

Articles of the Month – January 2021

Mandibular advancement device therapy

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Changes in headache characteristics with oral appliance treatment for obstructive sleep apnea

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Link: Scientific Reports | (2021) 11:2568 | <https://doi.org/10.1038/s41598-021-82041-6>

Changes in headache characteristics in obstructive sleep apnea (OSA) patients following oral appliance treatment was investigated for the first time. Thirteen OSA patients with headaches treated with a mandibular advancement device were investigated. Level I polysomnography and Migraine Disability Assessment Questionnaire were completed before and after treatment. Various headache characteristics and concomitant conditions were analyzed. The patient was considered a headache responder when $\geq 30\%$ reduction in headache frequency following treatment. Differences in headache and polysomnographic parameters were compared between headache responder groups. Eight patients (62%) were headache responders. Eleven patients (85%) before and 7 (54%) after treatment reported morning headaches. Significantly more patients had bilateral headache in the responder group before treatment ($P= 0.035$). The severest headache intensity ($P= 0.018$) at baseline showed a significant decrease in the headache responder group after treatment. The time spent in N2 ($r = -0.663$, $P= 0.014$), REM sleep ($r = 0.704$, $P= 0.007$) and mean oxygen saturation ($r = 0.566$, $P= 0.044$) showed a significant correlation with post-treatment average headache intensity. Pre-treatment lower PLM index ($r = -0.632$, $P= 0.027$) and higher mean oxygen saturation levels ($r = 0.592$, $P= 0.043$) were significantly correlated with higher post-treatment severest headache intensity. Treatment with an oral appliance is beneficial for many OSA patients with headaches. It should be considered as an alternative treatment in headache patients with mild to moderate OSA.

EADSM comment:

Headache is a fairly common symptom among sleep apnea patients. Interestingly, patterns of headache seems to change with MAD therapy. A previous RCT showed in secondary outcomes no difference to a placebo device, but a change in types of headaches, frequency and intensity in the active group, but not the placebo group.

Marklund M., Carlberg B., Forsgren L., Olsson T., Stenlund H., Franklin K.A. (2015) Oral Appliance Therapy in Patients With Daytime Sleepiness and Snoring or Mild to Moderate Sleep Apnea: A Randomized Clinical Trial. *JAMA Intern Med*, 175, 1278-1285.

Larger RCTs with the primary aim to investigate headaches are needed.

Sleep Breath. 2021 Jan 4.
doi: 10.1007/s11325-020-02183-1.

The effects of continuous positive airway pressure and mandibular advancement therapy on metabolic outcomes of patients with mild obstructive sleep apnea: a randomized controlled study

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Link: <https://link.springer.com/article/10.1007/s11325-020-02183-1>

Background Moderate and severe obstructive sleep apnea (OSA) have been independently associated with dyslipidemia. The results of metabolic improvement with continuous positive airway pressure (CPAP) have been controversial. Less evidence exists regarding this issue in mild OSA. A current treatment for mild OSA is mandibular advancement device (MAD) therapy, but its effectiveness on the metabolic profile needs to be compared with CPAP. The purpose of this study was to compare MAD vs CPAP vs no treatment on the metabolic profile during 6 and 12 months of follow-up in patients with mild OSA.

Methods The inclusion criteria were patients with mild OSA, both genders, ages 18 to 65 years, and body mass index (BMI) of < 35 Kg/m². Patients were randomized in 3 groups (CPAP, MAD, and control). The evaluations included physical examination, metabolic profile, and full polysomnography at baseline, 6 months, and 12 months of follow-up.

Results Seventy-nine patients with mild OSA were randomized in three treatment groups, with mean age (\pm SD) of 47 ± 9 years, 54% men, and AHI 9.5 ± 2.9 events/h. MAD and CPAP reduced AHI at 6 and 12 months compared to the control group. MAD adherence was higher than CPAP at 6 and 12 months. Despite lower adherence compared to MAD, CPAP was more effective in reducing total cholesterol over 12 months (baseline 189.3 ± 60.2 mg/dl to 173.4 ± 74.3 mg/dl) and low-density lipoprotein cholesterol (LDL-c, baseline 112.8 ± 54.9 mg/dl to 94.5 ± 67.4 mg/dl).

Conclusions After 1 year of treatment, CPAP was superior to MAD in reducing total cholesterol and LDL-c in patients with mild OSA.

EADSM comment:

The first longer term data on metabolic outcomes of MADs compared with CPAP in mild OSA patients show a favor for CPAP, despite poorer adherence than with MAD. More studies are needed in this complicated topic.

Semi-fixed versus fixed oral appliance therapy for obstructive sleep apnea: A randomized crossover pilot study

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Link: [Semi-fixed versus fixed oral appliance therapy for obstructive sleep apnea: A randomized crossover pilot study - ScienceDirect](#)

Background/purpose: Although mandibular advancement oral appliances (OAs) are the most widely used and accepted therapeutic modality for obstructive sleep apnea (OSA), whether these maxillary and mandibular appliances should be semi-fixed or fixed remains uncertain. This randomized crossover pilot study compared the efficacy, side effects, and patient preference of semi-fixed and fixed OAs for the treatment of OSA. **Materials and methods:** Patients with mild to moderate OSA were recruited and randomly assigned to either the semi-fixed or fixed OA group, whereby they used their assigned OA for the first 4 weeks, followed by assessments for sleep parameters (including the Apnea-Hypopnea Index [AHI]) and temporomandibular joint pain as a side effect. After a two-week washout period, patients were switched to the alternative OA for 4 weeks, followed by repeated assessments. Patient preference was assessed at the end of the completed treatment period. **Results:** Fifteen patients were enrolled and completed the full study protocol. Both types of OAs were efficient in reducing the patient's AHI in comparison to baseline (i.e., without OA). However, there was no significant difference in AHI reduction between the semi-fixed and fixed OA devices. Regarding the side effect of temporomandibular joint pain and patient preference, the semi-fixed OA device was superior to the fixed OA device on both measures. **Conclusion:** While both semi-fixed and fixed OAs are effective in treating patients with OSA, semi-fixed OAs are superior in regards to both patient preference and reduced side effects. Thus, semi-fixed OAs may be the preferred therapeutic modality for OSA.

EADSM comment:

Small study comparing a fixed oral appliance with a semi-fixed one. No difference in AHI between designs, but less side effects and higher patient preference for the semi-fixed. The semi-fixed appliance was a "traction type" of appliance, which might explain why there was no difference in AHI, since this design is particularly intended to avoid a backward movement of the mandible, when the jaw opens up.

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doi: 10.1093/sleep/zsab015. Online ahead of print.

Health Outcomes of Continuous Positive Airway Pressure versus Mandibular Advancement Device for the Treatment of Severe Obstructive Sleep Apnea: an Individual Participant Data Meta-analysis

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Link: <https://academic.oup.com/sleep/advance-article/doi/10.1093/sleep/zsab015/6119670>

Study objectives: The impact of therapy with continuous positive airway pressure (CPAP) and mandibular advancement device (MAD) has not been directly compared in patients with severe obstructive sleep apnea (OSA). The purpose of this individual participant data meta-analysis was to compare the treatment effects of CPAP and titratable MAD on sleepiness, quality of life, sleep-disordered breathing severity and sleep structure in patients with severe OSA.

Methods: Randomized controlled trials (RCTs) that included severe OSA patients were identified in order to compare the impact of the two treatments. Individual data from severe OSA patients were extracted from the databases and pooled for analysis.

Results: Of the 7 studies identified, 3 crossover RCT and one parallel-group RCT corresponding to 151 patients and 249 observations (125 in the CPAP treatment arm and 124 in the MAD treatment arm) were included in the analysis. Titratable MAD had a similar impact to CPAP on major patient-centered outcomes (sleepiness and quality of life). CPAP was more effective in reducing AHI and ODI. However, the two treatments had a similar impact on sleep structure with an increase of N3 and REM sleep. Finally, treatment adherence and preference were largely in favor of MAD.

Conclusion: This meta-analysis suggests that MAD represents an effective alternative treatment in severe OSA patients intolerant to CPAP or who prefer alternate therapy.

EADSM comment:

Interesting study design with the selection of the severe patients from previous RCTs. Results show similar outcomes as previous meta-analyses, with higher efficacy on AHI of CPAP, but similar outcomes on symptoms and adherence. The results are, however, short-term and it is necessary to study, whether the effects persist long-term.

CPAP combined with oral appliance therapy reduces CPAP requirements and pharyngeal pressure swings in obstructive sleep apnea

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Link: [CPAP combined with oral appliance therapy reduces CPAP requirements and pharyngeal pressure swings in obstructive sleep apnea \(physiology.org\)](https://doi.org/10.1152/jappphysiol.00393.2020)

Oral appliance (OA) therapy is the leading alternative to continuous positive airway pressure (CPAP) for obstructive sleep apnea (OSA). It is well tolerated compared with CPAP. However, $\geq 50\%$ of patients using OA therapy have incomplete resolution of their OSA. Combination therapy with CPAP and oral appliance (CPAP + OA) is a potential alternative for incomplete responders to OA therapy. This study aimed to determine the extent to which combination therapy reduces therapeutic CPAP requirements using gold-standard physiological methodology in those who have an incomplete response to OA therapy alone. Sixteen incomplete responders [residual apnea/hypopnea index (AHI) > 10 events/h] to a novel OA with a built-in oral airway were recruited (3 women:13 men, aged 31-65 yr, body mass index: 22-38 kg/m², residual AHI range: 13-63 events/h). Participants were fitted with a nasal mask, pneumotachograph, epiglottic pressure catheter, and standard polysomnography equipment. CPAP titrations were performed during non-rapid eye movement (NREM) supine sleep in each participant during three conditions (order randomized): CPAP only, CPAP + OA (oral airway open), and CPAP + OA (oral airway closed). OSA was resolved at pressures of 4 ± 2 and 5 ± 2 cmH₂O during CPAP + OA (oral airway open) and CPAP + OA (oral airway closed) conditions versus 8 ± 2 cmH₂O during CPAP only ($P < 0.01$). Negative epiglottic pressure swings in oral airway open and closed conditions were normalized to CPAP only levels [-2.5(-3.7, -2.6) vs. -2.3(-3.2, -2.4) vs. -2.1(-2.7, -2.3) cmH₂O]. Combined CPAP and OA therapy reduces therapeutic CPAP requirements by 35%-45% and minimizes epiglottic pressure swings. This combination may be a therapeutic alternative for patients with incomplete responses to OA therapy alone and those who cannot tolerate high CPAP levels. **NEW & NOTEWORTHY** Combined CPAP and oral appliance therapy has been suggested as an alternative for incomplete responders to oral appliance therapy. We used a novel oral appliance incorporating an oral airway together with CPAP to show that pharyngeal pressure swings were normalized at reduced CPAP levels. Our findings demonstrate that using CPAP and oral appliance together may be a beneficial alternative for incomplete responders to oral appliance therapy and intolerant CPAP users due to high-pressure requirements.

EADSM comment:

Exciting combination therapy device, although Oventus is not yet available in Europe.

OSA in general

Does gender matter: sex-specific aspects of symptoms, outcome, and therapy of obstructive sleep apnea

[Sophia E Schiza](#)¹, [Izolde Bouloukaki](#)

Link: https://journals.lww.com/co-pulmonarymedicine/Fulltext/2020/11000/Does_gender_matter_sex_specific_aspects_of.7.aspx

Purpose of review: Obstructive sleep apnea (OSA) has historically been considered as a male disease. As a result, female individuals with OSA were often under-diagnosed and under-treated compared with male individuals. However, recent data suggest that several OSA-associated adverse cardiovascular outcomes are more pronounced in women.

Recent findings: This review provides a summary of the most relevant recent evidence with regard to sex-specific OSA characteristics, including atypical symptoms, greater quality of life impairment and several more pronounced adverse outcomes in female individuals compared with male individuals. It also provides updated evidence on the influence of female gender on under-treatment of OSA with limited evidence supporting gender differences in the effects of OSA treatment.

Summary: There is evidence suggesting gender-based differences in the frequency, severity, clinical presentation, and outcomes of OSA. The recognition of these gender differences could improve screening with development of female-specific screening instruments, early diagnosis, and individualized therapeutic plans towards better disease management and its outcomes.

EADSM comment:

Women seem underdiagnosed and untreated, despite quite similar prevalence and consequences of untreated disease, although with different patterns.

Respirology. 2020 Nov 2.

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Clusters of sleep apnoea phenotypes: A large pan-European study from the European Sleep Apnoea Database (ESADA)

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Link: <https://onlinelibrary.wiley.com/doi/10.1111/resp.13969>Affiliations expand

Background and objective: To personalize OSA management, several studies have attempted to better capture disease heterogeneity by clustering methods. The aim of this study was to conduct a cluster analysis of 23 000 OSA patients at diagnosis using the multinational ESADA.

Methods: Data from 34 centres contributing to ESADA were used. An LCA was applied to identify OSA phenotypes in this European population representing broad geographical variations. Many variables, including symptoms, comorbidities and polysomnographic data, were included. Prescribed medications were classified according to the ATC classification and this information was used for comorbidity confirmation.

Results: Eight clusters were identified. Four clusters were gender-based corresponding to 54% of patients, with two clusters consisting only of men and two clusters only of women. The remaining four clusters were mainly men with various combinations of age range, BMI, AHI and comorbidities. The preferred type of OSA treatment (PAP or mandibular advancement) varied between clusters.

Conclusion: Eight distinct clinical OSA phenotypes were identified in a large pan-European database highlighting the importance of gender-based phenotypes and the impact of these subtypes on treatment prescription. The impact of cluster on long-term treatment adherence and prognosis remains to be studied using the ESADA follow-up data set.

EADSM comment:

More and more knowledge becomes now available regarding various subtypes of OSA, which will be of help in future precision medicine. MADs were prescribed primarily in two of the clusters. One cluster consisting of only men, the other of only women, representing mainly healthier, younger and less obese patients. 12% of this female cluster and 10% of the male cluster were treated with MADs. Among the other 6 clusters, MADs were used in only a few percent (1.4-5.6%), probably mostly among CPAP-intolerant patients.