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Effectiveness of Narval CC™ device in the treatment of obstructive sleep apnea

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ABSTRACT

Mandibular advancement devices (MAD) are used in sleep apnea with varying results. We aimed to examine whether or not a MAD should be an integral treatment modality in the care of our patients with obstructive sleep apnea.

We designed a feasibility study and included 32 patients after meeting inclusion criteria. Only 3 patients did not finish the second sleep study exam. The intervention was an individually designed MAD and a sleep study exam was performed prior and post treatment. The outcome objective was an apnea-hypopnea index of under 10 and with a 50% reduction.

Patient population had a baseline AHI of 19.0 and mean reduction of AHI with MAD treatment to 13.3 yielding a MAD efficacy rate of 31% when outcome objectives were applied. The average reduction in AHI was 24.8% with 9 of the 29 patients actually experiencing an increase in AHI with MAD treatment. When there was a reduction in AHI using the MAD device the AHI reduction rate was 49.1% and there was a tendency for better treatment outcome when apnea-hypopnea was predominantly supine.

A mandibular advancement device serves as an important treatment modality in the care of patients with obstructive sleep apnea due to patient satisfaction and compliance. The broad range of treatment response to our MAD device highlights the importance of performing a sleep study exam after initiation of treatment with a MAD but also illustrates the complexity and need for individually tailored treatment for patients with obstructive sleep apnea.

1. Introduction

Obstructive sleep apnea (OSA) is a disease where there is a respiration effort but due to upper airway collapse there is a decreased air flow to the lungs. The severity of OSA is described in part by using the apnea hypopnea index (AHI). The clinical cut-off is 5 events/hour, <15 events/hour is mild, ≤30 is moderate and >30 events/hour is considered severe sleep apnea.

OSA is a common sleep disorder affecting 10–20% of males and 5–9% of females in the age group 30–60 years. Obstructive sleep apnea syndrome (OSAS) has a prevalence of 2–4% and 1–2% in men and women respectively in Denmark [1].

The symptoms of OSA are snoring, excessive sleepiness, loss of energy, irritability, daydreaming, anxiety or depressive mood problems, and reduced cognitive functions such as ability to concentrate [2]. In addition, in the longer term, associations with sequelae such as arterial hypertension [3,4], cardiac arrhythmias, pulmonary hypertension and right-sided heart failure [5,6] are seen. Often patients feel significantly disabled by these symptoms and want treatment. At present, in Denmark, the conventional treatment of mild to severe OSA is continuous positive airway pressure (CPAP) regardless of the severity of OSA. The treatment with CPAP is effective, but has the significant disadvantage that it requires advanced equipment and frequent compliance problems. With a mandibular advancement device (MAD) less compliance problems are observed [7,8]. MAD's are constructed to protrude the mandible and thus the tongue, the tongue base and the epiglottis thereby enlarging the upper airway preventing airway collapse during sleep [9]. Several studies have shown that MADs also have a therapeutic effect on OSA(10). A comparison between nasal CPAP and MADs in patients with mild to moderate OSA showed no difference in treatment efficacy [11]. Although MAD's in the treatment of OSA in general are less efficacious than CPAP in reducing AHI

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they are used more frequently and preferred by more patients [12]. Recent studies have also shown that a custom MAD such as the MAD device used in this study is superior to thermoplastic design which can be bought over the counter [10]. It has also been shown that MAD's, like CPAP, in addition to reducing AHI also has a corresponding reducing effect on cardiovascular sequelae making MAD devices a potential treatment option for mild to moderate OSA [13–15].

Treatment of OSA patient remain difficult because of compliance and variability in treatment response to for example MAD devices. In our study we decided to try to qualify our titration of the Narval CC™ device at one month followup using acustic pharyngometry because it has shown some promise as a prognostic marker for treatment response [16].

Since OSA is considered a chronic disease and its management therefore is likely to be life-long having alternative treatment options to CPAP is vital if the goal is a treatment option for as many patients as possible.

We have therefore examined the feasibility and the efficacy of a custom made MAD in patients suffering from mild to moderate OSA in a pragmatic clinical setting.

2. Materials and methods

This prospective feasibility study protocol was registered and approved with The Danish Data Protection Agency (18-000315) and the regional ethical committee (REG-202-2017).

The primary outcome was a reduction in AHI of 50% or more and an AHI <10. Secondary outcome was alleviation of associated symptoms quantified by reduction in Epworth sleepiness score (ESS).

2.1. Study population

Patients from the Sleep Clinic at the Department of Otorhinolaryngology and Maxillofacial Surgery, Zealand University Hospital, Køge, Denmark were offered to participate in the study. Prior to inclusion they were examined by an otorhinolaryngologist and had a cardiorespiratory monitoring (CRM) performed. Patients over 18 years of age with mild to moderate AHI were invited to participate if any of the exclusion criteria were not encountered. Patients were excluded if they had less than 10 teeth in each jaw, dental prosthetics, no dental appointments within the last 12 months, prior temporomandibular disorder, plans of larger dental procedures, lack of cooperation with acoustic pharyngometry or if they had excessive daily tiredness defined as ESS above 15.

If included, patients had a nurse consultation where ESS, were filled out and measurements including blood pressure, weight, height and BMI were obtained along with questions concerning medication, smoking and drinking habits. Afterwards two consecutive nights of CRM were performed in the patients home and if the mean AHI was between 5 and 30 they were referred to a Narval CC™ certified dentist. The dentist performed a 3D scan of the patients teeth and an acoustic pharyngometry to evaluate vertical displacement of the custom titratable MAD device. The MAD device was then shipped to the patient and after 1 month of use the patient would have a second appointment with the dentist to evaluate if the device needed to be titrated. After 2 months of nightly use the patients had a second consultation with the same nurse and the same questionnaire and ESS was performed followed by two consecutive nights of CRM wearing the MAD. Lastly, all the patients who had finished the trial were contacted by the author with recommendation on future treatment options of their OSAS.

All patients included in the trial were evaluated by the same lead author (JHT) prior to enrolment and after completion of the second CRM. All patient's MAD devices were fitted and titrated by the same Narval CC™ certified dentist who also coauthors the article (PK). During and after the 1.st month of use and after completion the participants filled out a questionnaire concerning average daily use of the MAD device each week, potential side effects and satisfaction on a numeric rating scale (NRS).

The number of participants needed in the study was 32 based on a power calculation prior to the study aiming to find a 50% reduction in AHI before and after MAD treatment with a type 1 error of 0.05, type 2 error of 0.2 and with 1 standard deviation.

From February 2019 to October 2019 we enrolled a total of 45 patients in the study. Thirty-two patients were referred to the dentist for Narval CC™ mandibular advancement device and 29 patients completed to study (see Fig. 1) and thus within a 10% drop-out rate.

2.2. Sleep recordings

A Nox T3 CRM device (Nox Medical) was used for data collection and Noxturnal Software System was used for data analysis. Patients were instructed by a specialist nurse in how to use the equipment. The patients were instructed to do two consecutive nights of recording. All recordings were evaluated by both the specialist nurse and one of the authors (JHT) for error and excluded if the device had not been used properly. Patients were included if one night was of sufficient quality and quantity and if not, the patient was asked to repeat the test. Quality was defined as signal quality above 95% and quantity of at least 6 h of sleep.

2.3. Statistical analysis

Statistical analysis was performed in the statistical environment R statistics version 3.6.

We evaluated the changes in AHI, ODI, snore index and ESS from baseline to the follow-up visit using the Wilcoxon-signed-rank-test. Data was evaluated by non-parametric statistics as data were not normally distributed evaluated by Shapiro-Wilks test. We considered a p-value below 0.05 significant.

3. Results

Table 1 shows the baseline data before and after treatment with Narval CC™ of the 29 patients who completed the study. It is seen that there was a significant reduction in total AHI, AHI in supine position, ODI and snore index. Of the 29 patients who finished the study 25 patients were titrated at the follow-up appointment with dentist Poul Kirketerp.

The outcome measure were achieved, defined as a 50% reduction in AHI and AHI <10, for 9/29 of the patients yielding an efficacy rate of 31% for the MAD device at follow-up. The average reduction in AHI was 24.8% ranging from −106% to 90%. When there was a reduction in AHI using the MAD device the reduction rate was 49.1%. A box-plot in Fig. 2 shows the statistically significant reduction in AHI pre- and post-treatment for patients who completed the study. It also illustrates the difference in response to the treatment.

All patients completed the questionnaire and the results are shown in Table 2. It is seen that pain and dental and jaw soreness are mentioned by approximately 50% of the participants but also that 83% would advocate this treatment to others and there was a high satisfaction rate on NRS.

4. Discussion

In this study 9/29 patients met outcome measures using the

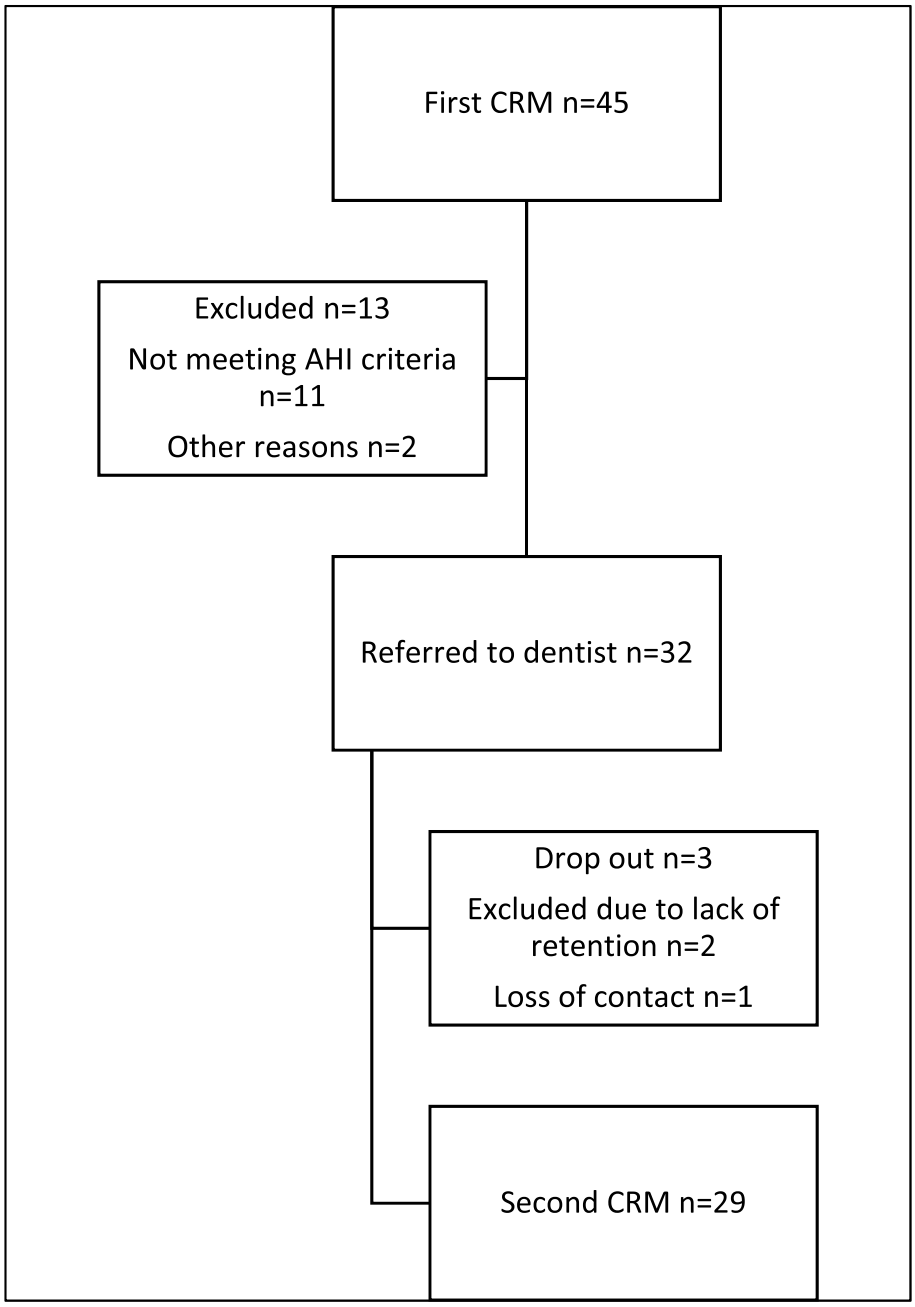

Fig. 1. Patient inclusion and exclusion flowchart.
CRM – Cardiorespiratory monitoring, AHI – apnea hypopnea index.

Table 1
Baseline data for the 29 participants completing the study.
BMI – Body mass index, MAP – Mean arterial pressure, ESS – Epworth sleepiness score, AHI – Apnea hypopnea index, ODI – Oxygen desaturation index.

	At baseline mean/(SD)	With treatment mean/(SD)	p-value
Age (years)	56		
BMI (kg/m2)	30.4 (5.8)	30.1 (5.1)	ns
MAP (mmHg)	101.78 (12.1)	101.8 (22.8)	ns
ESS (points)	6.8 (3.9)	4.5 (2.8)	ns
Total AHI (events/h)	18.95 (5.7)	14.25 (8.9)	0.005
AHI supine (events/h)	36.58 (22.8)	22.5 (16.7)	0.003
AHI non-supine (events/h)	10.86 (6.1)	10.17 (8.72)	0.247
ODI (events/h)	17.46 (5.5)	13.75 (8.6)	0.017
Snore index (%)	20.09 (16.4)	10.21 (14.0)	0.02

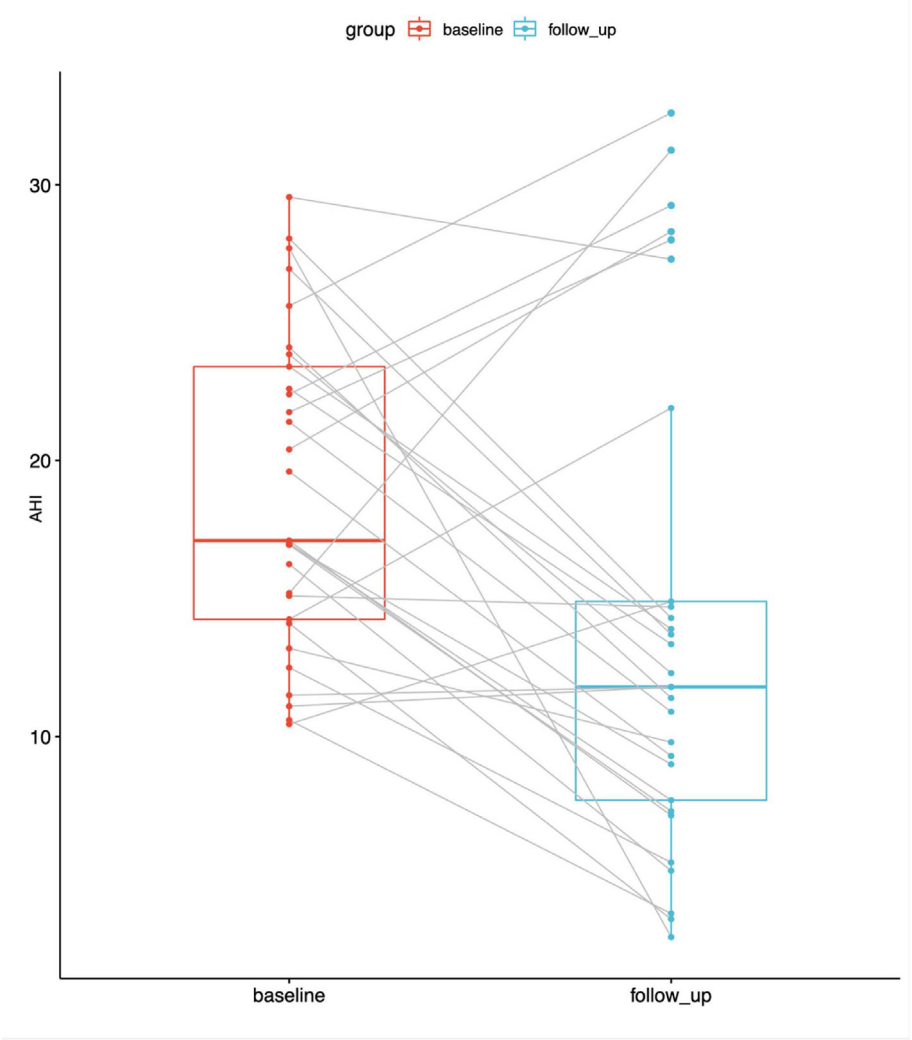

Fig. 2. Treatment response prior and post mandibular advancement device illustrated using a boxplot were the lines define – Q1, median and Q3.
AHI – Apnea hypopnea index.

Table 2
Patient evaluation after use of the mandibular advancement device.

Average MAD usage			(h/night)/range
First week			6.0 [2–8]
Second Week			6.5 [3–8]
Third week			6.9 (2.5–8)
Subjective side effects	**Yes**	**No**	**Do not know**
Has the MAD device caused pain? (n/%)	10 (34.5)	18 (62.1)	1 (3.4)
Has the MAD device caused dental soreness? (n/%)	16 (55.2)	12 (41.4)	1 [3,4]
Has the MAD device caused soreness of the jaw joint? (n/%)	14 (48.3)	14 (48.3)	1 (3.4)
Would you recommend the mad device to others? (n/%)	24 (82.8)	1 (3.4)	4 (13.8)
Average assessment on 0-10 scale on subjective outcome (10 being the best possible)/range			8.3(4.4–10.0)

MAD = Mandibular advancement device.

Narval CC™ MAD device. We had a statistically significant reduction in AHI of 24.8% with a p-value of 0,005 although the efficacy of the treatment was seemingly inconsistent. Twenty out of twenty-nine patients showed an improvement in their AHI but the remaining patients included showed a rise in AHI. Interestingly, a sub analysis of AHI improvement pre- and post-treatment showed a statistically significant response to treatment in the supine AHI but not the non-supine AHI prompting the notion that MAD device mechanism of action serve better in treatment of patients with dominant supine sleep apnea. This has also been suggested in prior studies [17–19]. This correlates with MAD device mechanisms of protruding the mandible as to create space antero-posteriorly in hypo- and oropharynx. This might also explain the treatment failure in patients treated with MAD device because the effect of treatment with a MAD device on velopharyngeal collapse and lateral collapse are more variable [20]. Petri et al. concluded in their

prospective study of 62 OSA patients treated with MAD's that predominant non-supine AHI was inversely related to treatment success defined as a 50% reduction in AHI and a residual AHI <10(18). Cavaliere et al. has elaborated on the subject in a study where Drug-Induced Sleep Endoscopy (DISE) was performed and found a treatment response relationship depended on location of the collapse in the upper airway. They found that the presence of palatal and base of tongue collapse was associated with greater response to treatment, while the presence of oropharynx or lateral wall collapse showed a tendency towards an association with a less favorable treatment outcome [19]. Both A. Vroegrop et al. and Cavaliere et al. used a simulation bite, called maximal comfortable protrusion (MCP), during DISE to evaluate predictability of treatment outcome and while the location of collapse and the percentage of multilevel collapse varied from 87.2% to 65.0%, respectively, both studies showed positive significant association between simulation bite on the upper airway patency during DISE and treatment response [19,21]. The patients who had a negative treatment outcome using the MAD device in our study could therefore be explained by having upper airway collapse at anatomical localization not addressed or even worsening the collapse by using a MAD device. Patients who had a negative treatment outcome were questioned as to changes in medicine, sickness and alcohol intake prior to second CRM but no significant changes were found and therefor it remains unanswered as to why some patients worsened with treatment.

Our study has some limitations. The number of patients completing the study was small but just within the sample size of our power calculation. Furthermore, our method for determining AHI was by way of Nox T3 CRM and not with Polysomnography (PSG) as normally is the gold standard for AHI measurements. However, this was intentional to extrapolate our findings to the current way to diagnose and monitor treatment response in our pragmatic clinical setting. Furthermore our study goal was to evaluate MAD's potential role in treatment of OSA patients within Danish guidelines. Therefore our study does not have a non-treatment group or Placebo-MAD group and therefor there is risk of intentionally overlooked placebo effect.

Our study was treatment respons in OSA patients when the Narval CC™ device was used and therefor our results cannot be directly extrapolated to all MAD devices.

A strength was that we performed pharyngometry to adjust the MAD device as optimal as possible at the initial adjustment and after a month to correct potential disadvantages.

Patient satisfaction was high although soreness of teeth and jaws were frequently mentioned as a problem. Despite this usage of the Narval CC™ MAD device was highly satisfactory and patients would even recommend this device to others.

5. Conclusion

In conclusion our study found a statistically significant reduction in AHI of 24,8% and that 9/29 patients included had an AHI reduction of 50% or more and an AHI <10 after treatment with Narval CC™ MAD device. Our results demonstrates a broad range of responses to treatment with our MAD device and emphasizes the need for follow up with AHI measurements if this modality is chosen for treatment for mild to moderate OSA. The high satisfaction rate shows this MAD device has a role in treatment of this group of patients who cannot tolerate CPAP and who fulfills certain criteria as mostly AHI in supine position.

We propose further studies should aim to better qualify patient selection in the treatment of mild to moderate sleep apnea with MAD devices and that DISE might be suitable for evaluation hereof.

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CRediT authorship contribution statement

Johan H. Therchilsen: Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Poul Kirketerp:** Conceptualization, Methodology, Study design, Resources, Project administration. **Preben Homøe:** Conceptualization, Methodology, Study design, Resources, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: One of the authors, Poul Kirketerp is a dentist specializing in treatment of obstructive sleep apnea and one of the MAD devices he uses is a Narval MAD. He has no specific investment in the brand but nevertheless we decided to perform the study so that Poul Kirketerp has not been involved in patient selection, data collection, analysis or writing. He has been presented to the manuscript and only had minor revision recommendations.

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References

[1] Jennum Poul, Tønnesen Philip. Obstruktiv søvnapnø-syndrom. Ugeskr Læger 2014;11:1032–4. 2014;176:V11120679.
[2] Vanek J, Prasko J, Genzor S, Ociskova M, Kantor K, Holubova M, et al. Obstructive sleep apnea, depression and cognitive impairment. Sleep Med 2020 Aug 1;72:50–8.
[3] Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000 May 11;342(19):1378–84.
[4] Marin JM, Agusti A, Villar I, Forner M, Nieto D, Carrizo SJ, et al. Association between treated and untreated obstructive sleep apnea and risk of hypertension. JAMA 2012 May 23;307(20):2169–76.
[5] E S, Cw W SR, Et L, Ab N, Fj N, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 2001;163(1):19–25.
[6] Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet (London, England) 2005 Mar;365(9464):1046–53.
[7] Sutherland K, Vanderveken OM, Tsuda H, Marklund M, Gagnadoux F, Kushida CA, et al. Oral appliance treatment for obstructive sleep apnea: an update. J Clin Sleep Med 2014;10(2):215–27.
[8] Vecchierini MF, Attali V, Collet JM, d'Ortho MP, El Chater P, Kerbrat JB, et al. A custom-made mandibular repositioning device for obstructive sleep apnoea-hypopnoea syndrome: the ORCADES study. Sleep Med 2016 Mar 1;19:131–40.
[9] Ryan CF, Love LL, Peat D, Fleetham JA, Lowe AA. Mandibular advancement oral appliance therapy for obstructive sleep apnoea: effect on awake calibre of the velopharynx. Thorax 1999;54(11):972–7.
[10] Venema JAMU, Rosenmöller BRAM, de Vries N, de Lange J, Aarab G, Lobbezoo F, et al. Mandibular advancement device design: a systematic

review on outcomes in obstructive sleep apnea treatment. Sleep Med Rev 2021 Dec 1:60.
[11] Aarab G, Lobbezoo F, Hamburger HL, Naeije M. Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnea: a randomized, placebo-controlled trial. Respiration 2011 Apr;81(5):411–9.
[12] Ferguson KA, Cartwright R, Rogers R, Schmidt-Nowara W. Oral appliances for snoring and obstructive sleep apnea: a review. Sleep 2006 Feb 1;29(2):244–62.
[13] Bratton DJ, Gaisl T, Wons AM, Kohler M. CPAP vs mandibular advancement devices and blood pressure in patients with obstructive sleep apnea: a systematic review and meta-analysis. JAMA 2015 Dec 1;314(21):2280–93.
[14] Iftikhar IH, Hays ER, Iverson MA, Magalang UJ, Maas AK. Effect of oral appliances on blood pressure in obstructive sleep apnea: a systematic review and meta-analysis. J Clin Sleep Med 2013;9(2):165.
[15] Anandam A, Patil M, Akinnusi M, Jaoude P, El-Solh AA. Cardiovascular mortality in obstructive sleep apnoea treated with continuous positive airway pressure or oral appliance: an observational study. Respirology 2013 Nov;18(8):1184–90.
[16] Van Gaver H, Op de Beeck S, Dieltjens M, De Backer J, Verbraecken J, De Backer WA, et al. Functional imaging improves patient selection for mandibular advancement device treatment outcome in sleep-disordered breathing: a prospective study. J Clin Sleep Med 2022 Mar 1;18(3):739–50.
[17] Marklund M, Persson M, Franklin KA. Treatment success with a mandibular advancement device is related to supine-dependent sleep apnea. Chest 1998 Dec;114(6):1630–5.
[18] Petri N, Christensen IJ, Svanholt P, Sonnesen L, Wildschiødtz G, Berg S. Mandibular advancement device therapy for obstructive sleep apnea: a prospective study on predictors of treatment success. Sleep Med 2019;54:187–94.
[19] Cavaliere M, De Luca P, De Santis C, Scarpa A, Ralli M, Di Stadio A, et al. Drug-induced sleep endoscopy (DISE) with simulation bite to predict the success of oral appliance therapy in treating obstructive sleep apnea/hypopnea syndrome (OSAHS). Transl Med @ UniSa 2020 Sep;23:58–62.
[20] Ciscar MA, Juan G, Martínez V, Ramón M, Lloret T, Mínguez J, et al. Magnetic resonance imaging of the pharynx in OSA patients and healthy subjects. Eur Respir J 2001 Jan;17(1):79–86.
[21] Vroegop AVMT, Vanderveken OM, Dieltjens M, Wouters K, Saldien V, Braem MJ, et al. Sleep endoscopy with simulation bite for prediction of oral appliance treatment outcome. J Sleep Res 2013 Jun;22(3):348–55.