TURKISH JOURNAL of ORTHODONTICS

DOI: 10.4274/TurkJOrthod.2022.2022.54

Original Article

Starting Mandibular Advancement Device Therapy in Patients with Good Protrusive Capacity: A Randomized Pilot Study

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Cite this article as: Marklund M. Starting Mandibular Advancement Device Therapy in Patients with Good Protrusive Capacity: A Randomized Pilot Study. *Turk J Orthod.* 2023; 36(3): 158-164.

Main Points
- Obstructive sleep apnea patients with a good protrusive capacity may experience unnecessary side effects with the mandible advanced by 70% at start.
- The advancement measured in millimeters correlated with the occurrence of severe side-effects, r=0.64, in this group of patients.
- The patients had difficulty estimating whether they had started with a smaller or larger advancement.
- A description in both millimeters and per cent will facilitate comparisons between patients with varying protrusive capacities.

ABSTRACT

Objective: Discomfort has been related to the poor acceptance of a mandibular advancement device (MAD) in patients with obstructive sleep apnea. The present study compared severe initial side effects between a smaller and a larger degree of mandibular advancement in patients with a good protrusive capacity.

Methods: Consecutive patients with obstructive sleep apnea and a good protrusive capacity (≥8 mm) were randomized to start treatment with the mandible advanced by either 70% of maximum protrusion ($Adv_{70\%}$) or by 4 mm (Adv_{4mm}) in a pilot study with a parallel design. The main outcome was tenderness or pain in the teeth or jaws using a 0-10 visual analogue scale (VAS) (from "not at all" to "very extensive") or excluded use because of side effects during the first week of treatment. Secondary outcomes included salivation problems and bite changes.

Results: Eighteen patients were randomly selected and 17 patients fulfilled the study protocol. Four patients in the $Adv_{70\%}$ group and none in the Adv_{4mm} group reported severe tenderness or pain (VAS ≥7) on five or more of the seven days (p=0.03). The degree of mandibular advancement measured in millimeters correlated with the number of days with severe side effects, r=0.64 (p=0.006). The secondary side effects were minor.

Conclusion: Starting MAD treatment with 70% mandibular advancement was related to more severe side effects during the first week of treatment compared with a smaller fixed millimeter value in patients with a good protrusive capacity in this pilot study.

Keywords: Oral appliances, mandibular advancement devices, mandibular repositioning appliances, side-effects, obstructive sleep apnoea

INTRODUCTION

The repositioning of the lower jaw anteriorly to facilitate breathing during sleep is the key mechanism of a mandibular advancement device (MAD) for treating patients with obstructive sleep apnea (OSA). Treatment with MAD may, however, also cause side effects leading to poor adherence,[1,2] in accordance with what has been found for treatment with positive airway pressure (PAP).[3] Good adherence already during the first week of treatment has been related to the long-term acceptance of both MAD and PAP.[4,5] Several routines have been suggested to identify the most effective jaw position for the MAD, as it will differ from patient to patient.[2,6] The American

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Received: May 6, 2022
Accepted: December 22, 2022
Epub: September 20, 2023
Publication Date: September 29, 2023

Academy of Dental Sleep Medicine has published the results of a task force that evaluated all the steps in the procedure of finding the therapeutic position of the mandible, from the beginning of treatment through the titration process to verifying the outcome with a follow-up sleep apnea recording.[2] These differences pertain to the posterior reference point used for measuring the advancement, whether the advancement should be measured in percent or in millimeters, and the appropriate magnitude of the initial advancement.

The degree of mandibular advancement can be measured either from the most retruded position of the lower jaw that the patient can achieve in a gauge or from centric occlusion, which is defined as the position with the maximum intercuspation of the teeth. Alternatively, it is also possible, although maybe more complex, to measure the advancement from a centric relation. The distance between centric occlusion and centric relation is usually also negligible.[7] The most retruded position in a gauge will be more posteriorly located than centric occlusion, as the mandible tends to rotate backward when the jaw opens up in the gauge.[7,8] Moreover, the location of the most retruded position in the gauge can vary from patient to patient,[8] making comparisons of mandibular advancement uncertain, whether measured in percent or in millimetres.

A titration procedure starting at a smaller degree of mandibular advancement is often recommended.[9] However, larger advancements, intended to provide a higher likelihood of direct treatment success, may also be used. Aarab et al.[10] conducted a study to compare the efficacy of a mandibular advancement device (MAD) at four different degrees of mandibular advancement (0%, 25%, 50% and 75%) in a random order measured from centric occlusion.[11] After approximately three weeks of using each mandibular position, they conducted interviews and found that initial side effects were more common with advancements of 50% or 75% than with smaller ones. In another study by de Ruiter et al.[12] MAD therapy was initiated with a 60% mandibular advancement, which was measured using a gauge.[12] Four of 36 patients reported severe side effects or discomfort while wearing the device. Two patients opted to switch to a smaller mandibular advancement, which reduced their problems. A mandibular advancement of 50% to 60% corresponds to an advancement of three to nine millimeters in sleep apnea patients. These patients have been reported to have a protrusive capacity between five and 15 millimetres.[7]

This randomized pilot study aimed to compare severe side effects during the first week of treatment between two different starting jaw positions. The idea for this randomized pilot study originated from our positive experiences with significantly reduced immediate pain at the start of treatment when we switched from monoblock devices to duoblock devices some years ago. When using monoblock devices, patients usually start with the mandible advanced to the anticipated therapeutic position. In contrast, adjustable duoblock devices allow for smaller initial advancements followed by a titration procedure. This approach appeared to be beneficial in allowing patients to adapt to an advanced mandibular position. We measured the advancement in millimetres, but percentage values of advancement are advancement are suitable for suitable for identifying the therapeutic mandibular position. Patients with a good protrusive capacity may, however, face a higher risk of experiencing large initial advancements if they start at an anticipated therapeutic position identified by a percentage value. This is because larger protrusive ranges lead to proportionally larger millimeter values with percentage advancement. Therefore, for this pilot study, only patients with a good protrusive capacity were selected. One advancement was intended to provide a relatively higher chance of direct treatment success. Therefore, a relative measure was chosen to provide a sufficiently advanced jaw position for all patients with different protrusive capacities. The other advancement was intended to represent a small initial advancement. An absolute value was chosen, which would result in a stable initial small advancement without interfering with the degree of advancements in the other randomization group. The null hypothesis for this study was that there would be no difference in severe side effects between the two starting positions.

METHODS

Consecutive patients referred from the Pulmonary Department at the University Hospital, Umeå University, Umeå, Sweden to the Dental School, Department of Orthodontics were asked to participate in the study. These patients had previously been undergone examination by a pulmonary physician and including a respiratory polygraphy (Level III) before MAD treatment. The patients underwent an odontological examination including measurements of the protrusion capacity defined from centric occlusion with maximum intercuspation of the teeth. Centric occlusion was reproduced on a wax index (Alminax, Kemdent, Swindon, England) and subsequently identified on plaster casts by marking two occluding teeth in the premolar area. The maximum protrusion capacity was measured on the central incisors.

The inclusion criterion for participation in the study was being treatment-naïve patients with a mandibular protrusive range of ≥8 mm. Exclusion criteria comprised recent or ongoing temporomandibular disorders, having too few teeth to anchor the appliance, unwillingness to participate, and fear of side effects or other problems that interfered with the opportunity for the subjects to fulfill the study protocol. All subjects provided informed consent before taking part in the study.

The patients were randomized using a block design, with four patients in each block to ensure even distribution between the two arms: $Adv_{70\%}$ with 70% maximum mandibular protrusion and Adv_{4mm} with 4 mm mandibular advancement. A computer-generated table was utilized for this randomization and it was kept by a person outside the study staff to maintain blinding. The participants were informed about the aim of the study, which involved comparing two different starting positions in terms of

side effects. During the visit for device delivery, the patients only tested the appliances to ensure their suitablitiy for wear. They received repeated information about the study protocol at this stage. The patients, but not the dentist, were blinded regarding the randomization group. This blinding was intended to prevent any bias in reporting side effects. This way, the dentist could make an immediate decision on how to proceed if the patient experienced initial problems with the device. The main outcome was tenderness or pain in the teeth or jaws using a 0-10 visual analogue scale (VAS) or exclusion from using the device due to these side effects during the first week of treatment. Secondary aims were assessed using the same scale and included salivation problems during appliance wear and occlusal changes after the appliance had been removed.

The patients were given the option to choose between the two types of appliances available at the clinic: a fin coupling type of device (SomnoDent Fusion™) or a traction type device (NarvalCC™) (Figure 1). All patients were advised to use elastic bands to secure the degree of mandibular advancement during the night.[13,14] For this study, two different degrees of advancement were chosen. The first degree involved 70% of maximum protrusion (resulting in ≥5.6 mm advancement in the patients with ≥8 mm protrusive capacity) and this advancement was intended to provide the patients with a mandibular position that could give immediate treatment success. The second advancement was a fixed millimeter value of 4 mm (resulting in ≤50% advancement) and intended to represent a milder treatment start in terms of side effects. Both measurements of advancement were assessed from centric occlusion, providing a standardized reference point for the evaluation.

A construction bite in wax was taken with the mandible advanced by approximately four millimeters, considering the comfort level for each patient. The teeth and jaw position with the construction bite in place were then scanned and sent to dental laboratories for fabrication of the appliances. Upon receiving the delivered appliances, adjustments were made on plaster casts based on the jaw position taken directly from each patient. These adjustments were made to achieve the randomized degree of advancement specific to each individual patient. Subsequently, the devices were tried out on the patients. The degree of initial mandibular advancement was measured with bite registration between the upper and lower parts of plaster casts. The randomized mandibular position was then achieved using the adjustment mechanism on the device.

Questionnaires

Shortly before the treatment's commencement, the patients completed a first questionnaire each day of the week, which assessed tenderness or pain in the teeth or jaws and salivation problems using a VAS graded from 0 to 10 (ranging from "not at all" to "very extensive"). Upon treatment initiation, they answered a second questionnaire daily during the first week of appliance use. These questions included inquiries about the excluded use of the appliance, the occurrence of tenderness or pain in the teeth or jaws during the day or night, and problems with chewing due to tenderness or pain, all reported on the VAS. Using the same scale, they reported the problems related to hypersalivation or dry mouth that disturbed sleep and bite changes. Before the finalization of the study, the patients responded to a third questionnaire, indicating their willingness to continue treatment. The response options ranged from "absolutely", "likely", "not likely", "absolutely not" or "don't know". In addition, the participants were asked to indicate whether they believed they had used larger or smaller advancement or did not know.

The ethical approval was obtained from the Ethics Committee of Umea University (EPN2018/44-31).

Statistical Analysis

The data were presented as median and interquartile range (IQR). Severe tenderness or pain was identified by the 75th percentile of the results reported in the study. The Mann-Whitney U test for independent samples was used to test differences in baseline characteristics and the occurrence of severe side effects during the first week between the two randomization groups. Fisher's exact test was used to compare the occurrence of severe tenderness or pain, appliance design, patients' estimation of the degree of advancement, and differences in sex distribution between the randomization groups. Spearman's rank correlation was used to study the relationship between mandibular advancement and the number of nights on which the patients had reported severe tenderness or pain or had excluded use because of these side effects. A p value of less than 0.05 was considered significant.

RESULTS

Thirty-five consecutive eligible patients were asked to participate in the study from March 2018 until June 2019. Out of these, seventeen patients were excluded for various reasons, including unwillingness to participate or lack of time (7), the need for dental treatment (1), desire for small initial advancement due to fear of jaw pain or bite changes, or recent temporomandibular disorder (6), and problems with device delivery (3). Eighteen patients were randomized, but due to the misunderstanding of the second questionnaire by one patient, the data from day two to day seven were partially or entirely unanswered. Therefore, 17 patients (12 men) were included in the analysis (Table 1). Among 17 patients, 9 had mild OSA, 7 had moderate OSA, and 1 had severe OSA (AHI 31). The final degree of advancement, presented in both percentage and millimeters, for the randomization groups is summarized in Table 2. In the $Adv_{70\%}$ group, the advancements differed by around 2 millimeters between the patients.

Fifteen out of the 17 patients responded to the first daily questionnaire before starting MAD therapy (Table 3). During the first week of treatment, four patients (13 nights) in the $Adv_{70\%}$ group and one patient (3 nights) in the Adv_{4mm} group did not

Table 1. Patient characteristics (n=17)

	Total sample (n=17)		$Adv_{70\%}$ group (n=8)		Adv_{4mm} group(n=9)		
	Median	IQR	Median	IQR	Median	IQR	p value
Age (yrs)	56.4	46.8-61.3	51.8	31.9-59.6	60.4	53.6-62.2	0.123
Apnoea-hypopnoea index (AHI)	13	10-20	11	6-19	16	12-23	0.134
BMI (kg/m^2) (n=7 in $Adv_{70\%}$)	25.8	24.8-29.1	27.3	25-29.8	25	23.6-27.2	0.313
ESS (n=5 in $Adv_{70\%}$ and n=8 in Adv_{4mm})	8	2-12	8	1-12	9	2-14	0.460
Maximum protrusion (mm)	10	8.5-11.5	10.3	8.5-11	10.0	8.5-12.5	0.560
Overjet (mm)	3.0	2.3-4.0	3.0	2.1-3.8	3.0	2.3-5.0	0.461
Overbite (mm)	4.0	2.5-6.0	2.8	1.8-5.8	4.0	3.3-6.0	0.310
Height between incisors (mm)	5.5	5.0-6.5	5.5	5.1-6.4	6.0	5.0-6.8	0.557
Elastics use (nights) (n=6 in each group)	7	4-7	6	4-7	7	3-7	0.818
	n		n		n		
Male (%)	12 (71)		5 (63)		7 (78)		0.620
Fin/traction type of device	13/4		5/3		8/1		0.294

*Statistical significance p<0.05. The Mann-Whitney U test for independent samples and Fisher´s exact test were used to test differences between randomization groups

Table 2. Degrees of advancement in millimeters and percent of maximum protrusion in the randomization groups

	$Adv_{70\%}$ (n=8) group		Adv_{4mm} (n=9) group		
	Median	Minimum-maximum	Median	Minimum-maximum	p value
Advancement (mm)	7.2	5.6-7.7	4.0		<0.001*
Advancement (%)	70		40	31-50	<0.001*

*Statistical significance p<0.05. The Mann-Whitney U test for independent samples was used to test differences between randomization groups

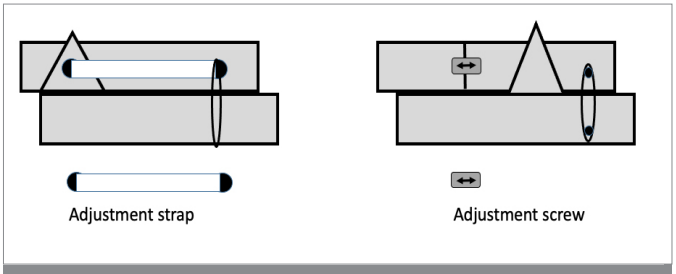

Figure 1 . The illustration of the traction type of MAD (left) and the fin coupling type of MAD (right). The traction type of the appliance is adjusted by different lengths of the straps. The fin coupling type of device is adjusted using a screw in the upper jaw, which pushes the lower jaw forward with the help of a wing.

use their appliances due to tenderness or pain in the teeth or jaws. These occasions were graded as worst pain. The median VAS score for tenderness or pain in the teeth or jaws during the week was two nights/days (IQR 0 to 7) (n=17).

The number of nights and days with severe tenderness or pain in the teeth or jaws before appliance use and during the first week of treatment, using a VAS cut-off of 7 (75^{th} percentile), are summarized in Table 3. Four patients in the $Adv_{70\%}$ group and none in the Adv_{4mm} group reported a score of ≥7 on VAS on five or more of the first seven nights (75^{th} percentile) of treatment (p=0.03) (Figure 2). There was a correlation (r=0.64, p=0.006) between the advancement of the mandible in millimeters

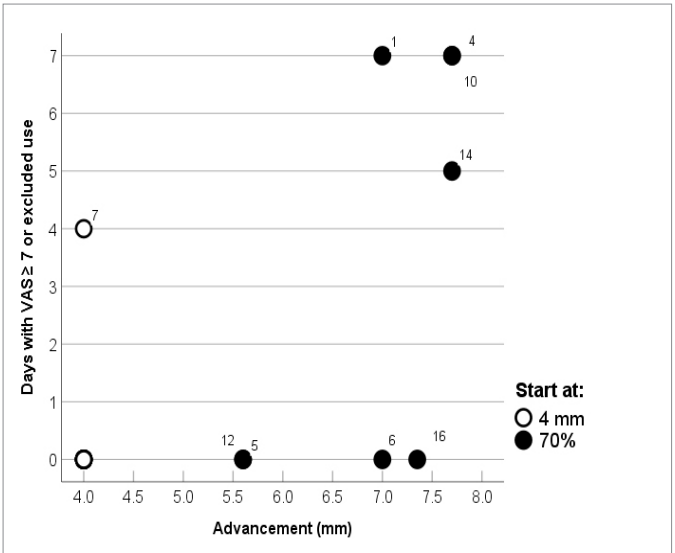

Figure 2. Scatter plot illustrating the relationship between the degree of mandibular advancement (mm) and the number of nights that the patients had reported tenderness or pain ≥ 7 on VAS or excluded use because of such side effects. Labels refer to patient identification.

and the occasions on which the patients reported severe side effects during the first week. Salivation problems or experienced bite changes were small and did not differ between the randomization groups (Table 3).

Table 3. Symptoms during the week before treatment and during the first week of treatment

The number of nights and days with severe symptoms (VAS ≥7)	Total sample (n=17)		$Adv_{70\%}$ (n=8) group		Adv_{4mm} (n=9) group		Between randomization groups
	Median	IQR	Median	IQR	Median	IQR	p value*
Without treatment							
Tenderness or pain in teeth or jaw¤	0	0-0	0	0-0	0	0-0	1.00
Salivation problems¤	0	0-0	0	0-0	0	0-0	1.00
During the first week of treatment							
Tenderness or pain in teeth or jaw or not used	0	0-5	3	0-7	0	0-0	0.055
Start on day:			1,1,1,3	n=4	4	n = 1	
Occlusal changes¤¤	0	0-1	0	0-4	0	0-0	0.110
Salivation problems¤¤	0	0-2	0	0-3	0	0-1	0.677

¤n=7 in $Adv_{70\%}$
n=8 in Adv_{4mm}
¤¤n=7 in $Adv_{70\%}$
*Statistical significance p<0.05. The Mann-Whitney U test for independent samples was used to test differences between randomization groups. IQR, Interquartile range

All 15 patients who responded to the third questionnaire expressed a desire to continue treatment, with 13 patients responding as "absolutely" and 2 patients responding as "likely." There was no difference in the responses between the randomization groups (p=0.2). The two patients who did not respond to the questionnaire belonged to separate randomization groups.

In the Adv_{4mm} group, four out of the eight responding patients (50%) correctly believed that they had used the smaller advancement, three patients thought they had used the larger one, and one patient was unsure. In the $Adv_{70\%}$ group, two of the seven responding patients (29%) correctly believed they had used the larger advancement, four patients thought that it was the smaller one, and one patient was unsure. There was no significant difference between the randomization groups in terms of patient perception (p=1.00).

DISCUSSION

In this study, the first week of MAD therapy was evaluated regarding side effects and the null hypothesis was rejected. Patients with a good protrusive capacity of ≥8 mm who initiated MAD treatment with 70% mandibular advancement experienced more severe tenderness or pain compared to those who began with 4 mm of advancement. The degree of mandibular advancement correlated with the patients' reports of severe side effects. However, there were only a few reports of severe early salivation problems or disturbances due to a change in bite during the first week of treatment in this sample.

Severe tenderness or pain lasting for 5 days or more was observed exclusively in patients belonging to $Adv_{70\%}$ group (Figure 2). These patients had undergone the largest advancements in the study, with advancements of seven millimeters or more (Table 2). Among these patients, severe side effects commenced on day one for three patients and on day three for one patient (Table 3). Only one patient from the Adv_{4mm} group reported any severe side effects and they were experienced for only four days. These side effects occurred during the last days of the week (Table 3). This patient had used 50% advancement, which was the largest advancement in the Adv_{4mm} group. This study is the first to evaluate the first week of MAD treatment regarding side effects that might disrupt treatment initiation. The findings shed light on this aspect of the treatment and provide support for the notion of commencing treatment with a smaller degree of mandibular advancement before proceeding to titration.

There was a positive correlation (r=0.64, p=0.006) between the assessment of mandibular advancement in millimeters and the occurrence of severe side effects during the first week among patients with a good protrusive capacity in this study. Using a percentage value to define the degree of mandibular advancement results in multiple millimeter values being used. Therefore, providing a measure of both the advancement and the protrusive capacity in millimeters with a percentage description would facilitate comparisons between patients with varying protrusive capacities. In our $Adv_{70\%}$ group, the patients' maximum protrusive capacity varied between eight and 11 millimeters, leading to mandibular advancements between 5.6 and 7.7 mm (Table 2). Sleep apnea patients may, however, protrude their mandibles up to 15 mm,[7] measured from centric occlusion, which corresponds to 11.5 mm with 70% advancement. It is also unknown if patients with a good protrusive capacity would require a larger mandibular advancement resulting from a percentage degree of advancement to achieve an optimal degree of pharyngeal widening.

Millimeter and percentage values of mandibular advancement were utilized in this study. Kazemeini et al.[15] conducted a comparison of personalized titration procedures and found no differences regarding final mandibular positioning or final AHI between them. One method started treatment in the maximally comfortable mandibular position followed by subjectively

accomplished titration. The other two methods utilized titration during polysomnography or drug-induced endoscopy. Although side effects were not evaluated in that study, it demonstrated that a subjectively guided titration procedure might yield similar final results on AHI as methods that commence at the most effective mandibular positioning.

The efficacy of MAD after titration is finalized is not proportional to the degree of advancement, according to a meta-analysis conducted by Bartolucci et al.[16] This conclusion is supported by three recent studies. Ma et al.[17] found no dose-dependent effect of mandibular advancement on the apnea and hypopnea index in the entire sample of 42 patients, although the relationship strengthened in patients with increased severity of OSA. In that study, patients with milder OSA could be effectively treated with an average advancement of 4 mm or 40% of maximum protrusion, while patients with more severe OSA needed an average advancement of 6 mm or 70% of maximum protrusion.[17] A pilot study[18] utilized pharyngometry to determine the optimal degree of advancement and found that the effective mandibular position was located 5 mm less advanced compared to 70% advancement, as measured in the gauge.[18] Furthermore, Anitua et al.[19] reported that treatment success was achievable with an advancement of zero or only a few millimetres. The generalized suggestion made by Aarab et al.[10] of starting at 50% advancement to balance the treatment effect with side effects can be modified. The above studies and the results of the present study indicate that even smaller percentage or millimeter values could be considered at the start of treatment to avoid unnecessary side effects. This is particularly relevant for patients with a good protrusive capacity, who may be at risk of side effects with routine percentage advancement at the beginning of treatment.

In the present study, thirteen patients had used the fin coupling type of MAD, and four patients had chosen the traction type of device.[20] Both types of appliances are equipped with lateral adjustment mechanisms, which provide more similar types of forces on the teeth compared to a centrally located type of adjustment mechanism.[20] However, the same study also revealed differences in the distribution of forces among various types of lateral adjustment mechanisms. This finding highlights the importance of using the same type of device in future studies, that aim to evaluate the side effects of MAD.

Only six out of the 15 patients (40%) who responded to the third questionnaire were able to identify whether they belonged to the smaller or the larger advancement group. This finding is consistent with previous research that indicates patients often have difficulty identifying changes in their dental occlusion. Additionally, many patients find it challenging to notice bite changes that occur over prolonged use of an MAD.[21] Consequently, it may be difficult for many patients to accurately assess how far forward their mandibles are repositioned at the beginning of treatment. Therefore, it might be beneficial to start with a gentle advancement to minimize potential side effects and discomfort.

Study Limitations

The sample size of this study was small. Nevertheless, the primary aim was to preliminarily evaluate the strength of a clinical observation. The inclusion criteria ensured that only patients with a good protrusive capacity of 8 mm or above were included. Therefore, it would be of interest to conduct further studies to investigate whether patients with smaller protrusive capacities can tolerate larger percentage degrees of advancement, which correspond to smaller millimeter values. Additionally, including more objective measures in such studies would be valuable.

The sample mainly comprised mild and moderate patients with OSA, a group of patients who generally require smaller therapeutic advancements.[17,22] These milder OSA patients constitute the majority of patients referred to our clinic; thus, finding more severe OSA patients who might require larger advancements was challenging. The particular aim of this pilot study was to investigate patients with a good protrusive capacity due to the lack of knowledge in this subgroup of patients regarding initial side effects. A recent study reported that no mild to moderate OSA patients experienced pain after 2-3 months of treatment with either 50% or 75% mandibular advancement, but information about the patients' protrusive capacity was not provided.[22] Future studies should be designed to provide more insight into the relationships between mandibular advancement, the efficacy of the device concerning disease severity and the patients´ protrusive capacity.

No cephalograms were taken for this pilot study. In future studies, new analysis methods could be employed to account for potential differences in skeletal mandibular shapes may influence the actual degree of mandibular movement.[23] It is important to recognize that the same degree of mandibular protrusion, as measured in relation to the teeth, may result in variable actual mandibular advancements in relation to the skull and pharynx.

Finally, it would have been ideal for a person outside the study, unaware of the randomization groups, to delivere the appliances to avoid possible bias. Initially, this was the intention; however it later became impossible due to the lack of personnel at the time of the study.

CONCLUSION

According to this pilot study, starting treatment with mandibular advancement device (MAD) for sleep apnea at 70% of the maximum mandibular advancement was associated with more severe tenderness or pain in patients with a good protrusive capacity during the first week of treatment compared to starting with a lower degree of advancement.

Ethics

Ethics Committee Approval: The ethical approval was obtained from the Ethics Committee of Umea University (EPN2018/44-31).

Informed Consent: All subjects signed informed consent.

Peer-review: Externally peer-reviewed.

Funding: The author declared that this study has received no financial support.

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