Review Article

A systematic review on the effectiveness of titratable over nontitratable mandibular advancement appliances for sleep apnea

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Abstract

Background: Mandibular advancement appliances are being tested for use in patients with obstructive sleep apnea (OSA). However, the effectiveness of titration of these appliances does not have conclusive evidence. Systematic reviews help us to compile all available clinical evidence using statistical principles. Hence, the aim of this systematic review is to identify the effectiveness of titratable over nontitratable mandibular advancement appliances in patients with mild to moderate OSA. This review objective is to identify if titration of these appliances produce significant benefits over fixed appliances.

Materials and Methodology: Electronic databases were searched to identify eligible studies based on set inclusion criteria. Data extraction form was created and the data were extracted. The participants were mild to moderate OSA patients who received mandibular advancement appliances. Studies included a comparison between titratable and nontitratable mandibular advancement appliance.

Results: Of the five included studies, three were observational and two were a randomized trial. All these studies were conducted in adults. The outcome attributes were polysomnographic readings and apnea-hypopnea index (AHI). A significant heterogeneity was seen between the eligible studies and hence a meta-analysis could not be performed.

Conclusion: The results from this systematic review did not show significant advantages of titratable appliances, although titratable appliances performed better from individual studies as regards to reduction in AHI and polysomnography. The reason is the lack of sufficient clinical trials on the same. More high quality randomized controlled trials comparing titratable and fixed appliances have to be initiated to get to conclusive evidence.

Keywords: Mandibular advancement device, mechanical appliance, sleep apnea

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INTRODUCTION

Obstructive sleep apnea (OSA) is a potentially serious sleep disorder. This is characteriszed by repeatedly stop and start breathing during sleep. There are several types of sleep apnea, but the most common is OSA. This type of apnea occurs when throat muscles intermittently relax

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and block the airway which leads to a noticeable sign of snoring.[1]

Oral appliances or more commonly the mandibular repositioning appliances have been reported to provide reversible, simple, and cost-effective treatment for patients with primary snoring in mild to moderate OSA.[2] These appliances cover all the teeth and they hold the mandible forward to relieve the obstruction. They can be used in a titratable or nontitratable manner.

The titratable appliances are two-piece appliance and they advance the mandible in increments whereas the nontitratable appliances are rigid single piece appliance which brings about maximum protrusion when inserted.[3] Theoretically, mandibular advancement by titration decreases the stress produced on the TMJ and surrounding structures.[3] The incremental mandibular advancement has been shown to produce greater degree of advancement as compared to single step advancement of mandible.[4]

Few randomized controlled trials and observational studies compared titratable and fixed appliances in patients with mild to moderate sleep apnea. Systematic reviews and meta-analysis in the past identified the utility of oral appliances in sleep apnea[5,6] though these reviews addressed the effect of titration there were few studies that were not included for the analysis. Hence, this systematic review was compiled to identify the advantages of titratable over nontitratable mandibular advancement appliances used in patients with mild to moderate sleep apnea with snoring.

MATERIALS AND METHODOLOGY

Information sources and search strategy

The protocol for this review was registered with the international prospective register of systematic reviews (PROSPERO) with the registration number CRD42016045721. The review protocol can be accessed at http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp. A through literature search was conducted and was completed on August 14, 2016. The primary database used was medline (via PubMed), Cochrane Central Register of Clinical Trials and Database of Abstracts of Reviews of Effects. The search strategy used was (mandibular advancement device) and mandibular advancement appliance. This search was further supplemented by hand searching of relevant references from review articles and other eligible studies. No limits were applied to the year of study, but studies published only in English language were included.

Eligibility criteria

Only those studies with the following requirements were included in the present study:

1. Type of participants: Patients diagnosed with mild to moderate sleep apnea using apnea-hypopnea index (AHI) or polysomnography
2. Types of intervention: Titratable or adjustable mandibular advancement appliance therapy
3. Comparison: Nontitratable or nonadjustable mandibular advancement appliance therapy
4. Outcome: The outcomes reported were posttreatment AHI, polysomnography, Epworth Sleep Scale questionnaire.

Study procedure

Both the authors independently screened the above-mentioned databases for studies and independently reviewed abstracts for suitability. Full-texts articles were obtained for those found to be eligible and for those that were inconclusive on the abstract screening. A pretested data extraction form was created and both the authors independently extracted the following data from each eligible study: trial site, year, trial methods, participants, interventions, and outcomes. Disagreement between the authors was resolved through discussion. A significant heterogeneity was seen between the eligible studies and so meta-analysis was not attempted. The present systematic review was conducted and presented in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[7] Cochrane risk of bias tool was used for assessing the risk of bias of randomized controlled trials and Newcastle-Ottawa scale for nonrandomized controlled trials and observational studies.[8,9]

RESULTS

Search results

A total of 166 articles were identified using the search strategy. Full-text and reference screening of the obtained article led to three more studies that could be included. After through screening of all the obtained 169 papers, 5 studies were eligible for final inclusion which fit into the set inclusion criteria. The PRISMA flow diagram is presented in Figure 1. Table 1 lists the key studies included.[10-14]

Key features of the included studies

Of the five included studies, three were observational (two were prospective cohort and one was a retrospective review) and two were short-term cross-over randomized trial. All these studies were conducted in adults. The

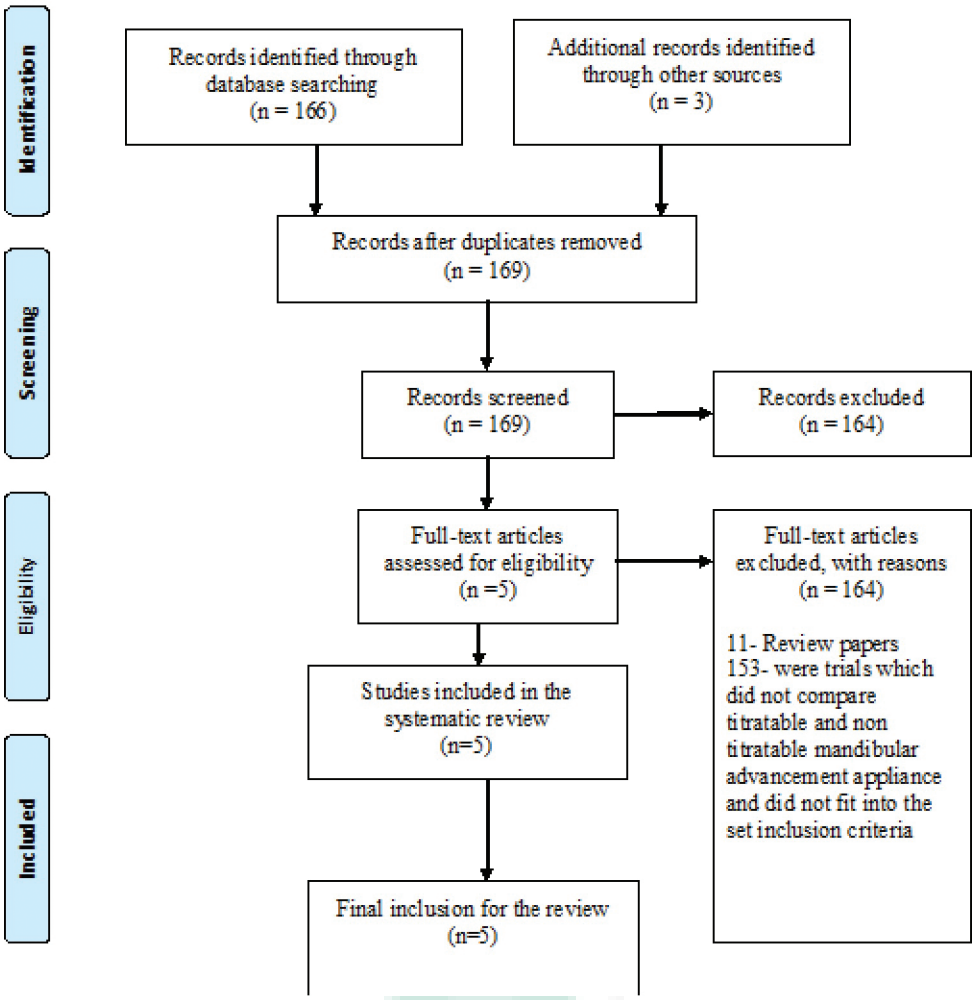

Figure 1: Preferred reporting items for systematic reviews and meta-analyses flow diagram

outcome attributes were polysomnographic readings and AHI. The study design and principles between the studies exhibited clinical heterogeneity. Hence, the principles of meta-analysis could not be applied. Risk of bias of randomized studies according to Cochran's tool [Table 2] showed high risk in terms of randomization sequence generation and allocation concealment. There was no mention regarding the blinding of participants, or the personal and the bias of blinding remains unclear. For studies that were nonrandomized, minimal risk of bias was observed as measured by Newcastle-Ottawa scale [Table 3].

Considering the results obtained from the studies that were included and compiled as a systematic review, there is a tendency for the titratable oral appliances to produce a better reduction in polysomnographic and AHI measurements although a statistically significant improvement cannot be calculated due to inability to perform the meta-analysis. However, results from individual studies provide evidence that titratable appliances could produce favorable results as regards to reduction in AHI and polysomnography. None of the studies made an attempt to identify the adverse effects of using these appliances on the TMJ and the surrounding musculature and structures. Furthermore, these studies were limited to short duration, and the long-term effects of these appliances on sleep apnea could not be studied in detail.

DISCUSSION

This systematic review identifies the advantages of using a titratable mandibular advancement appliance compared to nontitratable appliances in cases of mild to moderate sleep apnea. Eligible studies were identified from electronic databases, and four studies were included for the final review. Unfortunately, only one out of these was a short-term crossover randomized controlled trials. The others were either retrospective or prospective studies. The most important limitation in the included studies was that there was significant clinical heterogeneity between the studies which makes it difficult to compile evidences and conclude.

Table 1: Key characteristics of the included studies

Author	Study design	Participants	Intervention	Control	Outcome	Key results
Lettieri CJ 2011[10]	Retros pective review	922 patients diagnosed with mild or moderate sleep apnoea by polysomnography. Data was incomplete from 117 patients	602 patients on adjustable or titratable mandibular advancement device	2013 patients on non-adjustable mandibular advancement device	AHI less than 5 with resolution of sleepiness Polysom nography Epworth Sleep Scale (ESS)	AHI on therapy: Titratable - 7.6±9.7 Fixed - 10.0±12.4 % Reduction in AHI: Titratable - 74.4 Fixed - 64.9 ESS: Titratable - 9.7±4.1 Fixed - 10.6±4.3
Friedman M 2010[11]	Prospective, non randomised	87 patients diagnosed with mild or moderate sleep apnoea by AHI and Epworth sleep scale	41 patients with adjustable or titratable mandibular advancement device	46 patients on non-adjustable mandibular advancement device	AHI Polysom nography	Mean AHI from Polysomnogram: Baseline / OA Therapy Titratable 45.09±21.99 / 12.75±13.23 Fixed 26.65±12.02 / 13.09±12.21
Landry-Schonbeck A 2009[12]	Short term randomized cross over	12 patients diagnosed with moderate sleep apnoea using polysomnographic recordings	12 patients on adjustable or titratable mandibular advancement device for 4 weeks	12 patients on non-adjustable mandibular advancement device for 4 weeks	Polysom nographic recordings	% Reduction from Baseline Fixed - 34% reduction Titrated at 25% - 39% Titrated at 75% - 47%
Sari E 2011[13]	Prospective non randomised	24 patients diagnosed with mild or moderate sleep apnoea using polysomnography and AHI	12 patients on adjustable or titratable mandibular advancement device	12 patients on non-adjustable mandibular advancement device	Polysom nography and AHI	Polysomnogram readings: Titratable / Fixed AHI (total sleep) 10.0±4.3 / 10.0±4.5 Total sleep time 289±87.5 / 272±92.4 Sleep efficiency 87.4±8.0 / 88.2±8.9
Lawton HM 2005[14]	Prospective randomized cross over trial	16 patients diagnosed with mild to moderate obstructive sleep apnoea using body mass index and AHI	16 patients on Herbst appliance in cross over manner	16 patients on non-adjustable twin block in cross over manner	ESS and VAS	Herbst / Twin block ESS 8 (4-18) / 8.5 (3-17) AHI 25.5 (0-45) / 34 (9-63)

Table 2: Risk of bias of randomized controlled trials using Cochrane risk of bias tool

Study ID	Randomization sequence bias	Allocation concealment bias	Blinding bias	Incomplete outcome bias	Selective reporting bias
Landry-Schönbeck *et al*., 2009[12]	High	High	Unclear	Low	Low
Lawton *et al*., 2005[14]	High	High	Unclear	Low	Low

Table 3: Risk of bias as per Newcastle-Ottawa scale for observational and nonrandomized studies

Study	Selection				Comparability	Outcome			Total score
	Representativeness of the cases	Selection of control cohort	Ascertainment of exposure	Absence of outcome at the start of study		Assessment	Duration	Adequacy	
Lettieri *et al*., 2011[10]	1	1	1	1	1	1	1	1	8
Friedman *et al*., 2010[11]	1	1	1	1	1	1	1	1	8
Sari and Menillo, 2011[13]	1	1	1	1	1	1	1	1	8

Appliance therapy for mild to moderate OSA has been into practice for many years in cases of mild to moderate sleep apnea. These appliances are either prefabricated or custom made.[2] Considering the amount of diverse appliances available in the market it becomes impossible for the clinician to decide on the appliance that could produce predictable results with less adverse effects on the perioral structures.

Mandibular advancement devices and tongue retaining devices have been prescribed more commonly and they are usually custom made. However, mandibular advancement devices have been more commonly used by clinicians.[5,6] Mandibular advancement devices open the airway by moving the mandible forward. As the jaw is moved forward, the collapsible part of the airway is held open by the forward movement of the tongue and other airway muscles. These appliances also improve the strength and rigidity of the airway by increasing the muscle activity of the tongue and other muscles of the airway. The forward movement produced by these appliances could be an incremental movement produced by titratable appliances or a complete movement produced by nontitratable appliances.[15,16] The decision on using a titratable or nontitratable appliance can only be based on the evidence available from literature. Due to the lack of such evidence this systematic review was attempted.

The new era of appliance therapy for sleep apnea with incremental protrusion of the mandible has been reported to be efficacious in producing better reduction in AHI.[5,6] However, the number of randomized controlled clinical trials on which this could be based are very few. The clinical practice guideline (American Academy of Sleep Medicine 2015) for treatment of sleep apnea with appliances suggests the use of custom made titratable appliances over nonadjustable prefabricated appliances.[17] Unfortunately, there were only four studies that were identified and only one was a short-term randomized cross-over trial. The success of treatment of OSA can be defined from the reduction in AHI and also comparing baseline polysomnography with posttreatment polysomnogram.[17-19] A systematic compilation of the available studies was attempted and results from individual studies supported the use of titratable oral appliances for better reduction of AHI and polysomnographic readings when used in patients with mild to moderate sleep apnea. However, the adverse effects on the long-term use of these appliances lack evidence. Because of the clinical heterogeneity of the included studies, a meta-analysis could not be performed.

To conclude, there is a definite lack of randomized controlled trials that could identify the effect of titration of oral appliances for sleep apnea. This paper will serve as a basis on which future trials could be based. If the clinical heterogeneity between the studies could be minimized the principles of network meta-analysis could be applied to compile the evidences and could identify a possible conclusion.

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Conflicts of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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