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Research Article

Efficacy of Mandibular Advancement Device Therapy in Patients with Sleep-Related Breathing Disorders- A Retrospective Study

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Abstract

Purpose: Mandibular Advancement Devices (MAD) are a common treatment option in patients with Obstructive Sleep Apnea (OSA) and Continuous Positive Airway Pressure (CPAP) intolerance. The aim of the present study is to examine the efficacy of the Somnodent®-flex MAD in a cohort selected by pre-therapeutic Drug-Induced Sleep Endoscopy (DISE).

Methods: In a retrospective cohort study, 135 patients were examined with Somnodent®-flex. Apnea-Hypopnea Index (AHI) and Oxygen-Desaturation Index (ODI) was measured with respiratory polygraphy before therapy and 12 months after using MAD in 112 patients. Daytime sleepiness using the Epworth Sleepiness Scale (ESS), Fatigue Severity Score (FSS) and snoring index (0-10), were assessed by means of a questionnaire in 94 patients. The consequent side effects were then documented.

Results: After having used MAD, the AHI was reduced by 39.6% (-9.4/h) from 23.8 ± 15.9/h to 14.4 ± 12.5/h, the ODI was reduced by 37.6% (-7.1/h) from 18.9 ± 16.2/h to 11.8 ± 11.0/h, the mean ESS by 4.4 from 7.5 ± 5.0 to 3.2 ± 2.9 and the FSS by 10.4 from 30.4 ± 16.2 to 20.0 ± 14.1. Snoring was reduced by 5.3 from 8.2 ± 1.8 to 2.9 ± 1.8 on a VAS. The study found all noted changes to be significant. Furthermore, a mean usage time of 6.3 hours was reported with 82.8% daily use after 12 months. A low rate of registered side effects in long-term MAD usage were observed.

Conclusion: The Somnodent®-flex MAD is an effective treatment option for therapy of OSA. However, patient selection using pre-therapeutic Drug-Induced Sleep Endoscopy (DISE) showed similar results as reported in the literature for unselected groups of patients.

INTRODUCTION

OSA is a condition characterized by the repetitive closure of the upper airway during sleep. This is caused by a reduction in tonic and phasic contraction of the pharyngeal muscles during sleep [1]. Hypopnea is a partial reduction of airflow and apnea is a complete occlusion of the upper airway. This result in oxygen desaturation and sleep fragmentation [2]. Some of the major symptoms that OSA patients might experience are headaches in the morning, excessive daytime fatigue, reduced quality of life, and short-term memory loss. This serious disorder affects up to 49% of middle-aged men and 23% of women over the age of 30 [2].

CPAP is the gold standard treatment for moderate to severe OSA. Randomized trials have shown CPAP benefits in daytime sleepiness, blood pressure, quality of life, and endothelial dysfunction [3,4]. Large-scale studies have demonstrated that CPAP also reduces the risk of fatal and non-fatal cardiovascular events in severe OSA [5]. However, the clinical effectiveness of CPAP is often limited by lacking patient and partner acceptance, denial of CPAP, and low compliance. Studies in the field have shown that around 30% of all patients are non-compliant with receiving CPAP treatment [6]. MAD therapy has emerged as a non-invasive alternative to CPAP for the treatment of snoring and mild to moderate OSA with a focus on retro lingual upper airway obstructions [7]. Compared to CPAP, MAD in general shows lower efficacy but higher nightly compliance and has therefore often an equal effect on daytime sleepiness and general quality of life [8]. Prospective studies have shown the efficacy of MAD in reducing respiratory disturbance index, blood pressure, improved sleepiness, sleep quality, and both the subject`s and bed partners' satisfaction [9-11].

The goal of the present study is to investigate the efficacy and side effects of MAD therapy in OSA patients and habitual snorers after topo diagnostic investigation using Drug Induced Sleep Endoscopy (DISE) as a selection tool. Comparative studies suggest

that DISE in comparison to awake evaluations alters surgical treatment plans in approximately 50% of OSA patients [12] and can be applied to improve understanding of the anatomical basis for MAD failure, incomplete response or intolerance [13]. We hypothesise that using DISE while applying a chin lift as selection tool, treatment success may be better as compared to historical controls.

MATERIAL AND METHODS

One of the devices on the market for the treatment of snoring and OSA is the "Somnodent®-Flex" device, which was developed and patented by SomnoMed. The Somnodent® device contains two subunits (Figure 1), which are not directly connected and allow little vertical jaw movements. This raises the comfort as compared to monobloc devices with locked maxilla and mandible components [14]. A dental check-up before treatment as well as dental hygiene is essential. After creating a dental cast, an optimal protrusion was constructed. In this first session, the desired degree of protrusion was defined before the final device is manufactured. The device was individually designed to allow readjustments and a better fit. In a second session, the final mandibular device was handed out and the protrusion was adapted. The therapeutic protrusion range is usually set at 60% of the maximal protrusion.

The inclusion criteria were as follows:

1) AHI > 5/h,
2) Reduction of upper airway obstruction through chin lift during DISE,
3) Tonsils grade < 3,
4) No untreated dental or periodontal diseases,
5) No relevant nocturnal nasal obstruction as reported by the patient.

Figure 1 Mandibular Advancement Device consisting of the upper and lower jaw plate, composed of a body component with two opposed upstanding flanges, located in the buccal area of the lower posterior teeth.

The exclusion criteria were:

1) AHI< 5/h,
2) no relevant opening of the upper airway by chin lift during DISE,
3) untreated dental disease or insufficient number of teeth,
4) impaired nasal breathing during the night. A written informed consent was obtained from all participants before inclusion.

The primary objective endpoints were AHI and ODI reduction. Daytime sleepiness, fatigue, and snoring intensity were secondary subjective endpoints. Habits such as the consumption of alcohol, nicotine, and sleeping pills were considered in our questionnaire as well as the amount of sporting activity. All patients had a thorough ENT examination and DISE. During the DISE, we used a combination of Midazolam and Propofol, which was administered with a target-controlled infusion. Brain activity was monitored with Bispectral Index (BIS) with frontal electrodes attached to the forehead. The BIS was calculated every 15 seconds from the Electroencephalogram (EEG) signals [15].

At a BIS score of 60-70, the upper airway was evaluated with a focus on the velopharyngeal and oropharyngeal obstruction patterns. A chin lift with an estimated 60% of maximal protrusion was conducted to simulate the effect of a MAD. Only patients with a sufficient opening of the upper airway during this maneuver were offered a MAD. Before the treatment began, all patients had a polygraphy (Noxturnal T3) and were asked about their daytime sleepiness using the Epworth Sleepiness Scale (ESS), level of fatigue using the Fatigue Severity Score (FSS), and intensity of snoring using a VAS. Daytime sleepiness with and without MAD was assessed using the ESS, which is a self-administered questionnaire that rates how likely dozing off during the day is (0-10 points = normal, 10-24 points = severe daytime sleepiness) [16]. The FSS is a self-report questionnaire that assesses a subjective measurement of daytime fatigue, being largely independent of depression and daytime sleepiness. The range of possible scores is 1-7, with higher scores reflecting greater fatigue (< 36 points = not suffering from fatigue, > 36-63 severe fatigue) [17]. AHI was recorded as total AHI for the whole recorded night. AHI and ODI were analyzed for the whole cohort. Responders were defined according to the Sher criteria when treatment the AHI was reduced to < 20/h and > 50% from baseline [18]. Analogously for ESS, responders were defined when ESS value was reduced through treatment < 10 and a reduction from baseline of > 50% is achieved. As responder on the snoring VAS, we defined a value reduced through treatment to < 3 and a reduction from baseline of > 50%. The Visual Analogue Scale (VAS) for snoring was evaluated by the bed partner with and without the device (0 = not existent; 10 = severe).

The follow-up visit was at 12 months after the MAD was fitted. Polygraphy was conducted with MAD and patients answered the questionnaires regarding ESS, FSS, and snoring VAS. Any side effects of the MAD such as hyper salivation, experiencing of foreign body, occlusion disorder, mandibular joint complaint, receding gums and pain were recorded. Every patient was recommended to undergo a dental check-up before fitting the MAD to minimize the risk of temporomandibular joint complications, changing the degree of occlusion, hyper salivation, and pressure points on the gingiva. The compliance of the MAD was assessed by frequency of use and thoroughly questioned if there was a specific individual reason for not using the device. These factors were self-reported through questionnaires. The resulting data was entered in R Studio (Boston, USA) V4.1.3 and analyzed using descriptive and explorative analysis. The paired t-test, Wilcoxon signed-rank test, and the Spearman correlation for continuous variables were used for exploratory data analysis. Categorical data were analyzed using the Chi-squared test. The level of significance was defined as $p < 0.05$.

RESULTS

Between December 2007 and May 2017, 135 patients were fitted with a MAD at the ENT clinic of the KSBL. In 53 cases, the previous therapy was CPAP, which was abandoned by the patients. In 15 cases the previous therapy had been an unsuccessful Uvulopalatopharyngoplasty (UPPP) and in 37 cases a septoplasty. Other previous therapies included 26 turbinoplasties, three Fairbanks incisions, seven uvuloplasties, and three hyoid suspensions. Out of the 135 patients 112 had follow-up sleep study and 94 filled out the questionnaires to evaluate ESS, FSS, snoring, adverse reactions, and MAD usage. The study group consisted of 118 (87.4%) men and 17 (13.6%) women. The average age was 55.1 years (standard deviation ± 11.7 years). Body Mass Index (BMI) was 27.7 ± 4.2 kg/m2. Nicotine was consumed by 17.8% (24) and alcohol consumption by 48.9% (66). Sporting activity was performed by 88.2% (119). Sleep medication was used by 22.2% (19).

The pretherapeutic mean total AHI for all patients (n =135) was 23.8/h ± 15.8/h. After 12 months of using MAD, the mean AHI was 14.4/h ± 12.5/h ($p < 0.001$ paired t-test, shown in (Figure 2)). According to Sher criteria, 43/112 (38.4%) patients were responders [18]. We found a significant difference in total AHI reduction for patients AHI < 10/h and AH I > 10/h. The total reduction of AHI was 28% in the AHI < 10/h group and 48% in the AHI > 10/h group. The pretherapeutic mean ODI was 18.9/h ± 16.2/h. After 12 months, the mean ODI was 11.8/h ± 11.0/h ($p = 0.002$ paired t-test, shown in (Figure 3)). Pretherapeutic mean ESS was 7.5 ± 5.0 and 3.2 ± 2.9 after 12 months with MAD ($p < 0.001$ Wilcoxon singed-rank test, shown in (Figure 4)).

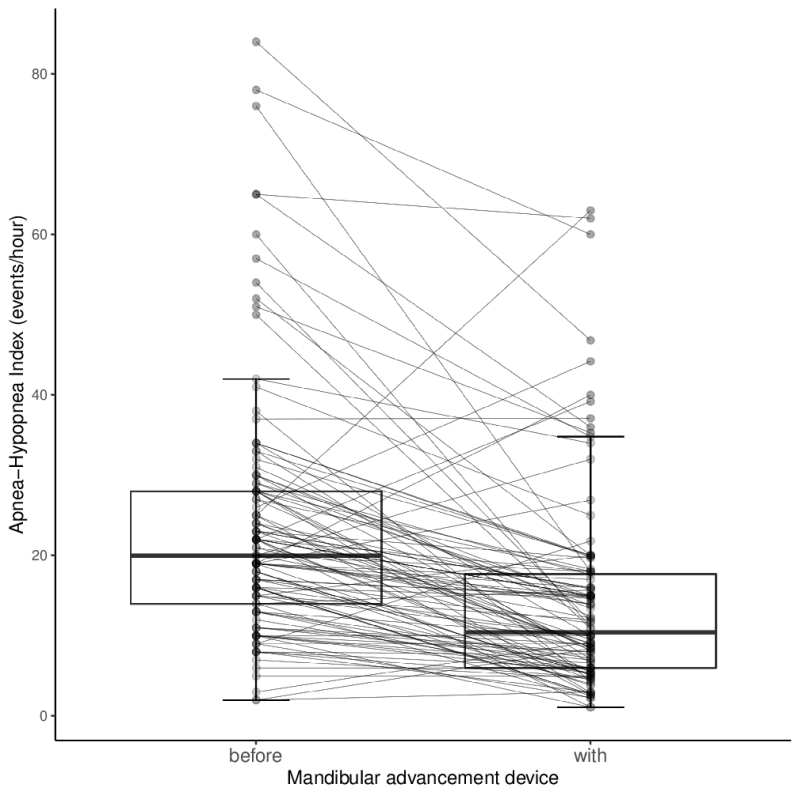

Figure 2 Apnea-Hypopnea Index before and with mandibular advancement device.

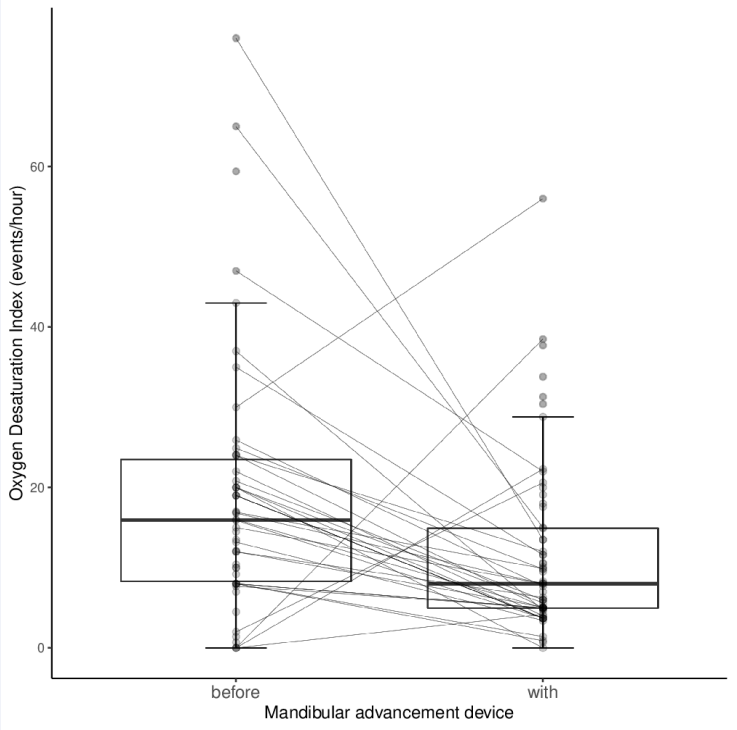

Figure 3 Oxygen Desaturation Index before and with mandibular advancement device.

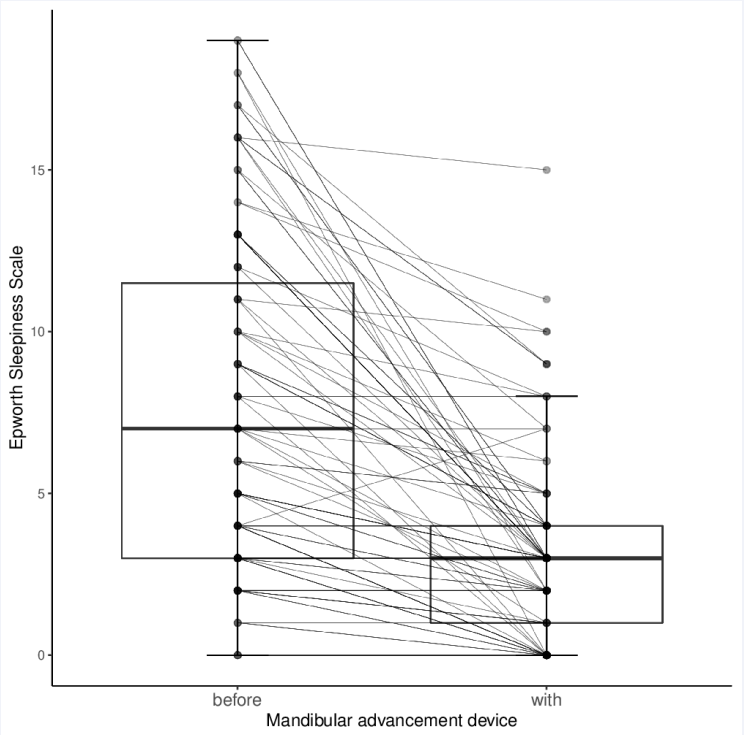

Figure 4 Epworth Sleepiness Scale before and with mandibular advancement device.

Responders regarding sleepiness with ESS < 10 and a > 50% reduction to baseline were 58/99 (58.6%) patients. Men reported significantly lower ESS (3.0 *vs* 4.8, $p = 0.04$) under treatment compared to women, however, the reduction was similar in both genders. Mean FSS pretherapeutic was 30.4 ± 16.2 and 20.0 ± 14.1 after 12 months with MAD ($p < 0.001$ Wilcoxon signed-rank test). Men reported significantly lower FSS (18.5 *vs* 30.4, $p = 0.01$) under treatment compared to women, however, the reduction was similar in both groups. The snoring index measured with VAS was 8.2 ± 1.8 before treatment. After 12 months of using the MAD, the VAS snoring index was reduced to 2.9 ± 1.8 ($p < 0.001$ Wilcoxon signed-rank test). 56/90 (73.3%) patients were responders on the snoring index. The average duration of use was 6.2 hours per day. MAD was used on daily basis by 77/94 (83%) of the participants.

Adverse reactions in order of relevance were hypersalivation 8/91 (8.8%), foreign body sensation 7/89 (7.9%), occlusion disorder 6/85 (6.6%), mandibular joint complaint 5/87 (5.4%), receding gums 4/87 (4.4%) and pain 2/89 (2.2%). Women reported slightly more adverse events, however, the difference was not statistically significant ($p = 0.06$). There appears to be no correlation between reported adverse events and usage time of the MAD ($p = 0.98$) or reduction in AHI ($p = 0.27$). There was a borderline significant correlation between reported adverse events and ODI reduction ($p = 0.04$). There was no correlation between reported adverse events and reduction in ESS ($p = 0.71$) and reduction in FSS ($p = 0.13$), but a significant correlation between adverse reaction and a reduction in snoring. Patients with fewer adverse reactions to MAD report to have a bigger reduction in snoring intensity ($p = 0.03$). Adherence to therapy was good with 85% of participants reporting using the MAD over 6 hours per night and 82.8% reported using it every night.

DISCUSSION

Several systematic reviews and meta-analyses have shown a clinical effectiveness of treatment of OSA with MAD therapy [11]. Roughly, MAD therapy is not effective in one out of three patients. The costs of MAD therapy in Switzerland are approximately 1600 Euros, a considerable waste in case of MAD failure. Here is certainly room for improvement. We were interested to see if the use of DISE with chin lift would increase the success rate, as compared to historical controls. Somewhat in contrast to our expectations, our success rate was not higher than results reported in literature.

The most important objective parameters to monitor the treatment efficacy are decrease of the AHI and ODI. Most of the studies reported in the literature were conducted in unselected patient populations, while we report results in a highly selected patient cohort using DISE with chin lift. We were able to demonstrate a significant total reduction of AHI by 40%. Reports in the literature using various types of MAD devices show similar results [19,20]. In a retrospective cohort study without previous DISE using Somnodent®, an AHI reduction of 48% was found with a pretherapeutic mean AHI of 18.5/h [21] compared to our pretherapeutic mean AHI of 23.8/h. With similar reduction of AHI in unselected patient populations, the question of the significance of DISE before MAD treatment must be raised. However, further prospective randomized-controlled trials would be needed to further address this question. Subgroup analysis addressing this question should focus on collapse patterns, palatal coupling and other parameters in DISE, which might be favorable or unfavorable indicators for success with MAD.

We showed a significant reduction in total AHI. According to Vecchierini et al., who used a patient-driven study protocol for 40 OSA diagnosed patients, the AHI average decrease was varying between 33% and 57%. Our results are comparable with the findings from Vecchierini et al. It is important to mention that our study used a different MAD system to that of Vecchierini et al, who used a MAD with a compression-based triangle and connector articulation [20]. We were also able to show a reduction of total ODI by 38% although the impact on oxygen desaturation parameters is less systematically reviewed in the literature [20].

A subjective measure for effective treatment is daytime sleepiness assessed using the ESS. A significant total reduction by 4.3 points (57.3%) could be achieved with the MAD used in this study. Therefore, the responder rate was 58.6%. Similar results were reported in a retrospective analysis with another type of MAD (type "Somnodent-Herbst") [22] and the RespiDent Butterfly MAD consisting of two clips [19]. The FSS reflects daytime fatigue which can be the consequence of various conditions other than sleep disorders, especially depression. A significant reduction of FSS was achieved, by using the MAD in this study. In total, the initial pretherapeutic FSS was reduced by 34.4%. We found no relevant literature, which evaluates the FSS in OSA therapy using MAD. Snoring with MAD treatment was significantly reduced after 12 months, corresponding to a responder rate of 73.3%. This is comparable to the study by Terryn et al. describing a treatment success of 65% to 75% in patients [23].

As with all devices used in OSA therapy, compliance is crucial for the efficacy of the therapy. Over 85% of participants used the MAD in this study over 6 hours per night. This is comparable with Gotsopoulos et al. study, evaluating oral appliance therapy in relation the blood pressure in a randomized controlled trial [24]. A secondary important factor for compliance is the number of adverse reactions occurring during long-term usage of MAD. In our study 21.7% (20/90) of the frequent users of MAD experienced in total 37 adverse reactions during the long-term usage over 12 months. Relevant adverse reactions, defined as 6 or higher on a visual analogue scale are in order of relevance hypersalivation, foreign body sensation, occlusion disorder, mandibular joint complaint, receding gums and pain. In comparison to other already published studies, the rate of side effects is rather small in our cohort. In a large cohort study with 260 patients evaluating long-term effects in a 2-3 year follow-up by Marklund et al., up to 34% of frequent users of MAD experienced side effects like hypersalivation, dry mouth, and lips, problems with the temporomandibular joint, and occlusal change occurred [25]. The MAD used in the cohort study

by Marklund et al. was a monobloc Mandibular Repositioning Appliance (MRA), pushing the mandible 4-6mm forward. We can conclude from these results, that the acrylic duo bloc system, used in our study generates fewer side effects in comparison to a monobloc system which is in accordance with the literature, reporting better compliance and fewer side effects for duo-bloc systems compared to mono-bloc ones [26]. In the literature, the number of complications varies from 0 up to 70%, depending on follow-up time, type of MAD, and the assessed side effects [7]. In general, short-term side effects are overly sensitive teeth and hypersalivation occurring during the first 6 months of MAD usage.

Our study is not without limitations. Compliance was calculated based on patient self-report about usage. Ideally, compliance would have been calculated based on objective usage as assessed by a thermochip. Secondly we used polygraphy, while a full night polysomnography would have been even more precise. Finally, we realize that a chin lift is not a very precise procedure, and it might be not a true reflection of the effect of MAD. Other groups (Antwerp) are working with a simulation bite during DISE, while others (Amsterdam) used a temporarily MAD, manufactured just before DISE in the hope this will mimic the effect of the definitive MAD better [27-30]. However, more research on the usefulness of such procedures is warranted.

CONCLUSIONS

Our study suggests that MAD devices such as the duo-bloc Somnodent® device are a reasonably effective tool in OSA patients that are CPAP-intolerant. We registered a reduction of AHI with the MAD of 40%. With that, we can show the effectiveness of the MAD on respiratory parameters. Our study confirmed that daytime sleepiness, fatigue, and snoring showed a significant improvement measured with ESS (57.3% reduction), FSS (34.4% reduction), and snoring (64.5% reduction). The study also noted a low rate of adverse reactions in long-term MAD usage over 12 months. However, pretherapeutic DISE with chin lift does not improve treatment outcome.

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