-reitoria de pesquisa
unicamp

Cidade Universitária "Zeferino Vaz", 30 de junho de 2021.

SIGAD: Of. CEP nº 94/2021

Prof. Dr. Almiro José Machado Junior
Pesquisador Responsável

REF.: DISPENSA DE APRESENTAÇÃO DE PROJETO DE PESQUISA PARA AVALIAÇÃO DO SISTEMA CEP-CONEP.

Prezado Senhor,

Informamos que a pesquisa intitulada "**AVANÇO MANDIBULAR ORTOPÉDICO/ORTODÔNTICO EM CRIANÇAS COM SÍNDROME DA APNÉIA OBSTRUTIVA DO SONO: REVISÃO GUARDA-CHUVA**", para fins de dissertação de mestrado do Programa de Pós-Graduação em Ciência da Cirurgia, da Faculdade de Ciências Médicas, cuja aluna pesquisadora é Carolina Cozzi Machado, destina-se a fazer uma síntese de revisões sistemáticas sobre a eficácia dos aparelhos ortodônticos/ortopédicos de avanço mandibular no tratamento da apneia obstrutiva do sono em crianças.

Deste modo, baseados no projeto anexado ao documento, o estudo não necessita tramitar pelo Comitê de Ética em Pesquisas envolvendo Seres Humanos, tendo em vista que será realizada uma revisão guarda-chuva serão selecionados artigos de revisão sistemática e metanálises das seguintes bases de dados: PubMed, EBSCO (Dentistry & Oral Sciences Source), LILACS Ovid, SciELO Web of Science, EMBASE Bireme, BBO Bireme electronic databases e Cochrane Library.

Ressaltamos que se houver qualquer alteração no escopo do projeto, na qual envolva seres humanos, o CEP/Unicamp deve ser informado para fins de deliberação sobre essas mudanças.

Atenciosamente,

Dra. Renata Maria dos Santos Celeghini
COORDENADORA DO COMITÊ DE ÉTICA EM PESQUISA
UNICAMP

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13083-887 Campinas – SP
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Fone: (019) 3521-7187
cep@unicamp.br

Anexo B. Apresentação em congresso.

CONGRESSO BRASILEIRO DO SONO

Associação Brasileira do Sono

abms

ABROS

Associação Brasileira de Odontologia do Sono

XVIII CONGRESSO BRASILEIRO DO SONO 2021

CERTIFICADO

Certificamos que o Trabalho Científico intitulado MANDIBULAR ADVANCEMENT APPLIANCES IN PEDIATRIC OBSTRUCTIVE SLEEP APNEA: AN UMBRELLA REVIEW

dos autores Carolina Cozzi Machado, Fátima Rosana Albertini, Almiro José Machado Junior

foi apresentado no Congresso Brasileiro do Sono, realizado no Centro de Convenções Frei Caneca,

12 a 15 de Dezembro de 2021, na forma de apresentação: Pôster.

São Paulo, 15 de dezembro de 2021

Dra. Andrea Bacelar
Presidente da ABS

Rowdley Robert Rossi
Presidente da ABROS

Dr. Pedro Rodrigues Genta
Presidente da ABMS

Dr. Luciano Ribeiro Pinto
Coordenador de Projeto da ABS

Anexo C. Registro Prospero.

You have 1 records

My other records

These are records that have either been published or rejected and are not currently being worked on.

ID	Title	Status	Last edited
CRD42021285521	MANDIBULAR ADVANCEMENT APPLIANCES IN PEDIATRIC OBSTRUCTIVE SLEEP APNEA: AN UMBRELLA REVIEW **To enable PROSPERO to focus on COVID-19 registrations during the 2020 pandemic, this registration record was automatically published exactly as submitted. The PROSPERO team has not checked eligibility.**	Registered	15/11/2021

Anexo D. Aceite do artigo.

Sleep Science - Article Approved 938 MANDIBULAR ADVANCEMENT APPLIANCES IN PEDIATRIC OBSTRUCTIVE SLEEP APNEA: AN UMBRELLA REVIEW

De: Sleep Science - GNPapers (gnpapers@gnpapers.com.br)

Para: cozzimachado@yahoo.com.br

Data: terça-feira, 31 de janeiro de 2023 19:12 BRT

Sleep Science

Dear Dr. Machado, Cozzi CC

Article Number: 938
Title: MANDIBULAR ADVANCEMENT APPLIANCES IN PEDIATRIC OBSTRUCTIVE SLEEP APNEA: AN UMBRELLA REVIEW

We are pleased to inform that your article has been accepted for publication in Sleep Science. Your manuscript will now be transferred to our production department and it will proceed to copy-editing and production. If we need any additional information to create the proof, we will let you know.

Thank you for submitting this work to Sleep Science. We are most pleased to have it in the Journal and we hope you consider us again for future submissions.

Please let me know if you have any questions.

Sincerely,

Dr. Monica Levy Andersen
Editor-in-chief