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Therapeutic efficiency analyses of mandibular advancement devices using polysomnography, smartphone sleep applications, and simple pulse oximetry

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ABSTRACT

Aims: Oral appliances are non-invasive solutions for obstructive sleep apnea (OSA). The aim of the present study was to determine the therapeutic efficiency of mandibular advancement devices (MAD), using polysomnography (PSG), smartphone sleep applications (SSA), and simple pulse oximetry (SPO) for OSA patients.

Methods: Totally 18 mild-moderate OSA patients (8 females and 10 males, aged between 34 and 83 years) with subjective snoring complaints were selected. The diagnostic PSG tests were accepted as initial PSG. Each patient was subjected to SPO and SSA at 3 different nights at home. The mean diagnostic values of oxygen desaturation index (ODI), snoring intensity score (SIS) and snoring percentage (SP) were obtained. Non-titratable-customized MADs (NTC-MAD) with 60-75% of maximal mandibular protrusion were fabricated. SPO and SSA measurements were repeated at the 1st, 4th, 12th, and 24th weeks of the treatment process. At the 24th week of the treatment, the PSG tests were repeated and all PSG, SPO, and SSA values were compared with initial diagnostic values.

Results: There was no significant difference in body mass index and neck circumference values during the treatment ($p>0.05$). The success rate of NTC-MAD treatment was about 68.7% according to the success criterion of MAD treatment as the decrease of apnea-hypopnea index below 5 per hour. ODI, SIS, and SP values showed a significant decrease during the treatment ($p<0.01$). A maximum decrease in SPO and SSA data were obtained at the 12th week of NTC-MAD use ($p<0.05$).

Conclusions: NTC-MADs significantly decreased snoring intensity and frequency and may be accepted as effective devices in the treatment of OSA.

Introduction

Obstructive sleep apnea (OSA) is one of the common syndromes of sleep-related breathing disorders according to the "International Classification of Sleep Disorders-3" (1,2). OSA, which causes snoring and sleep fragmentations, resulting in excessive day time sleepiness, originates from apneas and hypopneas (2). OSA severity is defined as mild for apnea-hypopnea index (AHI) ≥ 5 and <15 , moderate for AHI ≥ 15 and ≤ 30 , and severe for AHI >30 events/h (2).

The principal treatment methodology for OSA patients is positive airway pressure (PAP) (2,3). In patients with mild to moderate OSA, oral appliances such as mandibular

advancement devices (MADs) and tongue advancement devices are alternately indicated especially for patients intolerant to continuous PAP therapy (3).

The American Academy of Dental Sleep Medicine (3) recommended titratable-customized MADs (TC-MAD) for patient comfort and the ability to permit modifications in the amount of mandibular protrusion for treatment efficacy. However, several studies (4-7) demonstrated similar therapeutic efficiency of non-titratable-customized MADs (NTC-MADs) in the treatment of simple snoring (SS) and OSA.

The treatment efficacy of oral appliances is generally identified by polysomnography (PSG). Important physiological

sleep markers such as AHI, oxygen desaturation index (ODI), and respiratory disturbance index are obtained with PSG (2,3,8). However, the rareness of qualified PSG centers and late appointment times are still the main factors restricting its usage. Pepin et al. (9) proposed measurement and comparison of snoring sound magnitudes as an alternative method for the follow-up of SS and OSA patients and claimed that at least 15% of snorers had an AHI >15 events/h. It was shown that the acoustic characteristics of snoring differed between SS and OSA patients (10).

The latest remarkable developments in the telecommunication industry and smartphone technologies have enabled to monitor and compare magnitudes of snoring at home by using a wide range of smartphone sleep applications (SSA). Manufacturers of SSA claim that these applications enable users to record snoring sounds, snoring frequencies, and snoring intensities.

The effect of oral appliances on SS and OSA has been studied extensively by using PSG, type-3 home sleep study device, and subjective questionnaires. However, there are no studies in the literature evaluating the therapeutic effects of MADs in OSA patients using both SSA and simple pulse oximeter (SPO). The aim of the present study was to determine the efficacy of NTC-MAD therapy on snoring intensity, snoring frequency, and oxygen desaturation periods in patients with snoring problems using SSA and SPO methods.

Methods

The present study was approved by the Clinical Trials Ethics Committee of Gulhane Military Medical Academy (Ankara, Turkey) (2015-KAEK-84/ 24th December 2015) and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study. The present study was registered at ClinicalTrials.gov (NCT04427111). The participants were selected from OSA patients presenting with subjective snoring (n=37) to the Department of Prosthodontics between December 2015 and January 2017. The exclusion criteria for the study were; having severe OSA, having previous surgery for OSA, and carrying a high risk of cardiovascular, respiratory, neurological or psychiatric disorders (n=12). Patients with an inadequate dental anchor for MAD treatment, temporomandibular joint dysfunction, and Angle Class 3 maxillomandibular relation (n=7) were also excluded. OSA patients who were not eligible for MAD treatment were informed and directed to other treatment options. Totally 18 mild-moderate OSA patients with subjective snoring complaints were included in the study. Of 18 patients, eight patients (44.4%) were female and 10 patients were (55.6%) male. The average age of the patients was 49.33 years, ranging between 34 and 83 years.

PSG, ODI, and SSA values were used to determine and compare the therapeutic efficacy of NTC-MAD treatment in

the present study. The diagnostic PSG values of the subjects (before NTC-MAD use) were accepted as initial PSG (PSG-i) values. Final PSG (PSG-f) measurements were performed after 24 weeks of NTC-MAD treatment with NTC-MADs *in situ*. Body mass index (BMI) and neck circumference values were also recorded before NTC-MAD treatment and at the 24th week of the treatment of NTC-MAD. The success criterion of NTC-MAD treatment was defined as the decrease of AHI below 5 per hour. To detect a reduction in AHI, a minimum sample size of 13 participants was considered to obtain 80% power at a 95% confidence to demonstrate a significant difference in AHI of three months after the NTC-MAD therapy, as previously reported (4). A 10% dropout rate was assumed. It was indicated that 15 pairs of subjects demonstrated the therapeutic effect of NTC-MAD in the present study.

To determine initial ODI (ODI-i) values, all subjects were first informed about the proper usage of SPO (Beurer PO 80, BEURER GmbH, Ulm, Germany) in detail. Subjects were instructed to press the start button and attach the device's probe on the extremity of their index finger before falling asleep. To determine initial SSA values, all subjects were first informed about the proper usage of SnoreLab SSA software (Reviva Softworks Ltd., London, UK). Then, the subjects were instructed to download SSA on their smartphones. All subjects were recommended to place their smartphones next to their bed with the microphone facing towards the subjects, to keep the charger connected, and to sleep alone at the quietest room of the home during SSA recordings. Also, the subjects were instructed to use SSA and SPO in-home environment during sleep for three nights due to minimizing the environmental impact on recordings. The average SSA and SPO values obtained in three nights were calculated and initial mean values of ODI, snoring intensity score (SIS), and snoring percentage (SP) were obtained.

After obtaining ODI-i and SSA values, NTC-MADs were fabricated. Irreversible hydrocolloid impressions (Italglin Chromatic Alginate, BMS, Capponoli, Italy) were made from both dental arches. The impressions were poured with type 3 dental stone (Denstone 3, Ata Yapı Ürünleri San. ve Tic. Ltd., Turkey). Autopolymerizing acrylic resin splints (Self Curing for Ortho Chrystal, BMS, Capponoli, Italy) in 2-2.5 mm thickness were fabricated on the models of upper and lower jaws and were tried intraorally. Interferences on maximal retrusive and protrusive positions were eliminated. Maximal mandibular protrusion value (MMPV) and retrusive positions were marked on splints (Figure 1A, 1B). To determine efficient mandibular protrusion value (EMPV), MMPV was measured for each patient and the 60-75% (4,11) of MMPV was calculated and marked (Figure 1C). An interincisal space of 6 mm was set for each patient (4). The most comfortable protruded mandibular position situated between 60 and 75% of MMPV was determined according to

patient response and registered with wax rims. (Figure 1D) The registered models were mounted on a semi-adjustable articulator (AAA43002 CT, Amann Girrbach Artex, Koblach, Austria). The upper and lower acrylic resin splints were secured to each other in the posterior region with auto polymerizing acrylic resin and NTC-MADs were obtained. Subsequently, the NTC-MADs were trimmed, polished, and placed on dental arches (Figure 1E, 1F). The patients were instructed to wear their NTC-MAD every night. After the initial of NTC-MAD therapy, each patient performed the previously described ODI and SSA procedures at the 1st, 4th, 12th, and 24th weeks of the treatment protocol.

Consequently, totally 17 measurement values for each subject were recorded; PSG-i values, PSG-f values, ODI-i values, ODI 1st week values (ODI-1w), ODI 4th week values (ODI-4w), ODI 12th week values (ODI-12w), ODI 24th week values (ODI-24w), initial SIS (SIS-i) values, SIS 1st week values (SIS-1w), SIS 4th week values (SIS-4w), SIS 12th week values (SIS-12w), SIS 24th week values (SIS-24w), initial SP values (SP-i), SP 1st week values (SP-1w), SP 4th week values (SP-4w), SP 12th week values (SP-12w) and SP 24th week values (SP-24w) were obtained.

Statistical Analysis

All statistical analyses were performed with the SPSS 22.0 software package (SPSS Inc., Chicago, Ill). Continuous variables were expressed as the means with standard deviations. The

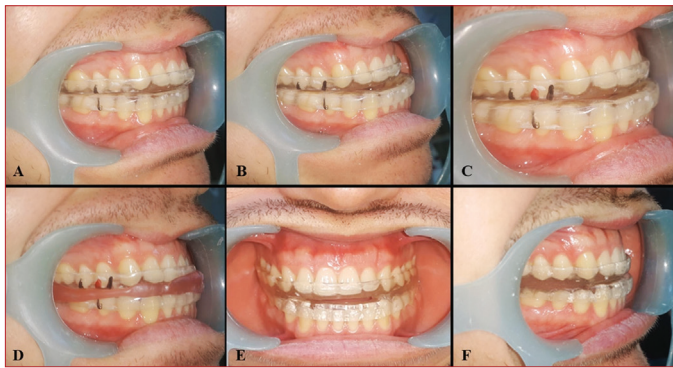


Figure 1. Setting the mandibular protrusion rate at 60-75% of the maximal mandibular protrusion. A) Retrusive position, B) maximal mandibular protrusion value (MMPV), C) efficient mandibular protrusion value (EMPV) (60-75% of MMPV). D) Fixing EMPV with wax rims. E and F) Intraoral views of non-titratable customized mandibular advancement device

Kolmogorov-Smirnov test was used to confirm that the data were within the ranges of normal distribution. The t-test (two-tailed for paired samples) was used to compare the differences between initial and final values. To evaluate the effect of MAD on ODI, SIS, and SP, one-way repeated measures analysis of variance test (ANOVA) was used. The Bonferroni-Holm correction was used to correct the multiple comparisons. The type 1 error probability associated with this test was set as ($\alpha=0.05$).

Results

All patients completed the study protocol. No significant difference was found between the mean BMI and neck circumference values comparing the 1st (BMI=29.62±5.56 kg/m² and neck circumference=38.22±4.12 cm) and 24th weeks (BMI=28.84±5.10 kg/m² and neck circumference=38.22±4.12 cm) of the treatment [$t(17)=1.748$, $p=0.98$ and $t(17)=1.758$, $p=0.97$ respectively].

PSG-i and 24th week (PSG-f) mean PSG values were shown in Table 1. In the comparison of PSG-i and PSG-f values, it was determined that all AHI, ODI, and SI values were significantly decreased. The average decrease of AHI, ODI, and SI values were 5.67±3.66/h ($p<0.001$), 4.25±3.49/h ($p<0.001$) and 51.48±51.25/h ($p=0.005$), respectively. According to PSG results, the success of NTC-MAD treatment was 68.7% for OSA patients.

The mean ODI, SIS, and SP values were depicted in Table 2. Intragroup comparison of ODI, SIS, and SP at 5 different time intervals (ANOVA) showed a significant difference ($p<0.001$). A significant difference was found between ODI-i and ODI-1w, ODI-4w, ODI-12w, and ODI-24w ($p<0.05$). The highest decrease in ODI values was reached at the 12th week of the treatment. No significant difference was found between ODI-12w and ODI-24w ($p=0.181$) (Figure 2A). As with ODI values, a significant difference was also found between SIS-i and SIS-1w, SIS-4w, SIS-12w, and SIS-24w ($p<0.001$) except SIS-12w and SIS-24w ($p=0.113$) (Figure 2B).

Intragroup comparison of SP values showed that there was a significant difference at 5 different time intervals ($p<0.001$). The Bonferroni-Holm correction displaced no significant difference between SP-i and SP-1w ($p=0.56$), SP-4w and SP-12w ($p=1$) and SP-12w and SP-24w ($p=0.510$) (Figure 2C).

Table 1. Initial polysomnography (PSG) and 24th week PSG-final data (mean value±standard deviation)

	PSG-i	PSG-f	t value	p value
AHI (events/h)	10.59±5.23	4.91±2.6	6.574	<0.001*
ODI (events/h)	7.61±4.88	3.35±2.39	5.169	<0.001*
SI (events/h)	173.17±131.93	122,26±31,18	3.48	0.005*

*Indicates significant changes for intragroup comparison (t-test).

AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, SI: Snoring index, PSG-i: Initial polysomnography, PSG-f: Final PSG

Discussion

The objective of the present study was to determine the efficacy of NTC-MAD therapy on snoring intensity, frequency, and oxygen desaturation periods in mild-moderate OSA patients with snoring problems. For the differential diagnosis of patients referring to snoring complaints, AHI was accepted to be the main physiological sleep parameter in the present study. Besides, the AHI values were also used for the evaluation of the NTC-MAD's treatment success in OSA patients (2,3).

MAD treatment success rate determined by AHI varies between 19% (12) and 71% (4). Age, gender, BMI, the severity level of OSA, and MAD type may influence the success of MAD

Table 2. Pairwise comparison of oxygen desaturation index, snoring intensity score and snoring percentage at different time intervals

	Time interval	Mean±SD	f value	p value
ODI	ODI-i	7.82±5.39	25.17	p<0.001*
	ODI-1w	6.62±4.48		
	ODI-4w	4.37±2.99		
	ODI-12w	3.5±2.67		
	ODI-24w	3.14±2.32		
SIS	SIS-i	72.96±31.14	39.45	p<0.001*
	SIS-1w	61.09±26.97		
	SIS-4w	48.85±24.35		
	SIS-12w	40.20±22.33		
	SIS-24w	36.03±22.14		
SP	SP-i	32.61±17.29	21.46	p<0.001*
	SP-1w	29.40±14.60		
	SP-4w	21.29±11.95		
	SP-12w	19.81±10.64		
	SP-24w	17.35±8.97		

*Indicates significant changes for intragroup comparison (ANOVA). SD: Standard deviation, ODI: Oxygen desaturation index, SIS: Snoring intensity score, SP: Snoring percentage

treatment (3,13,14). It is emphasized that EMPV is the most determinative parameter affecting customized MAD treatment success (3). Aarab et al. (4) reported that 50% to 75% of MMPV had higher treatment efficiencies. Marklund et al. (11) reported that using more than 75% of MMPV increased the complication probability.

In the present study, the NTC-MADs were fabricated by using 60-75% of MMPV to provide optimal treatment efficacy and to minimize the side effects. All patients use the appliances appropriately without side effects that restrict the use of appliances. The treatment success of the present study was similar to those in which EMPV was expressed as being the 60-75% of MMPV, either with TC-MADs or NTC-MADs (4,6,15-17). In these studies, the success of the MAD treatment is determined by full night PSG. However, the insufficient number of qualified sleep laboratories and the expensiveness of the PSG procedure obliged the clinicians to use home testing devices for the diagnosis and follow-up of sleep disorders. One of these home testing devices is SPO (18). SPOs are capable of calculating the ODI and monitoring automatically the desaturation fluctuations during sleep. The major concern about ODI is that hypopneas and short apneas do not always cause a 3-4% decrease in oxygen saturation. In such cases, the ODI parameter is far from being determinative (18).

Due to the coherence of AHI and ODI values in morbid obesity, ODI was especially used for the follow-up procedures of OSA in morbidly obese patients with AHI >10 (19). Recently, Ernst et al. (20) reported that the correlation between AHI and ODI was larger in patients with normal weight and proportionally decreased by the increase in BMI. This result highlighted the important role of ODI during the follow-up of OSA patients.

In the present study, a significant decrease in ODI (4.68 events/h) was found using NTC-MADs. Incoherence with our study, Ghazal et al. (21) reported a decrease of 4.50 events/h in ODI with TC-MADs. Similarly, Barnes et al. (22) found a decrease of 4.30 events/h in ODI with TC-MADs. Zhou and Liu

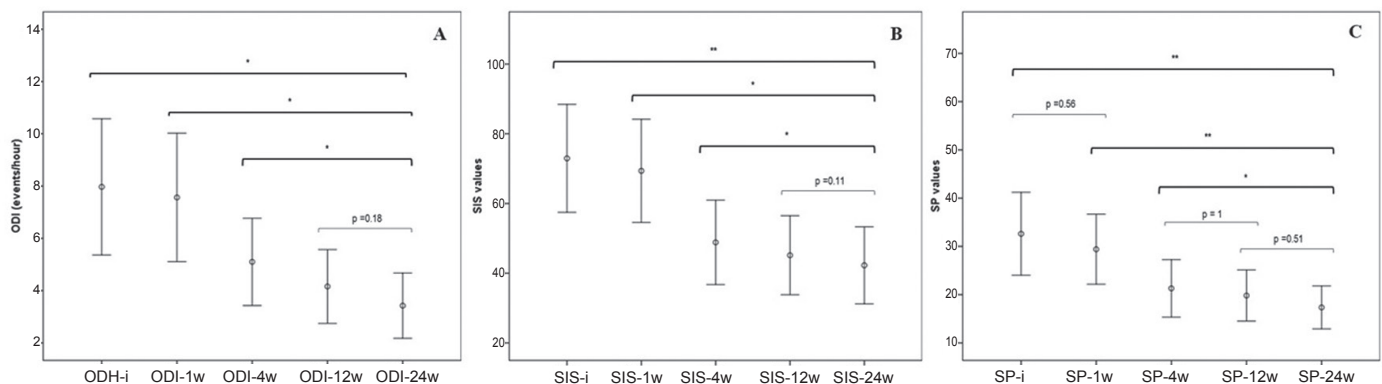


Figure 2. Multiple comparisons of simple pulse oximeter and smartphone sleep application values (Bonferroni-Holm correction) (*p<0.05, **p<0.01, 1. standard deviation). A) Oxygen desaturation index, B) snoring intensity score, C) snoring percentage

ODI: Oxygen desaturation index, SIS: Snoring intensity score, SP: Snoring percentage

(6) reported that compared to TC-MADs, NTC-MADs achieved an equivalent reduction in ODI in adult patients with OSA and reported a decrease of 25.00 events per hour in ODI with the use of an NTC-MADs. The authors physiologically determined individual EMPVs using the PSG test and titration for each patient. That proper method for determining EMPV explains the huge difference in ODI values compared to the present study.

In all of the above-mentioned studies, the mean differences in ODI were only determined at the end of the 12th or 24th weeks. There is not any study that reported the mean ODI difference in periodical time intervals within the treatment procedure. According to the results of the present study, it can be deduced that the maximum reduction in ODI can be achieved in 12 weeks.

MADs are not only indicated for the treatment of OSA patients but also for SS patients. The effects of MADs on snoring were mostly assessed by subjective tests such as questionnaires and visual analog scale (3,5). However, some researchers suggested using sensors and microphones in a soundproofing environment for recording and evaluating snoring sounds objectively (10,23). Snoring sound frequency could be evaluated as an important parameter for differential diagnosis between SS and OSA because the snoring sounds of OSA patients recorded in sleep laboratories have a frequency higher than 800 Hz (10) and SS patients usually have frequencies between 110 and 190 Hz (below 500 Hz) (23).

Remarkable technological advancement of communication provides recording snoring sounds at the patient's home by using smartphones. And also, SSAs monitor the snoring sounds as numeric data. Although there are many SSAs, few studies report about the reliability of SSAs. An excellent positive correlation was reported between SSAs and sleep laboratory sound recordings of 93% to 96% in a soundproof environment (24,25).

According to studies evaluating snoring sounds, the MAD treatment decreased SIS (26,27). Walker-Engström et al. (26) determined that NTC-MADs with 75% of MMPV caused a higher decrease in SIS. Besides, Bloch et al. (27) stated that NTC-MADs provided a greater reduction in subjective snoring intensity than TC-MADs. In the present study, SIS values started to decrease just from the 1st week of NTC-MAD treatment. O'Sullivan et al. (28) reported that MADs reduced SIS even at the first night. Smith and Battagel (29) reported that the use of MAD for a month caused a 64% reduction in SIS. However, the SIS reduction rate (43%) in this study was not as high as theirs. That difference may be explained with the determination difference of EMPV existing between two studies. While Smith and Battagel (29) used one-night titration to determine EMPV, a standard EMPV (60-75% of MMPV) was used in the present study. Considering the obtained SSA data, it was determined that the maximum reduction in SIS with the use of NTC-MADs could be obtained at the 12th week.

It was determined in the present study that SP significantly decreased (39%) at the 4th week and that level remained constant till the end of the study. Umemoto et al. (7) and Lee et al. (30) reported a 40% and 34% decrease in SP values, respectively, with the use of NTC-MADs. However, Umemoto et al. (7) found a decrease of 9% in SP values with TC-MADs while that of NTC-MADs was 40%. The authors concluded that due to their more stable and compact structure that keeps the mandible at a constant protrusive position, NTC-MADs were much more efficient in SP than TC-MADs.

Numerous sleep medicine authors recommended the use of TC-MADs due to some advantages like providing the titration of MADs to optimize its efficiency, keeping the mandible more flexible, and causing fewer side effects (2,3). However, NTC-MADs were used in the present study as in some previous studies (3,5,26,27) reporting that the treatment efficiencies of NTC-MADs and TC-MADs were similar. Further, some studies declared that NTC-MADs were more efficient in snoring due to structural characteristics (6,7). Besides, NTC-MADs are much more economic devices compared to TC-MADs, thus, low-costing NTC-MADs were used for SS and OSA patients with snoring complaints. The other limitations are that no information exists about how to calibrate SnoreLab to calculate SIS and SP and that SSAs may be affected by ambient sounds (25). A wide range of smartphones with various technological properties may lead to differences in the determination of MAD treatment success. Also, the age and susceptibility of the patients to the technology may affect the results of the sleep studies.

SSAs are still very new and there is not enough reliable information about them. However, technological developments can be considered as a messenger soon that SSAs, which have advanced algorithms that are less affected by smartphone hardware and ambient sounds, will take their place in the markets.

Conclusion

Within the limitations of this *in vivo* study, the following conclusions were drawn:

1. The use of NTC-MADs for 24 weeks was found to be an efficient method for decreasing AHI, ODI, SI, SIS, and SP.
2. Significant reduction in ODI and SIS was observed at the end of the 1st week and continued to decrease regularly until the 12th week.
3. A significant decrease in SP was determined at the 4th week.

It was concluded that NTC-MADs significantly decreased snoring intensity and frequency and they are effective devices in the treatment of SS and OSA.

Ethics

Ethics Committee Approval: The trial was approved by Clinical Trials Ethics Committee of Gülhane Military Medical Academy in Ankara, Turkey (protocol number: 2015-KAEK-84, date: 24th December 2015).

Informed Consent: All patients gave their written informed consent to participate in the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.E., Concept: B.E., B.P., C.S., Design: B.E., B.P., C.S., Data Collection or Processing: B.E., B.P., Analysis or Interpretation: B.E., Literature Search: B.E., Writing: B.E., B.P., C.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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