Articles of the Month – January 2022

MAD

J Clin Sleep Med. 2022 Jan 31.
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Cardiovascular and metabolic effects of a mandibular advancement device and continuous positive airway pressure in moderate obstructive sleep apnea: a randomized controlled trial

Julia A M Uniken Venema[1,2], Grietje E Knol-de Vries[3,4,5], Harry van Goor[6], Johanna Westra[7], Aarnoud Hoekema[1,2,8,9], Peter J Wijkstra[3,4,10]

Study objectives: It has been suggested that treatment for obstructive sleep apnea (OSA) reduces cardiovascular risk. So far, knowledge is limited about the difference in the reduction of this risk between mandibular advancement device (MAD) and continuous positive airway pressure (CPAP) therapy. The aim of this study was to compare the cardiovascular effects of MAD versus CPAP therapy in patients with moderate OSA.

Methods: Patients with an apnea-hypopnea index (AHI) of 15-30 events/h were randomized to either MAD or CPAP therapy. At baseline and after 12-months follow-up, 24-hour ambulant blood pressure measurements (ABPM) and laboratory measurements were performed. ABPM consisted of 24-hour, daytime and night-time systolic (SBP) and diastolic blood pressure (DBP), and heart rate (HR) measurements. Laboratory measurements consisted of serum lipid values, creatinine, high-sensitivity c-reactive protein, plasma glucose, hemoglobin A1c (HbA1c), proinflammatory cytokines, soluble receptor for advanced glycation end products (sRAGE), chemokines and adhesion molecules.

Results: Of the 85 randomized patients with moderate OSA, data were available for 54 patients (n=24 MAD, n=30 CPAP) at 12-month follow-up and showed that AHI significantly decreased with either therapy. In the MAD group, sRAGE and HbA1c were significantly higher after 12 months follow-up compared to baseline. No significant changes were found between MAD and CPAP treatment for all outcomes.

Conclusions: Treatment of patients with moderate OSA with either MAD or CPAP therapy had no profound effects on major cardiovascular risk factors after 12-months.

EADSM comment: A bit disappointing results, but in line with a previous study in mild OSA patients.
Guimaraes TM, Poyares D, Oliveira ESL, et al. The treatment of mild OSA with CPAP or mandibular advancement device and the effect on blood pressure and endothelial function after one year of treatment. *J Clin Sleep Med*. Feb 1 2021;17(2):149-158.

Sleep Breath. 2022 Jan 22.
doi: 10.1007/s11325-022-02569-3. Online ahead of print.

Link: https://link.springer.com/content/pdf/10.1007/s11325-022-02569-3.pdf

A pilot study on comparison of subjective titration versus remotely controlled mandibular positioning during polysomnography and drug-induced sleep endoscopy, to determine the effective protrusive position for mandibular advancement device therapy

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Study objectives: The aim of this pilot study was to evaluate the clinical effectiveness of subjective titration versus objectively guided titration during polysomnography (PSG) and drug-induced sleep endoscopy (DISE) in mandibular advancement device (MAD) therapy for patients with obstructive sleep apnea (OSA).

Methods: In this pilot cross-over study, patients underwent three titration procedures in randomized order: (1) subjective titration, (2) PSG-guided titration using a remotely controlled mandibular positioner (RCMP) and (3) DISE-assisted titration using RCMP. After each titration procedure, patients used the MAD for 1 month at the targeted protrusion obtained according to the preceding titration procedure. For each procedure, a follow-up PSG was performed after 1 month of MAD use in order to evaluate the efficacy of the MAD.

Results: Ten patients were included in the study. Overall, no significant differences in targeted optimal protrusion compared to maximal comfortable protrusion among the three titration methods were observed. There was no significant difference in reduction in AHI. In this study, PSG titration correctly classified 50% of patients as 'responder'. A higher predictive accuracy was found for DISE titration with a sensitivity of 83.3% and a specificity of 100%.

Conclusions: This pilot randomized cross-over trial showed no differences in optimal mandibular positioning and corresponding efficacy of MAD between subjective titration, DISE titration or PSG titration.

EADSM comment: A very welcome study comparing titration methods, favoring no particular one, which talks against choosing predefined values, such as 50,60 or 70%.

Sleep Breath. 2022 Jan 11.
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Link: https://link.springer.com/article/10.1007%2Fs11325-021-02561-3

Drug-induced sleep endoscopy improves intervention efficacy among patients treated for obstructive sleep apnea with a mandibular advancement device

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Purpose: To compare the short-term treatment effect of a mandibular advancement device (MAD) with and without previous drug-induced sleep endoscopy (DISE) on polysomnography (PSG) and other sleep apnea-related treatment outcomes (Short Form Health Survey [SF-36] and Epworth Sleepiness Scale [ESS]) among adults with mild, moderate, and severe obstructive sleep apnea (OSA). We hypothesized that using DISE would improve the efficacy of MADs on the sleep apnea parameters.

Methods: The study sample consisted of patients with OSA who were unable or unwilling to tolerate a CPAP device, divided into an experimental (with DISE) and a control (without DISE) group.

Results: Of 50 patients with OSA, 40 men (80%), mean age was 48.8 ± 12,3 years. The mean apnea-hypopnea index (AHI) score of both groups decreased significantly between baseline and the 8-week follow-up titration PSG with MAD in situ, from 31.7 ± 17.3 (mean ± SD) apnea-hypopnea episodes/h to 7.0 ± 6.4/h ($p < 0.0001$) in the experimental group, and from 22.5 ± 16.6 episodes/h to 11.4 ± 8.0/h ($p < 0.024$) in the control group. Capillary oxygen saturation (SpO_2) levels did not change significantly between the two timepoints for either group. The SF-36 ($p < 0.023$) and ESS ($p < 0.036$) results of both groups improved significantly between baseline and the 8-week follow-up after starting MAD treatment; however, the improvement in quality of life was significantly more pronounced in the experimental group than in the control group ($p < 0.0001$).

Conclusion: DISE provides a significant benefit to patients with OSA undergoing MAD treatment. It can be used as a valuable prediction tool in clinical practice for the management of patients with OSA, even those with moderate and severe disease.

EADSM comment: DISE might simplify the finding of good responders and an effective mandibular positioning. The nonrandomized study design makes it, however, difficult to know the strength of this method.

Sleep Breath. 2022 Jan 11.
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Link: https://link.springer.com/content/pdf/10.1007/s11325-021-02548-0.pdf

A multifactorial intervention to increase adherence to oral appliance therapy with a titratable mandibular advancement device for obstructive sleep apnea: a randomized controlled trial

Jie Liu[1], Victoria Sheets[2], Rachel Maerz[3], Ai Ni[4], Ulysses Magalang[5], Ching-Chang Ko[1], Allen Firestone[6]

Purpose: Obstructive sleep apnea (OSA) is a common chronic condition, associated with several conditions that account for leading causes of mortality. Adherence to treatment of a chronic condition is, along with treatment efficacy, a major determinant of treatment outcome. The aim of this study was to test whether or not a multifactorial intervention in addition to standard care increases adherence rates in patients using a titratable oral appliance for OSA.

Methods: All subjects were 18 years old or older, had a diagnosis of OSA, and were treated with an oral appliance with an embedded sensor to measure appliance wear time objectively. The control group received routine care, while the experimental subjects received an additional multifactorial intervention. Comparison of adherence was at 30 days (Phase I) and 90 days (Phase II) after appliance delivery.

Results: Data are reported for 82 subjects in Phase I (control 43; experimental 39) and 66 subjects in Phase II (control 36; experimental 30). There were no significant differences for age, sex, body mass index, and apnea-hypopnea index ($p > 0.05$) between groups. In both Phase I and Phase II, the mean number of nights the appliance was worn 4 or more hours and the mean time the appliance was worn nightly were significantly greater in the experimental than in the control group ($p < 0.05$).

Conclusions: Interventions were well received by subjects and can be carried out by auxiliary personnel. The experimental interventions resulted in clinically important and statistically significant improvements in patient adherence to treatment.

EADSM comment: Although short term adherence with MADs seems quite good, the longer term adherence decline, where methods to improve this are welcome.

NON-CPAP THERAPIES

Randomized Controlled Trial
Prog Orthod. 2022 Feb 1;23(1):3.doi: 10.1186/s40510-021-00397-x.

Link: https://progressinorthodontics.springeropen.com/track/pdf/10.1186/s40510-021-00397-x.pdf

Mini-implant assisted rapid palatal expansion (MARPE) effects on adult obstructive sleep apnea (OSA) and quality of life: a multi-center prospective controlled trial

Daniel Paludo Brunetto[1], Christoph E Moschik[2], Ramon Dominguez-Mompell[3], Eliza Jaria[4], Eduardo Franzotti Sant'Anna[5], Won Moon[4 6]

Introduction: Transverse maxillary deficiency is a high prevalent growth disorder within the adult population that may lead to serious health issues, such as detrimental malocclusions and higher risk of developing obstructive sleep apnea (OSA). Mini-implant assisted rapid palatal expansion (MARPE), as it expands the mid-face and augment the nasal and oral cavities dimensions, may reduce the airflow resistance and thus play an important role on OSA therapy in some patients. The main objective of the present trial is to assess MARPE effects on the sleep and quality of life of non-obese adult OSA patients with transverse maxillary deficiency.

Methods: A total of 32 participants were divided into intervention and control groups. They underwent physical evaluation, Epworth Sleepiness Scale (EES) and Quebec Sleep Questionnaire (QSQ), cone-beam computed tomography (CBCT) and home sleep testing (HST) for OSA before MARPE (T1) and 6 months after the intervention (T2).

Results: Questionnaires EES (daytime sleepiness) and QSQ (OSA-related quality of life) presented significant statistical differences between the groups. We also found clinical and statistical ($p < 0.01$) differences between the groups regarding the apnea/hypopnea index (AHI), as well as others HST parameters (mean oxygen saturation and snoring duration).

Conclusion: In our sample, MARPE (without any auxiliary osteotomy) showed a good success rate (85%) and promoted important occlusal and respiratory benefits. We observed important daytime sleepiness and OSA-related quality of life improvement, as well as the AHI (65.3%), oxygen saturation and snoring duration.

EADSM comment: More treatment alternatives are needed for the multicausal disease, OSA. Treatment of transverse deficiency has previously mainly been performed in pediatric OSA patients. To use this treatment modality also adults might be simplified with the developed knowledge about implants.

Am J Orthod Dentofacial Orthop. 2022 Jan 15;S0889-5406(21)00835-0.
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Link:
https://reader.elsevier.com/reader/sd/pii/S0889540621008350?token=DF8587233763598ABD5241AF44CA7B66AB96F68F463EB277F4D125DC768976C064995773B31C6F411E01E0A0C8676214&originRegion=eu-west-1&originCreation=20220205132552

Airway changes after fixed functional appliance treatment in children with and without morphologic deviations of the upper spine: A 3-dimensional CBCT study

Yousef Abdalla [1], Stavros Kiliaridis [2], Liselotte Sonnesen [3]

Introduction: Functional appliances (FA) have a positive effect on the upper airway volume and minimal cross-sectional area (MCA) in children. An association between morphologic deviations of the upper spine (MDUS) and reduced treatment response was found in appliances used to treat adults with obstructive sleep apnea. This study aimed to: (1) compare airway changes after FA treatment in children with and without MDUS and controls; (2) identify if MDUS causes a smaller upper airway.

Methods: Pretreatment and posttreatment cone-beam computed tomography scans were included from 21 children with MDUS and 42 without MDUS treated with a fixed FA, along with a pair-matched control group (matched for chronological age, skeletal age, gender, and mandibular inclination) who received orthodontic treatment for minor malocclusions without an FA. The influence of MDUS on changes in upper airway volume and MCA were evaluated with 3-dimensional cone-beam computed tomography scans using standardized, previously validated methods and mixed-effects linear regression.

Results: There was a significantly increased volume and MCA in the FA groups with and without MDUS compared with control (P = 0.003 and P = 0.049) and in the FA group without MDUS compared with the MDUS group (P = 0.008 and P = 0.011) after treatment. There was no significant pretreatment difference in airway dimensions between the MDUS and non-MDUS FA groups.

Conclusions: The airway response with fixed FA is significantly reduced in MDUS children. MDUS caused no significant pretreatment airway differences in children. However, MDUS may be important in predicting airway changes in FA treatment.

EADSM comment: It is satisfying that the airway might be modified during growth using functional appliances. But, according to the present results, there are different subgroups of patients that might benefit more or less from this intervention.

HYPOXIA

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Link: https://www.atsjournals.org/doi/10.1164/rccm.202108-1808OC?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

Daily Exposure to Mild Intermittent Hypoxia Reduces Blood Pressure in Male OSA Patients with Hypertension

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Rationale: Daily exposure to mild intermittent hypoxia (MIH) may elicit beneficial cardiovascular outcomes.

Objectives: To determine the effect of 15 days of MIH and in-home continuous positive airway pressure (CPAP) treatment on blood pressure in participants with obstructive sleep apnea (OSA) and hypertension.

Methods: We administered MIH during wakefulness 5 days/week for 3 weeks. The protocol consisted of twelve 2-minute bouts of hypoxia interspersed with 2 minutes of normoxia. End-tidal carbon dioxide was maintained 2 mmHg above baseline values throughout the protocol. Control participants were exposed to a sham protocol (i.e. compressed air). All participants were treated with CPAP over the 3-week period. Results are mean ± standard deviation.

Measurements and main results: Sixteen male participants completed the study (experimental n = 10, control n = 6). Systolic blood pressure at rest during wakefulness over 24 hours was reduced after 15 days of MIH (142.9 ± 8.6 vs 132.0 ± 10.7 mmHg, $P < 0.001$), but not following the sham protocol (149.9 ± 8.6 vs 149.7 ± 10.8 mmHg, $P = 0.915$). Thus, the reduction in blood pressure from baseline was greater in the experimental group compared to control (-10.91 ± 4.1 vs. -0.17 ± 3.6 mmHg, $P = 0.003$). Modifications in blood pressure were accompanied by increased parasympathetic and reduced sympathetic activity in the experimental group, as estimated by blood pressure and heart rate variability analysis. No detrimental neurocognitive and metabolic outcomes were evident following MIH.

Conclusions: MIH elicits beneficial cardiovascular and autonomic outcomes in males with OSA and concurrent hypertension.

EADSM comment: Interesting data, somewhat confirming previous studies supporting that some degree of hypoxia might be beneficial.

DAYTIME SLEEPINESS

Review
Heart. 2022 Jan 31;heartjnl-2021-319596.doi: 10.1136/heartjnl-2021-319596. Online ahead of print.

Link: https://heart.bmj.com/content/early/2022/01/30/heartjnl-2021-319596.long

Excessive daytime sleepiness: an emerging marker of cardiovascular risk

Joshua Bock[1], Naima Covassin[1], Virend Somers[2]

Excessive daytime sleepiness (EDS) is classically viewed as a consequence of insufficient sleep or a symptom of sleep disorders. Epidemiological and clinical evidence have shown that patients reporting EDS in tandem with sleep disorders (e.g., obstructive sleep apnoea) are at greater cardiovascular risk than non-sleepy patients. While this may simply be attributable to EDS being present in patients with a more severe condition, treatment of sleep disorders does not consistently alleviate EDS, indicating potential aetiological differences. Moreover, not all patients with sleep disorders report EDS, and daytime sleepiness may be present even in the absence of any identifiable sleep disorder; thus, EDS could represent an independent pathophysiology. The purpose of this review is twofold: first, to highlight evidence that EDS increases cardiovascular risk in the presence of sleep disorders such as obstructive sleep apnoea, narcolepsy and idiopathic hypersomnia and second, to propose the notion that EDS may also increase cardiovascular risk in the absence of known sleep disorders, as supported by some epidemiological and observational data. We further highlight preliminary evidence suggesting systemic inflammation, which could be attributable to dysfunction of the gut microbiome and adipose tissue, as well as deleterious epigenetic changes, may promote EDS while also increasing cardiovascular risk; however, these pathways may be reciprocal and/or circumstantial. Additionally, gaps within the literature are noted followed by directions for future research.

EADSM comment: Important analysis of relationships between daytime sleepiness, cardiovascular risk and sleep disorders, discussing hen and egg relationships.