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Effect of MAD (Mandibular Advancement Device) on Obstructive Sleep Apnea and Quality of Sleep

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Abstract: This study is intended to verify the efficacy of oral airway dilatation using MAD for the treatment of sleep apnea and quality of sleep compare to surgical treatment. The study performed an obstructive sleep apnea evaluation (polysomnography, endoscopy, degree of tonsillar hypertrophy, sleep apnea-related questionnaires and radiation inspection) with patients visiting sleep centers or otorhinolaryngology of three medical institutions due to sleep apnea. A total of 62 hospitalized patients with a chief complaint of snoring or sleep apnea were recruited. The 3 participants could not complete the study and dropped out; the 59 participants completed the study as planned. In the primary analysis of efficacy evaluation, the difference between the findings at baseline and visit 5 and the analysis for each medical institution were analyzed for AHI, PSQI, ESS and SaO_2. The mean AHI, indicating level of sleep apnea, at week 5 after treatment decreased. For PSQI for measuring the sleep quality, the measured value at visit 5 after treatment was increase. For ESS for measuring daytime sleepiness, the value also decreased. SaO_2 during sleep also increased and all of these results were statistically significant. In the secondary analysis of comparison of success rate there was no statistical difference between the success rate of airway dilation using MAD and the success rate of UPPP. The difference in the success rates among the medical institutions was also not statistically significant. These findings indicate that this product has the comparative advantage to the surgery in terms of less complications and the low cost.

Key words: MAD, obstructive sleep apnea, quality of sleep, medical institutions, complications

INTRODUCTION

Obstructive Sleep Apnea (OSA) is a sleep disorder and generally occurs in 2-7% of adults, especially 2% of middle-aged women and 4% of men with the risk of incidence in men being nearly <2 times as that in women (Sharples *et al*., 2016; Bhamrah *et al*., 2015; Ferguson *et al*., 1996). It is known that the causes of this disease are anatomical and neuromuscular factors causing the imbalance between the forces required opening and closing the upper airway (Gakwaya *et al*., 2014; Gerbino *et al*., 2014) which results in respiratory depression through partial or complete obstruction of the upper airway during sleep (Islam *et al*., 2015; Wang *et al*., 2015; Gomis *et al*., 2010). One of the symptoms, frequent awakening during sleep, can occur owing to the change in the chemical environment such as decreased blood oxygen or excessive carbonic acid which causes the respiratory muscle to overcome the reflex or obstruction of upper airway (Charbonneau *et al*., 1994). This is also recognized as a common cause of frequent sleepiness during day time which can damage cognitive function and cause a traffic accidents (Bhamrah *et al*., 2015; Ciavarella *et al*., 2009). Moreover, it is known as one of the causes of cardiovascular diseases such as hypertension, stroke, acute myocardial infarctio another metabolic disorders (Islam *et al*., 2015; Torr *et al*., 2015; Zamarron *et al*., 1999; Cadilhac *et al*., 2005) and can be a risk factor for increased mortality in severe cases (Borel *et al*., 2012). The currently known treatment for OSA is surgical and non-surgical treatment (Gerbino *et al*., 2014, Gomis *et al*., 2010; Epstein *et al*., 2009; Gay *et al*., 2006; Levendowski *et al*., 2007; Faria *et al*., 2013). The basic principle of surgical treatment is to prevent snoring and airway obstruction by removing a part of the area causing snoring and apnea due to anarrowed airway, based on the diagnostic findings of the nasal cavity and laryngopharynx (Epstein *et al*., 2009; Riley *et al*., 1993). However, this treatment has limitations because of drawbacks including hemorrhage and pain caused by surgery, discomfort due to post-surgical scars, complications, recurrence of symptoms and irreversibility and adverse effects of post-surgical medications (Riley *et al*., 1993; Esclamado *et al*., 1989;

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Katsantonis *et al*., 1987). Non-surgical treatment includes Continuous Positive Airway Pressure (CPAP) which is a "gold standard" (Ciavarella *et al*., 2009) and use of oral appliances (Hsieh *et al*., 2014; Guimaraes *et al*., 2015). Oral appliances include Mandibular Advancement Devices (MAD) that position mandible forward, Tongue Retaining Devices (TRD) that pull only the tongue forward and soft palatal lifters (Hoffstein, 2007). Among these, soft palatal lifter and TRD are rarely used owing to inconvenience and currently MAD is the most commonly used appliance (Hoffstein, 2007). The principle of its action is to indirectly pull the tongue and its base by pla cing the mandible forward, leading to the expansion of the space behind the tongue and the stabilization of pharyngeal wall (Epstein *et al*., 2009; Hoffstein, 2007). Its merits include convenient usage, no noise, reversible placement and noninvasiveness, owing to which patient compliance is high (Ferguson *et al*., 1996; Ferguson *et al*., 1997; Clark *et al*., 1996; Pitsis *et al*., 2002); its effect is better especially for patients with moderate to severe sleep apnea (Mehta *et al*., 2001). Oral appliances have been used for the treatment of sleep-related breathing disorders in the United States since the early 1990's and currently there are about 30 kinds of appliances approved by the FDA (http://www.fda.gov/,https://www.sleepassociation.org/).

However, intraoral devices made overseas were being imported for use as there were no intraoral devices being manufactured in Korea until a few years ago. A reliance on imported goods results in financial issues such as high costs while also complicating the process in clinical use, giving rise to procedural problems that can lead to longer periodsrequired for treatment procedures. Therefore, this study will verify the effects of the device through clinical trials using MAD which was originally developed in Korea and establish an airway expanding treatment using MAD by standardizing the treatment process.

MATERIALS AND METHODS

Study subjects: In this study, a total of 62 hospitalized patients with a chief complaint of snoring or sleep apnea were screened (31 from Seoul National University Bundang Hospital (SNUBH), 21 from Seoul National University Hospital (SNUH) and 10 from Chonbuk National University Hospital (CNUH). Mean age of them (53 males and 9 females) was 52.71±9.74. The 62 participants started the study by wearing MAD but 3 could not complete the study and dropped out; 59 participants completed the study as planned. Additional 1 participant, however did not complete two questionnaires (PSQI and ESS).

Manufcture of MAD: While the mandibular advancement measuring device (George Gauge) is placed inside the mouth, the device is induced to the normal mandible position (the general occlusion) and the moved level is recorded. Further, after inducing the mandible to the maximum position in front, the moved value is recorded. Then, after removing the device from the oral cavity, the baseline value and the maximum moved value are calculated. The movement of the mandible to the front needs to be within 60% of the maximum moved value and the range of mandibular advancement is determined within 60% based on a physician's judgment or the degree of a patient's inconvenience considering the difference in temporomandibular joints between patients. After determining the amount of mandibular advancement through the aforementioned procedure, resin casts of the maxilla and the mandible are taken to produce a mandibular advancement device suitable for the oral structure of each individual (Fig. 1). In this study, "Bio-Guard" designed and manufactured by Sleep and health, Co. (Jeonju, Korea) was used in order to prevent snoring and OSA caused by airway obstruction during sleep from various causes (Fig. 2).

Experimental procedures: At visit 1, the evaluation of OSA (polysomnography and surveys related to the symptoms of sleep apnea) was conducted in the patients hospitalized for sleep apnea at 3 university hospitals. The MAD customized at visit 1 was first worn at visit 2 and the moved value of mandibular advancement was adjusted as needed after checking if it was worn without temporomandibular joint inconvenience. Participants visited the hospitals every 1-2 weeks (visit 3-4) 3 weeks after the first wearing for additional fine adjustment until they adapted to the MAD and felt comfortable. However, if there was no need for additional adjustment without discomfort then phone consultation was conducted instead of hospital visit. If the subjects properly adjusted to the device during the adjustment period by visit 5 (week 5), polysomnography was scheduled at week 5 and they visited the hospital to receive the evaluation about OSA by using polysomnography as during screening.

Accessment related to sleep apnea

AHI (Apnea/Hypopnea Index): AHI is the number of incidences of apnea and hypopnea during 1 h of sleep; apnea in AHI is defined as complete cease of breathing for <10 sec and hypopnea is defined as <4% decrease of oxygen saturation in addition to <30% decrease of respiratory signal from the baseline.

Fig. 1: Measuring mandibular positions using George Gauge. George Gauge is consisted of 2 bite forks and a gauge (left). Middle panel shows George Gauge inserted in the mouth to measure mandibular position. The scale of the gauge marked as a rectangular was recorded after protruding mandible maximally (right)

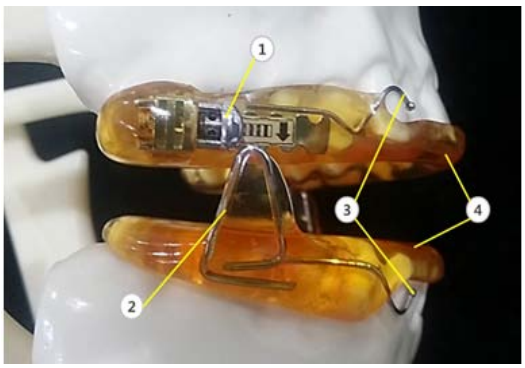

Fig. 2: Structural elements: a) Adjustment screw: the screw adjusts the advancing distance of the mandible; b) Projecting inclined-plate: when the mouth is closed, the plate touches the adjustment screw of the maxilla and pushes forward; c) Hook: it keeps the main body at the proper position; if necessary, elastic strings can be hung on the hook to prevent the mouth from opening; d) Main body: it is a pair of acrylic resin structures shaped like a bruxism splint. Each of a pair is placed on the upper and lower teeth, respectively. Element 1-3 are installed on the main body

SaO_2 (oxygen saturation): Oxygen saturation is the ratio (%) of dissolved oxygen in the blood and it declines as repetitive upper airway obstruction occurs and thus the airflow is not smooth in OSA patients. Therefore, the degree of alleviation of upper airway stricture after MAD installation was evaluated by comparing the SaO_2 before and after the treatment in this study.

PSQI (Pittsburgh Sleep Quality Index) questionnaire: PSQI is a questionnaire consisting of 7 items (subjective sleep quality, sleep latency, sleep time, sleep efficiency, degree of sleep disturbance, taking sleeping pills and presence of daytime disturbances) to evaluate sleep quality and the total score of PSQI is from 0-21 with the classification of poor sleep quality if the score is <5.

ESS (Epworth Sleepiness Scale) questionnaire: ESS consists of items regarding 8 situations in which one feels sleepy in daily life and the classification of daytime sleepiness was made if the total score was <10.

Evaluation standard of treatment success rate: Definition of treatment success was >10 in AHI at visit 5 and <50% decrease of AHI from the baseline. Treatment success rate wasthe ratio of the number of successfully treated patients to the number of participants who received the treatment with the experimental device.

RESULTS

The difference between the findings at baseline and visit 5: The difference between the findings at baseline and visit 5 and the analysis for each facility were analyzed for AHI, PSQI, ESS and SaO_2. Total 58 subjects involved in PSQI and ESS test (Table 1).

The baseline AHI was 34.78 on average, indicating very severe level of sleep apnea but the mean AHI at week 5 after treatment decreased to 14.74, showing about 20.04 point decline and this was statistically significant ($t = 10.63$, $df = 58$, $p<0.01$). For PSQI for measuring the sleep quality, the baseline was 5.98 but the measured value at visit 5 after treatment was 4.14, showing about 1.84 point increase ($t = 8.50$, $df = 57$, $p<0.01$). For ESS for measuring daytime sleepiness, the value also decreased by about 2.86 points ($t = 6.15$, $df = 57$, $p<0.01$). SaO_2 during sleep also increased by 5.16% ($t = -3.29$, $df = 58$, $p<0.01$). The difference of each evaluation variable between medical facilities was not statistically significant as shown by one-way ANOVA.

Comparison of success rates: This study compared the success rates of MAD and the current surgical treatment for OSA. To accomplish this we referred to the results of a meta-analysis on 54 studys that studied the effects of the surgical treatment (Sher *et al*., 2006). They found that 77 of 171 participants had an apnea index of >10 and their post-treatment AHIs decreased by <50% from baseline, reporting 45% success rate of surgery.The success rates of the surgical procedure and the success rates that used MAD in this study are compared using a χ^2-test (Table 2). The estimated success rate of MAD was 54.2% showing that the difference from that of surgical treatment was about 9.2% and there was no statistical difference between the success rate of oral dilation using MAD and the success rate of UPPP as shown by the χ^2-test

Table 1: OSA-related indices improved by mad treatment

Parameters	n	Mean±SD	t-values
AHI			
Baseline	59	34.78±17.00	10.63**
Visit 5	59	14.74±14.47	
PSQI			
Baseline	58	5.98±2.240	8.50**
Visit 5	58	4.14±1.810	
ESS			
Baseline	58	8.36±4.030	6.15**
Visit 5	58	5.50±3.080	
SaO_2			
Baseline	59	78.01±12.07	3.29**
Visit 5	59	83.17±7.400	

**p<0.01

Table 2: Comparison of mad and operation methods

Parameters	MAD	Surgery	χ^2
Success	32.0	77	1.49
Fail			(p = 0.222)
	27.0	94	
Success rate (%)	54.2	45	

(χ^2 = 1.49, df = 1, p>0.05). The difference in the success rates among the medical facilities was also not statistically significant (χ^2 = 4.70, df = 2, p>0.05).

DISCUSSION

Currently, the known treatments for snoring and OSA include surgical treatment, CPAP and OA (Gerbino *et al*., 2014; Gomis *et al*., 2010; Gay *et al*., 2006; Levendowski *et al*., 2007; Faria *et al*., 2013). Each treatment has merits and drawbacks: surgical treatment has a definite therapeutic effect by removing the causal area in cases in which symptoms are caused by anatomical reasons (Engstrom *et al*., 2000; Nelson, 2001) but it is irreversible and has the risk of complications related to anesthesia (Ciavarella *et al*., 2009; Esclamado *et al*., 1989; Katsantonis *et al*., 1987). CPAP is effective but low patient compliance due to severe discomfort when patients wear it (Gomis *et al*., 2010; Mehta *et al*., 2001) and OA has several merits to displace other treatments (Ferguson *et al*., 1996; Ferguson *et al*., 1997; Clark *et al*., 1996; Pitsis *et al*., 2002; Mehta *et al*., 2001) but has been used as an industrial product or a dental technology product without approval for its efficacy and safety in Korea.

This study was intended to verify the clinical efficacy of MAD manufactured in Korea and to evaluate its feasibility as a standard treatment to replace other treatment methods including surgery for OSA. The result showed that MAD treatment increased AHI, PSQI, ESS and SaO_2. This result is consistent with the study that compared the effects of MAD, a tongue retaining device and a soft palatal lifter and reported that AHI was decreased only in the MAD treatment, thereby showing an effect on sleep apnea (Barthlen *et al*., 2000). Moreover, the results of the studies examining the effects of MAD treatment using AHI and magnetic resonance imaging (Chan *et al*., 2010), AHI and oxygen saturation (Ciavarella *et al*., 2009) and AHI and ESS (Deane *et al*., 2009) were also consistent with this study. The success rate of MAD treatment in this study was not different from that of the surgical treatment provided in a meta-analysis (Sher *et al*., 1996). Furthermore, the success rates (55 and 53.8%) reported by studies using MAD (Ferguson *et al*., 1997; Sanner *et al*., 2002) that were similar to the one used in this study were almost the same as the success rate observed in this study (54.2%). This reveals that MAD, a non-surgical procedure, may show a similar success rate to a surgical procedure. It indicates that unless the case requires a surgical procedure due to anatomically unusual issues, MAD which is relatively inexpensive and rarely has side effects can be effectively used in treating obstructive sleep apnea. The success rate of MAD developed in Korea was almost equivalent to that of overseas products which implies that this product can achieve the effect of import substitution. The clinical logic of using MAD is that obstructive sleep apnea is caused by respiratory obstruction and thus it can be improved by expanding the narrow airway. The treatment goal of this study was to advance the mandible within 60% of the maximum amount of mandibular advancement. However, the amount of advancement was adequately adjusted in the process of treatment since each patient had different anatomical features of the oral cavity and different responses in terms of their discomfort in using MAD. Therefore, a correlation analysis was conducted on the two factors, since it is likely that there is certain relevance between the actual amount of advancement and the therapeutic effect. The result of the analysis showed that the correlation between the two factors was significant (r = 0.374, df = 39, p = 0.016) but not high. This result is consistent with the view that it is desirable to keep the amount of advancement at 6.0 mm or lower (Kim *et al*., 2011), since there was no direct correlation between the amount of mandibular advancement and the therapeutic effects. It seems that anamount of advancement that falls short of the predetermined amount that may also improve sleep apnea while an amount that exceeds it may not proportionately increase the therapeutic effect either. This implies that it is necessary to conduct extensive research as there may be various causes for a narrow airway in obstructive sleep apnea. This study also assessed the extraordinary reaction that occurred during the experiment every visit from visit 2 to after 3 months in orde to assess the safety of MAD in addition to its effectiveness. Moreover, it examined

anatomical variations by conducting a radiographic inspection on visit 1 and on visit 5 and after 3 months. The result showed that 91.8% of the participants showed slight discomfort which is toothache or temporomandibular pain caused by the forward movement of the mandible. Only one participant showed a severe extraordinary reaction but this turned out to be irrelevant to the treatment in this study and was cured with proper treatment. The radiographic inspection also did not reveal any anatomical abnormality of the maxilla and mandible.

On the other hand, this study showed positive results in various evaluations but also had limitations. The possibility of placebo effect could not be ignored as this study was intended to explore the effect of airway dilatation without including a control group. Further, research including not only a group receiving a similar intervention but also a control group without any intervention is required for accurate verification.

CONCLUSION

The results of this study showed that the MAD, "Bio-Guard" designed and manufactured by sleep and health, Co. In Korea, could be used effectively to improve sleep apnea. Moreover, this product for which efficacy has been proved through this study can be used in the future as an alternative treatment to the conventional irreversible surgical treatment, there by preventing surgical complications and reducing medical cost.

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