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Treatment Outcomes of Mandibular Advancement Devices between Rapid-Eye-Movement (REM)-Related and Not-REM-Related OSA Patients

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Purpose: Mandibular advancement devices (MAD) are used effectively and widely for the treatment of obstructive sleep apnea (OSA) and rapid-eye-movement (REM) dependency of the patients can affect the treatment outcome of OSA. The aim of this study was to compare treatment outcomes of MAD between REM-related and not-REM-related OSA patients.

Methods: Fifty-six consecutive patients with OSA who received MAD therapy were evaluated using full night polysomnography before and after insertion of the MADs. The patients were divided into REM-related (REM apnea-hypopnea index [AHI] at least two times higher than their non-REM AHI) and not-REM-related (REM AHI less than two times higher than their non-REM AHI) OSA groups.

Results: MAD is used for the treatment of OSA effectively. In respect of AHI, MAD therapy were effective both in REM-related OSA and not-REM-related OSA, but MAD therapy was more effective in not-REM-related OSA than REM-related OSA in overall sleep and non-REM sleep. SpO_2 saturations were improved after MAD therapy, but were not different between two groups. Epworth sleepiness scale scores were not improved after MAD therapy. Percentage of REM sleep was increased after MAD therapy but was not different between two groups.

Conclusions: MAD therapy was more effective in not-REM-related OSA than REM-related OSA and REM dependency can be a predictive factor of treatment outcome of oral appliance for OSA patients.

Key Words: Oral appliance; Polysomnography; Sleep apnea; Sleep, REM; Treatment outcome

INTRODUCTION

Obstructive sleep apnea (OSA) is a common sleep disorder affecting between 2% and 4% of the general population, characterized by recurrent episodes of complete or partial upper airway collapse, accompanied by intermittent hypoxemia and recurrent arousals from sleep.[1)]

Soft tissue constituting the inner wall of the soft palate or pharynx do not tolerate negative pressure during inspiration and collapse and the periodic cessation of breathing occurs repeatedly.[2)] This disorder cause daytime somnolence, reduction in cognitive performance, and cardiovascular diseases including hypertension, cardiac arrhythmias, nocturnal angina, and myocardial ischemia. OSA is related to age, obesity, and anatomical factors such as mandibular retrognathism, micrognathia, macroglossia, and tonsilomegaly.[3)]

Whereas upper airway collapse can occur during rapid-eye-movement (REM) and non-REM (NREM), we can sort OSA into REM-related OSA and not-REM-related OSA by the feature of REM and NREM sleep apnea. In REM sleep reduced pharyngeal muscle activity increases the tendency of upper airway collapse.[4-6)] REM-related OSA is a sleep disorder

in which apnea and hypopneas occurs mainly to REM sleep period. REM-related OSA was defined as REM apnea-hypopnea index (AHI)/NREM AHI ≥2 indicating a predominance of disordered breathing during REM sleep, whereas not-REM-related OSA was defined by REM AHI/NREM AHI <2.[7] It is well known that OSA is common in the elderly, in males, in individuals with high body mass index (BMI), and in individuals who sleep in supine position.[6,8] However, REM-related OSA is reported to occur more in younger patients, women, children, and patients with mild to moderate OSA.[9,10]

Treatment of OSA may include lifestyle modification, i.e., weight loss, sleep position training, upper airway surgery, continuous positive airway pressure (CPAP) and oral appliances. CPAP is the most widely suggested method because it provides the most reliable therapeutic modality, especially in severe OSA. But, there is poor compliance of patients who consider this therapy difficult to tolerate and unacceptable. For these reasons, several surgical and non-surgical procedures have been proposed as an alternative.

Among non-surgical therapies, good results have been obtained with the oral appliance. Oral appliances reduce apneas and improve sleep quality in mild to moderate OSA patients. Among oral appliance, mandibular advancement devices (MAD) are used effectively and widely. MAD is associated with extenuated upper airway collapsibility during sleep.[11-13]

The aims of this study were to compare MAD treatment outcomes between REM-related OSA and not-REM-related OSA patients.

MATERIALS AND METHODS

1. Subjects

Fifty-six consecutive patients who visited the Snoring and Sleep Apnea Clinic, Department of Oral Medicine in Seoul National University Dental Hospital (Seoul, Korea) complaint of snoring, sleep apnea, or daytime sleepiness and received MAD therapy were evaluated. The patients diagnosed as OSA based on an AHI ≥5 were included and who had the history of major surgery on the orofacial region were excluded in this study.

The patients were divided into REM-related and not-REM-related OSA groups. These criteria state that REM-related OSA patients have a REM AHI at least two times higher than their NREM AHI, and not-REM-related patients will have a REM AHI less than two times higher than their NREM AHI.

The study was approved by the Institutional Review Board of Seoul National University Hospital and informed consent was obtained from each patient.

2. Polysomnography Evaluation

Multi-channel recordings of electroencephalogram (EEG), submental and leg electromyogram (EMG), electrocardiogram (ECG), nasal thermistor, nasal pressure transducer, thoracic and abdominal piezoelectric belts, and oxygen saturation were conducted using Alice 4 (Respironics, Pittsburgh, PA, USA) polysomnography. Body position was also confirmed through direct observation of the patient by the technician using a low light camera and simultaneous digital recording with a posture tag at the thoracic piezoelectric belt.

3. Mandibular Advancement Device

All appliances used advanced the mandible and were custom made. The type of MAD used in this study was SNU appliance. The appliances were made by the respective laboratories and the degree of mandibular advancement was set to 50% of the patient's maximum protrusion. After a titration period during which incremental anterior adjustments of the mandible were made until the maximum comfortable limit was reached, an additional sleep study was performed with the MAD to determine treatment efficacy.

4. Statistical Analyses

Means and standard deviations of each variable were calculated. For baseline data, independent t-test and chi-square test were used to compare age, gender, BMI, Epworth sleepiness scale (ESS), and each polysomnography parameters between two groups.

Repeated measures ANOVA involving group (REM-related and not-REM-related OSA groups) as a between subjects factor and time (baseline, after MAD therapy) as a within subjects factor were used. Age was considered as a covariate.

RESULTS

Table 1 shows the demographic features of the subjects. The mean age of REM-related OSA (n=26) and not-REM-related OSA (n=30) were 41.8±10.5 and 47.3±10.9 years, respectively. There were more men than women in both groups. BMI of each group was 24.6±3.6 and 25.7±3.3. ESS scores were 7.4±3.7 in of REM-related OSA and 8.3±4.4 in not-REM-related OSA patient groups. There were no significant differences between in age, gender, BMI, and ESS scores between REM-related OSA and not-REM-related OSA patient groups.

Baseline levels of sleep study data of REM-related OSA and not-REM-related OSA were shown in Table 2.

Overall AHI (p<0.001) and NREM AHI (p<0.001) were significantly higher in not-REM-related OSA than REM-related OSA patients. There were no significant differences in REM AHI between two groups.

Percentage time with SpO_2 <90 (p=0.003) and lowest O_2 saturation (p=0.009) were significant different between REM-related OSA and not-REM-related OSA patients. There were no significant differences in mean O_2 saturation between two groups.

Table 3 shows the changes in apnea-hypopnea event variables before and after MAD therapy in each group. The main effect for time was significant (p<0.01) in each

Table 1. Demographic data of the subjects

Variable	REM-related OSA (n=26)	Not-REM-related OSA (n=30)	p-value
Age (y)	41.8±10.5	47.3±10.9	0.060[a]
Gender (male)	84.6	96.7	0.115[b]
BMI	24.6±3.6	25.7±3.3	0.266[a]
ESS	7.4±3.7	8.3±4.4	0.367[a]

REM, rapid-eye-movement; OSA, obstructive sleep apnea; BMI, body mass index; ESS, Epworth sleepiness scale.
Values are presented as mean±standard deviation or %.
[a]p-values were obtained from independent t-test.
[b]p-values were obtained from chi-square test.

Table 2. Sleep study data of both groups at baseline

Variable	REM-related OSA	Not-REM-related OSA	p-value
Overall AHI	13.1±10.5	39.4±29.5	<0.001
REM AHI	32.9±20.5	33.8±29.6	0.895
NREM AHI	9.3±8.6	39.9±29.7	<0.001
Percentage SpO_2 <90	1.8±2.4	8.4±11.2	0.003
Lowest O_2 saturation	84.5±6.4	78.2±10.1	0.009
Mean O_2 saturation	95.6±1.9	94.7±2.2	0.112

REM, rapid-eye-movement; OSA, obstructive sleep apnea; AHI, apnea-hypopnea index; NREM, non-REM.
Values are presented as mean±standard deviation.
p-values were obtained from independent t-test.

Table 3. Apnea-hypopnea event before and after MAD therapy in each group

Variable	Group	Treatment		p-value
		Before	After	
Overall AHI	REM-related OSA	13.1±10.5	8.3±9.1	Time<0.001
	Not-REM-related OSA	39.4±29.5	24.0±29.8	Group=0.001
				Time×Group=0.006
REM AHI	REM-related OSA	32.9±20.5	21.9±21.5	Time=0.002
	Not-REM-related OSA	33.8±29.6	27.8±29.2	Group=0.005
				Time×Group=0.342
NREM AHI	REM-related OSA	9.3±8.6	4.9±7.6	Time<0.001
	Not-REM-related OSA	39.9±29.7	23.1±30.3	Group<0.001
				Time×Group=0.001

MAD, mandibular advancement devices; AHI, apnea-hypopnea index; REM, rapid-eye-movement; OSA, obstructive sleep apnea; NREM, non-REM.
Values are presented as mean±standard deviation.
p-values were obtained from multivariate repeated-measures ANOVA.

apnea-hypopnea event variables, i.e., overall AHI, REM AHI, and NREM AHI are significantly decreased after MAD therapy (Fig. 1, 2).

The interaction between time (before and after MAD therapy) and group (REM-related and not-REM-related OSA patients) were significant in overall AHI (p=0.006) and NREM AHI (p=0.001), i.e., overall AHI and NREM AHI decreased significantly in not-REM-related OSA patients than REM-related OSA patients. However, the interaction between time and group was not significant in REM AHI (p=0.342), i.e., decrease of REM AHI after MAD therapy did not significantly differ between not-REM-related and REM-related OSA patients.

Table 4 shows the changes in oxygen saturation variables before and after MAD therapy in each group. The main effect for time was significant in each oxygen saturation variables. Percentage time with SpO_2 <90 (p=0.004), lowest O_2 saturation (p<0.001), and mean O_2 saturation (p=0.002) were significantly improved after MAD therapy. However improvement in these oxygen saturation variables did not significantly differ between not-REM-related and REM-related OSA patients.

Table 5 shows the changes in ESS score and duration of REM sleep before and after MAD therapy in each group. ESS score was not changed significantly after MAD therapy. The main effect for time was significant in duration of REM sleep. Duration of REM sleep was increased significantly after MAD therapy (p=0.006). However, decreases in duration of REM sleep did not significantly differ between not-REM-related and REM-related OSA patients.

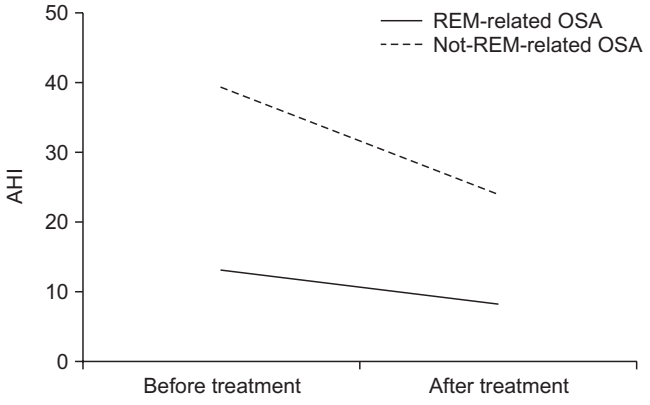

Fig. 1. Overall apnea-hypopnea index (AHI) changes after mandibular advancement devices therapy in each group. REM, rapid-eye-movement; OSA, obstructive sleep apnea.

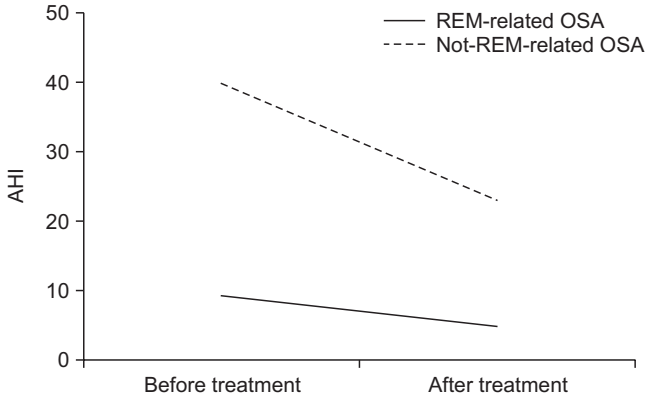

Fig. 2. NREM AHI changes after mandibular advancement devices therapy in each group. REM, rapid-eye-movement; OSA, obstructive sleep apnea; NREM, non-REM; AHI, apnea-hypopnea index.

Table 4. Oxygen saturation before and after MAD therapy in each group

Variable	Group	Before	After	p-value
Percentage SpO_2 <90	REM-related OSA	1.8±2.4	0.8±1.6	Time=0.004
	Not-REM-related OSA	8.4±11.2	4.3±6.4	Group=0.003
				Time×Group=0.073
Lowest O_2 saturation	REM-related OSA	84.8±6.3	87.8±6.9	Time<0.001
	Not-REM-related OSA	78.2±10.1	83.2±9.0	Group=0.007
				Time×Group=0.342
Mean O_2 saturation	REM-related OSA	95.5±1.9	95.9±1.5	Time=0.002
	Not-REM-related OSA	94.7±2.2	95.9±1.8	Group=0.345
				Time×Group=0.105

MAD, mandibular advancement devices; REM, rapid-eye-movement; OSA, obstructive sleep apnea.
Values are presented as mean±standard deviation.
p-values were obtained from multivariate repeated-measures ANOVA.

Table 5. ESS and REM sleep before and after MAD therapy in each group

Variable	Group	Before	After	p-value
ESS	REM-related OSA	7.6±3.9	7.2±3.8	Time=0.068
	Not-REM-related OSA	8.1±4.2	7.5±3.9	Group=0.704
				Time×Group=0.722
REM (%)	REM-related OSA	17.3±6.8	19.7±6.3	Time=0.006
	Not-REM-related OSA	15.2±6.3	18.6±5.8	Group=0.229
				Time×Group=0.626

ESS, Epworth sleepiness scale; REM, rapid-eye-movement; MAD, mandibular advancement devices; OSA, obstructive sleep apnea.
Values are presented as mean±standard deviation.
p-values were obtained from multivariate repeated-measures ANOVA.

DISCUSSION

REM-related OSA is OSA when AHI values are twice or more in REM sleep than in NREM sleep. When the difference is less than double, it is called not-REM-related OSA. In our present study, the overall AHI (all sleep stages combined) was significantly higher in the not-REM-related OSA group than in the REM-related OSA group. It means not-REM-related OSA is a more severe form of sleep apnea than REM-related OSA.

During sleep, the most pronounced decrease in muscle tone mainly occurs in REM sleep. Decreased muscle tonicity cause atony and the loss of tone in the dilator muscles lead to the obstructive breathing disorders. Such events could be associated with sleeping in supine position or with REM sleep. REM-related OSA was more common in patients with mild to moderate OSA than severe OSA. In our study AHI values were lower in the patients with REM-related OSA than in those with not-REM-related OSA. In another study, similar to the present study, REM-related OSA was found to be more common in patients with moderate OSA than in those with severe OSA.[14,15] REM AHI values are not significantly different between REM-related OSA and not-REM-related OSA, but NREM AHI values were higher significantly in not-REM-related OSA than in REM-related OSA. It means that not-REM-related OSA is more severe form of OSA and not-REM-related OSA has another cause of sleep apnea in addition to decreased muscle tonicity. Several studies reported that not-REM-related OSA is more common among patients with high AHI (≥30/h).[16-18] The effect of high NREM AHI values had on the overall AHI values were high, because NREM sleep consist of majority of sleep time.

Pevernagie et al.[19] reported that AHI values were higher in the supine position than in the lateral position only during NREM sleep. Sleep position should be considered of one of main factors that have a large impact on OSA features. Sleeping with the lateral posture and avoiding the supine position could represent an effective behavioral maneuver to decrease the number of apneas and hypopneas, improve sleep quality, and reduce daytime sleepiness in many positional OSA patients.

In our studies MAD therapy reduce AHI values effectively in both groups. Overall AHI and NREM AHI were reduced more effectively in not-REM-related OSA than REM-related OSA, but reduced REM AHI values were not different significantly between two groups. This means the effectiveness of MAD therapy during NREM sleep were higher in not-REM-related OSA than in REM-related OSA. This maybe the baseline NREM AHI is higher in not-REM-related OSA than REM-related OSA. The effectiveness of MAD therapy was similar during REM sleep in both groups. MAD makes its effect by expanding the upper airway. In our study, MAD therapy was very effective consequently in respect of AHI values. During REM sleep MAD therapy was effective and was not different in both groups. During NREM sleep, MAD therapy was effective but the effectiveness was different between two groups. As mentioned, not-REM-related OSA is more severe form of OSA than REM-related OSA. During NREM sleep, not-REM-related OSA shows high AHI values than REM-related OSA. NREM sleep in REM-related OSA is maybe thought as normal sleep or mild sleep disorders, so MAD therapy could be shown as not effective in comparison with NREM sleep in not-REM-related OSA.

OSA patients experience fluctuations in oxygen levels during sleep. Various factors have been reported to affect the severity of oxygen desaturation, such factors including sleep posture, sleep stage, and age, as well as gender and obesity.[20-23] In our study, percentage time with SpO_2 <90 was higher in not-REM-related OSA than REM-related OSA. Lowest O_2 saturation was lower in not-REM-related OSA than REM-related OSA. Mean O_2 saturation was not different between two groups. Percentage time with SpO_2 <90, lowest O_2 saturation, and mean O_2 saturation were improved after MAD therapy both two groups, but not different significantly between two groups.

OSA is a common chronic condition in adults. Its prevalence and severity are higher in men than in women.[20,24] However, some studies have reported that REM-related OSA is more common among women.[9,10] But in our studies no gender difference were found between two groups.

In conclusion, MAD is used for the treatment of OSA effectively. REM-related OSA and not-REM-related OSA show different features especially in NREM sleep. In respect of overall AHI, REM AHI and NREM AHI, MAD therapy were effective both in REM-related OSA and not-REM-related OSA, but MAD therapy was more effective in not-REM-related OSA than REM-related OSA in overall sleep and NREM sleep. REM dependency can be a predictive factor of treatment outcome of oral appliance for OSA patients.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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