Mandibular advancement devices: a real alternative to CPAP therapy? Protocol for a systematic review

H. Campos Silvaa, F. Malignob, O. Pinhoc, J. C. Pinhd

aFaculty of Engineering, University of Porto, Porto, PT (helenacamposilva@gmail.com). bFaculty of Dental Medicine, University of Porto, PT (fsilva@fmd.up.pt). cFaculty of Nutrition and Food Sciences, University of Porto, PT (oliviapinho@fcna.up.pt). dOcclusion and Orofacial Pain Unity, Faculty of Dental Medicine, University of Porto, PT (jpinho@fmd.up.pt).

Article History
Received 11 June 2019
Accepted 19 March 2020
Published 20 April 2020

Abstract
Background: Obstructive sleep apnea syndrome (OSAS) is characterized by interruption of breath during sleep. OSAS is related to hypertension, type II diabetes and obesity. This disease has various implications on patient’s quality of life. The gold standard for OSAS treatment is continuous positive airway pressure (CPAP). Due to the high level of patients that complain about CPAP therapy, mandibular advancement devices could play an important role in OSAS treatment. Objectives: The purpose of this review is to appraise scientific evidence concerning the effectiveness of Mandibular Advancement Devices (MADs) for OSAS treatment and look over MADs designs that are currently being used scanning for its efficacy. Data sources: Five databases will be accessed (SCOPUS, PubMed, Web of Science, Science Direct and Wiley Online Library) and 6 keywords will be combined. Study eligibility and criteria: This systematic review will only include study’s developed with humans diagnosed with OSAS and with more than eighteen years old. English is the only language accepted. Study appraisal and synthesis methods: Studies assessment will be made by two authors (HCS and FM) and organized in three different parts: screen all articles; screen all abstracts, screen all full texts. In all phases articles that don’t have interest for this systematic review will be excluded. Two review authors (HCS and FM) will also assess the risk of bias and the quality of evidence, taking as a reference the Cochrane Collaboration’s Tool.

1. INTRODUCTION

1.1 Background
Obstructive sleep apnea syndrome (OSAS) is a chronic condition, characterized by repeated interruption of breathing during sleep (Garbarino, Guglielmi, Sanna, Mancardi, & Magnavita, 2016; Hamoda, Almeida, & Pliska, 2019; Mulgrew et al., 2007; L. D. Sharples et al., 2016; Sjosten et al., 2009). OSAS displays as a reduction (hypopnea) or complete cessation (apnea) of airflow despite ongoing respiratory efforts (Force, 1999). OSAS is branded by loud snoring, excessive daytime sleepiness (EDS), impaired quality of life (QoL) and increased risk for cardiovascular disease (Epstein et al., 2009; Jo, Lee, Lee, & Kim, 2018; L. D. Sharples et al., 2016). Some studies suggest that males have double risk in developing obstructive sleep apnea and also that this disease become more prevalent in the middle age (L. D. Sharples et al., 2016).

OSAS is associated with comorbidities including type II diabetes, hypertension, insulin-resistance and obesity (Gupta, Simpson, & Lyons, 2016; L. Sharples et al., 2014).
According with The American Academy of Sleep Medicine (AASM), OSAS is mild if Apnea-Hypopnea Index (AHI) varies from 5-14 events/hour; moderate OSAS if AHI varies from 15-30 events/hour; and severe OSAS if AHI is greater than 30 events/hour (Force, 1999).

Along with weight reduction, OSAS therapy could be managed by positive airway pressure (PAP), surgery or oral appliance therapy (OAT) (Mehta & Correa, 2018; Mintz & Kovacs, 2018).

Continuous positive airway pressure (CPAP) therapy was first described in the early 1980s and, since then, CPAP therapy have become the gold standard for OSAS treatment (Mintz & Kovacs, 2018; Sullivan, Issa, Berthon-Jones, & Eves, 1981).

CPAP therapy improves OSAS symptoms reducing sympathetic activity, the risk for cardiovascular morbidities and mortality rates (Gupta et al., 2016; Randerath et al., 2011). Positive airway pressure is thought to be effective in reducing the apnea-hypopnea index (AHI) by providing pneumatic splinting of the upper airway during sleep (Gupta et al., 2016).

Despite the efficacy of CPAP therapy, many patients complain about discomfort promoted by the mask and local-side effects at the face (Gupta et al., 2016; Mintz & Kovacs, 2018; Randerath et al., 2011).

For mild to moderate OSAS oral appliance therapy is recommended (Ramar et al., 2015). The type of OAT used as therapy for OSAS, the mandibular advancement device (MAD), holds the mandible in a protrusion position or maintain the tongue forward (Mintz & Kovacs, 2018; L. D. Sharples et al., 2016).

Mandibular advancement devices are used in the mouth during sleep, maintaining the upper airway patency, preventing collapse (Serra-Torres, Bellot-Arcis, Montiel-Company, Marco-Algarra, & Almerich-Silla, 2016; L. Sharples et al., 2014). A wide variety of devices are available (L. D. Sharples et al., 2016), either adjustable or nonadjustable, prefabricated or custom made (Mintz & Kovacs, 2018; Serra-Torres et al., 2016).

MADs are considered less effective than CPAP (Engleman, Martin, Deary, & Douglas, 1994; Ferguson et al., 1997; Krieger et al., 1997) even though they present some advantages, such as, better tolerance and greater personal satisfaction (Serra-Torres et al., 2016).

There is a lack of information regarding the efficacy of MADs in OSAS treatment and due to a large variety of MADs designs there is no consistent information about the ideal configuration for a mandibular advancement device.

The purpose of this review is to appraise scientific evidence concerning the effectiveness of MADs for OSAS treatment and look over MADs designs that are currently being used scanning for its efficacy.

1.2 Objectives

The aim of this systematic review protocol is to provide the research methodology to evaluate the interest of mandibular advancement devices (MAD) for OSAS treatment. To this end, the proposed research will answer the following questions:

- Mandibular advancement devices could be used in every patient with OSAS?
- What are the advantages of MAD compared to CPAP therapy?
- How is the acceptance of MAD’s by patient?
- Polysomnographic study’s support the use of mandibular advancement devices?
- How is the ideal configuration of a MAD?
2. Methodology

2.1. Research framework

The preferred Reporting of Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines has been used to guide the reporting of this protocol (Moher et al., 2015; Shamseer et al., 2015).

2.2. Eligibility criteria

Type of studies

This review will mostly consider published articles and articles in press from the last five years in order to identity new evidence about the applicability of MADs for OSAS treatment.

Type of participants

This systematic review will only include both experimental and theoretical study’s developed with humans diagnosed with SAOS and with more than eighteen years old.

Language

The present review will only include articles in English.

2.3. Information sources

The search will be performed within five electronic databases: SCOPUS, PubMed, Web of Science, Science Direct and Wiley Online Library.

Only journal articles or articles in press from April 2015 to April 2019 will be accessed in order to obtain the most recent and relevant information related with the use of mandibular advancement devices in patients with obstructive sleep apnea syndrome.

The references list of the collected articles will be screened to search for additional records fulfilling the goals of the present review.

2.4. Search strategy

The systematic review will aim to focus on publications that use mandibular advancement devices for treatment of OSAS and indicate MADs advantages and limitations. Reviews that compare CPAP therapy with MADs therapy will also be include in order to understand patient’s reaction and adaptation to each one of these options.

A search using a combination of the following keywords “Mandibular advancement devices”, “CPAP therapy”, “OSAS”, “Polysomnography”, “MAD design”, “MAD compliance” will be conducted.

As the relevant articles are selected, the reference list of the key papers found will also be screened manually in order to avoid missing articles.

2.5. Study records

Data management

The retrieved search results from the different databases are going to be processed by EndNote® software to remove duplicates. As a part of the data extraction process, two review authors will independently evaluate all retrieved studies by cross-checking the title and abstract against the inclusion and exclusion criteria.

After initial screening, review authors will compare their selection of included studies and come to an agreement on ambiguous studies. When review authors differ, then the third author will be consulted to decide about the inclusion of the study.

Selection process
Along with the selected keywords, exclusion criteria such as date, document type, language and source of the document will be applied.

As each combination of keywords is entered, three exclusion phases will be applied:

- First phase: screen all article titles. Titles with interest (refer to Mandibular Advancement Devices) will be selected.

- Second phase: screen all abstracts of the previous selected article titles. Abstracts with interest will be selected (refer to MADs, OSAS, CPAP therapy). In case of any doubts the article will be include until phase three.

- Third phase: screen full text of the previously selected papers. All articles with interest for the research will be included.

The exclusion of any article after a full-text assessment will be justified and recorded.

Data collection process

All relevant data will be collected in a form sheet from Microsoft Excel® in order to simplify article analysis and comparison. Two independent authors are going to fill the document gathering all the data to answer the objectives and the research question.

Extracted information will include study general information, sample characteristics, study primary characteristics, study limitations and potential risk of bias.

2.6. Data items

Data collected from the selected articles will be summarized in descriptive tables with publication details and topics that were mentioned in the previous section: study general information (mean age range, gender, sample size), study outcomes and limitations, conclusions and risk of bias.

2.7. Outcomes and prioritization

From the review, the following primary outcomes are expected:

A. To determine current improvement on mandibular advancement devices for obstructive sleep apnea.
   a. Type of materials used to develop the device.
   b. If digital screening is applicable or if traditional impressions are preferably indicated.

B. To identify in which situations mandibular advancement devices are indicated.

C. To examine the quality of outcomes related with use of mandibular advancement devices regarding parameters such as patient adaptation, comfort and perception.
   a. Various studies reported that patient’s compliance is high with MADs but it’s important to understand how that parameters were accessed and compare them between studies.

If possible, a comparison of outcomes of the most evaluated parameters from different studies will also be made.

2.8. Risk of bias in individual studies

The risk of bias will be determined individually for each study in the systematic review. The following parameters will be assessed in the papers:

- Researchers calibration
- Age of the individuals included
- Physiological variables
- Psychological variables
 Calculation methods

The Cochrane collaboration tool for assessing the risk of bias will also be used to appraise the studies quality and risk of bias (Higgins et al., 2011).

2.9. Data synthesis

Data will be presented in a demonstrative method using both the narrative and tables (with information from the selected publications) to systematize relevant evidence accessed in the selected articles. Relationships within and between studies will also be investigated and included in the narrative.

The checklist from The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Statement is going to guide this process (Moher et al., 2015).

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