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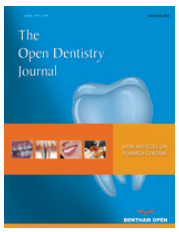

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RESEARCH ARTICLE

Mandibular Advancement Devices (MAD) as a Treatment Alternative for Obstructive Sleep Apnea Syndrome (OSAS)

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Abstract:

Background:

Continuous Positive Airways Pressure therapy (CPAP) is the gold standard treatment of the Obstructive Sleep Apnea Syndrome (OSAS), however, the scarce adherence to the therapy requires the evaluation of other therapeutic alternatives.

Objective:

The aim of the present study was to assess the effectiveness of Mandibular Advancement Devices (MAD) in subjects affected by OSAS who had interrupted the treatment with CPAP and to make comparative evaluations.

Methods:

Eighteen subjects (15 males and 3 females), aged between 27 and 60 years, with a diagnosis of moderate to severe OSAS were included. Inclusion criteria: polysomnographic examination before treatment (T0) and after 1 month from the beginning of the therapy with CPAP(T1), interruption of the treatment due to loss of compliance, Epworth Sleepiness Scale (ESS) questionnaire filled out at T0 and T1. Subjects started the treatment with MAD and polysonnographic examination was prospectively executed after 3 months (T2) and 1 year (T3). One-way analysis of the variance (ANOVA) was used to compare data of polysonnographic examination performed at T0, T1, T2 and T3 as well as the differences of ESS scores recorded at different timing.

Results:

Compared to baseline (T0), all functional parameters tested showed statistically significant differences at T1, T2 and T3 ($p < 0.001$), meanwhile no differences were found between data recorded after therapy with MAD (T2 and T3) and with CPAP (T1). Similar results were also found with the score of ESS among different timelines ($p < 0.001$).

Conclusion:

These findings suggest that MAD could be a valid alternative for the treatment of OSAS in those patients with scarce adherence to the CPAP therapy.

Keywords: OSAS, Sleep apnea, CPAP, Respiratory disease, Polysomnography, Quality of Life.

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1. INTRODUCTION

Obstructive Sleep Apnea/ipopnea Syndrome (OSAS) is a disorder characterized by episodes of airflow obstruction (apnea or hypopnea) during sleep. OSAS affects 25% of males and 15% of females in the general population, with increasing incidence in obese subjects [1]. Apnea is defined as breath interruption that lasts for more than 10 seconds, while hypopnea refers to a respiratory episode less than 10 seconds during which ventilation is reduced by at least 50% compared

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to the baseline; both conditions result in oxygen desaturations (at least 4 and 3% of the basal value, respectively) [2]. According to the Apnea Hypopnea Index (AHI), which represents the sum of ipopnea and apnea events per hour of sleep, OSAS can be classified as physiological (0-5 AHI), mild (5 -20 AHI), moderate (20-30 AHI) and severe (30 AHI) [3]. Subjects affected by OSAS usually report nocturnal symptoms such as habitual and persistent snoring, sleep breaks reported by the "bed-partner", awakenings with suffocation sensation defined as "choking", restless sleep with numerous movements and polyuria [4]. During daytime, subjects report drowsiness, headache, dry jaws and non-resting sleep sensation, asthenia, memory disorders, irritability, loss of interest, reduction in libido, changes in life habits with impaired relationship life [3, 4]. Concerning daytime symptoms, OSAS has great social importance as it is recognized as a frequent cause of road accidents due to so-called "sleep strokes while driving". [4, 5] Moreover, OSAS is associated with alteration of the microstructure and macrostructure of sleep and autonomic symptoms such as activation of the sympathetic, temporary increase in blood pressure, tachycardia [1, 5 - 7].

Polysomnography is the gold-standard examination for the diagnosis of OSAS. It allows the detection of blood pressure, electrocardiographic, electroencephalographic and electromyographic tracks, changes in body position and respiratory function during sleep, as well as the severity of OSAS by calculating the apnea-hypopnea Index (AHI) [8]. The polysomnography also assesses specific parameters such as: 1) the Desaturation Events Index (ODI), which corresponds to the number of respiratory events per hour of sleep during which blood oxygen saturation drops by at least 4% compared to baseline, 2) the average saturation of O2 (SpO2) and 3) desaturation time which is the time expressed in minutes or percentage, that the patient spends with a saturation of less than 90%, 85% or 80%, respectively.

Observational studies indicate that OSAS is an important risk factor for coronary heart disease, ischemic stroke and cardiovascular mortality [5 - 7, 9 - 13], and doubles the relative risk of developing heart failure regardless of other known risk factors [5]. In this regard, OSAS causes sleep fragmentation that increases respiratory stress, intermittent hypoxia and hypercapnia. These alterations can, in turn, lead to systemic and pulmonary arterial hypertension, greater incidence of cardiovascular and cerebrovascular disease, heart arrhythmias and, in the child, growth delay [2, 10, 14 - 16].

In the adult patient with OSAS, the treatment of choice is Continuous Positive Airways Pressure (CPAP) therapy, which consists of the continuous insufflation of positive pressure air in the nostrils during sleep [17]. This air flow creates a "physical wedge" that prevents the collapse of the upper airways, reducing the episodes of apnea and the associated nocturnal and daytime symptoms [18]. However, the scarce adherence to treatment with CPAP limits its effectiveness, in fact, approximately 25% of patients refuse to use CPAP or suspend the therapy after the first two weeks [19]. In children, minimally invasive treatments have recently been proposed, such as skeletal maxillary expansion [20 - 24] or functional therapies to stimulate mandibular growth [25 - 27].

The adherence to the treatment is still an important issue in the treatment of OSAS patients due to an unfavorable balance between economic and clinical commitment and the effectiveness of the therapy [28]. Thus, an alternative therapeutic approaches to the CPAP is needed considering the importance of the symptoms and the side-effects related to the OSAS.

In this regard, MAD appliances were found to reduce apnea-hypopnea index (AHI), albeit significantly below the effectiveness of CPAP [29 - 31], bykeeping the mandible in a forward position during sleep and maintaining upper airway patency [32]. The therapy with MAD appliance is more accepted by patients with a significant positive impact on the quality of life which, in turn, improves the compliance, the withdrawal rates and the wearing time. As a consequence, MAD has been widely recommended to patients with mild-to-moderate OSAS [33], despite a preliminary evaluation of the presence of temporomandibular disorders (TMD), it is mandatory in those patients referred for oral appliance therapy [34 - 39].

Moreover, there is no evidence of the effectiveness of MAD in subjects suffering from moderate to severe OSAS, despite it has been postulated that this therapy could be used as a substitute when these patients refuse or interrupt the therapy with CPAP [40, 41]. In this regard, the aim of the present study was to evaluate the effectiveness of the therapy with MAD, assessed via polysomnography and ESS score, in a cohort of subjects with a diagnosis of moderate to severe OSAS who had earlier interrupted the treatment with CPAP, and to make comparative evaluations between the two treatment options.

2. MATERIALS AND METHODS

This study followed the principles laid down by the World Medical Assembly in the Declaration of Helsinki 2008 Helsinki Declaration on medical protocols and ethics and received a positive response from the Approval Board of the School of Dentistry, University of Catania (protocol n. 14/19). The study sample included 18 subjects (15 males and 3 females), aged between 27 and 60 years, with the diagnosis of moderate to severe OSAS (AHI >30 events/h) and reporting the following inclusion criteria: polysomnographic examination before treatment (T0) and after 1 months from the beginning of the therapy (T1), short-term CPAP therapy with an interruption due to loss of compliance, 3) Epworth Sleepiness Scale questionarrie filled out at T0 and T1. Exclusion criteria were:periodontal disease, edentulous, or pain during protrusion maneuver. The included subjects were referred to our clinic seeking consultation for MAD appliance as an alternative treatment to the CPAP. During intra-oral examination, upper and lower dental impressions were recorded, also bite registration was taken in centric relation and at 60% of the maximum mandibular protrusion for the first mandibular advancement step. Subjects were treated with MAD equipped with an advancement screw that was firstly activated according to the initial mandibular protrusion (Fig. **1**). Patients were weekly monitored for the first months and when necessary, the mandibular advancement was gradually increased in order to reduce the number of apnea episodes and

snoring as low as possible. Polysonnographic examination was executed for 3 months (T2) and 1 year (T3) after the administration of MAD appliance in order to recordt he functional parameters and to make comparative evaluation with those recorded at T0, T1 and T2. The data recorded were the apnea/hypopnea Index (AHI), the number of apnea and hypopnea episodes, the percentage of oxigen saturation (SAO2) and the total time of desaturation below 90% (CT90). In this regard, the study featured a mixed design, i.e. retrospective recruitment process, including subjects treated with CPAP and prospective monitoring of patients in treatment with MAD. Subjects were also administered the Epworth Sleepiness Scale (ESS) in order to make a comparative evaluation with the data of sleepiness recorded at T0 and T1. Finally, patients were asked to fill out a questionnaires, including simple dichotomic answers, to evaluate patients' compliance and satisfaction with the usage of MAD.

2.1. Statistical Analysis

The normal distribution and equality of variance of the data were performed with Shapiro-Wilk Normality Test and Levene's test. Since data were normally distributed and showed equality of the variance, parametric statistical analysis was conducted. One-way analysis of the variance (ANOVA) was used to assess differences inthe functional parameters recorded during the polysonnographic examination performed at T0, T1, T2 and T3; post-hoc comparison tests were also performed by using the Scheffè test. One-way analysis of the variance (ANOVA) and post-hoc tests was also used to investigate the differences of ESS scores recorded at different timing. Data sets were recorded on a specific spreadsheet and analyzed using SPSS® version 24 Statistics software (IBM Corporation, 1 New Orchard Road, Armonk, New York, USA).

3. RESULTS

According to the one-way analysis of variance (ANOVA), all functional parameters recorded showed statistically significant differences among T0, T1, T2 and T3($p < 0.001$) (Table **1**). In particular, the post-hoc tests showed that there was a significant improvement in AHI, the number of apnea and hypopnea episodes, the SAO2 and CT90 at T1, i.e. after the first period of treatment with CPAP appliance ($p < 0.001$). Moreover, for each parameter recorded by the polysomnographic test, no differences were found among T1, T2 and T3, *i.e*. between the CPAP (T1) and the MAD (T2,t3) therapies (Table **1**).

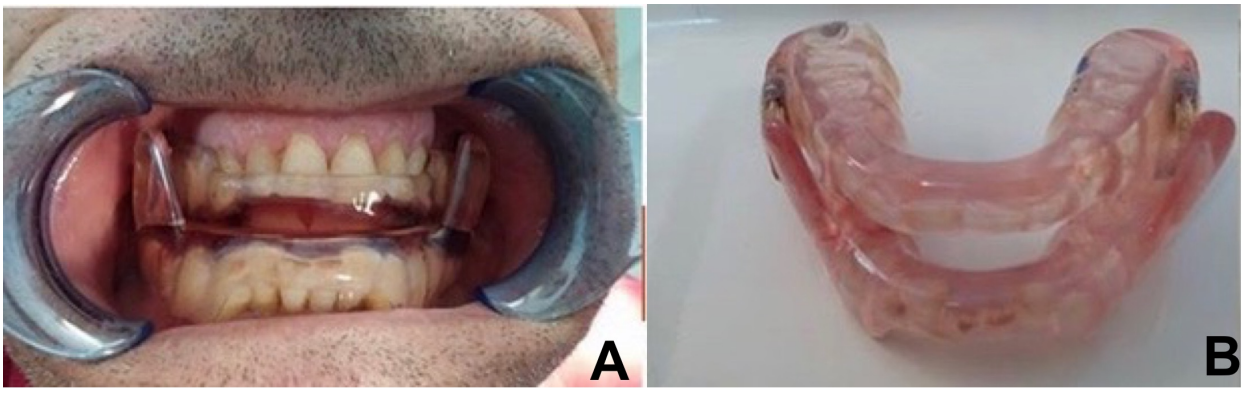

Fig. (1). Mandibular advancement device used in the present study. (**A**) intra-oral view, (**B**) extra-oral view.

Table 1. Comparative assessment of functional parameters recorded during polysomnographic examinations performed at T0, T1 and T2. AHI = Apnea Hypopnea Index; N = number; SAO2 = percentage of oxigen saturation; CT90 = total time of desaturation below 90% p values set at $p < 0.05$, according to the one-way analysis of variance (ANOVA) and post-hoc comparisons (Scheffè test).

Polysomnographic parameters	Examination Timing								
	T0 (a)		T1 (b)		T2 (c)		T3 (d)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Significance
AHI	34,25 (b,c)	10,82	2,67 (a)	1,21	3 (a)	1,55	4,11 (a)	1,03	$p < 0.001$
Apnea (N)	169 (b,c)	27,57	21,17 (a)	3,19	21,67 (a)	3,39	23,76 (a)	4,16	$p < 0.001$
Hypopnea (N)	215,5 (b,c)	76,87	5 (a)	1,79	11,5 (a)	5,28	13,45 (a)	3,9	$p < 0.001$
SaO2 (%)	91,5 (b,c)	2,35	95,33 (a)	1,37	94,67 (a)	1,75	94,03 (a)	1,32	$p < 0.001$
CT90	18,5 (b,c)	4,46	5,67 (a)	1,51	5,83 (a)	1,6	6,34 (a)	1,81	$p < 0.001$

Table 2. Comparative assessment of ESS score recorded at different timing (T0,T1 and T2). p values set at p < 0.05, according to the one-way analysis of variance (ANOVA) and post-hoc comparisons (Scheffè test)

	Examination Timing								
	T0 (a)		T1 (b)		T2 (c)		T3 (d)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Significance
ESS score	12.5 (b,c)	2.9	7.3 (a)	2.1	7.9 (a)	2.0	8,3 (a)	1,9	p < 0.001

Table 3. Grade Questionnaire is used to assess adherence to treatment and comfort with MAD devices.

Compliance Questionnarie
1. Do you have difficulty using the MAD? A. YES B. NO C. Sometimes
2. How many weekends per week does MAD use? A. Every other time B. 3-5 weekends per week C. 1-2 weekends per week
3. Have you irritation at the gum level and/or at the dental level since using MAD? A. YES B. NO C. Sometimes
4. Do you have muscle aches and/or noises when you open your mouth since you use MAD? A.SI B.NO C. Sometimes
5.Have chewing difficulties since using MAD? A. YES B. No C. Sometimes

Significant differences ($p < 0.001$) were also found in the mean ESS score, which decreased from 13.5 (T0) to 7.3 after CPAP therapy (T1), while no differences were found between the ESS score detected at T1 and 3 months (T2) and 1 year (T3) after therapy with MAD appliance (Table **2**). All patients provided consistent responses to the usage of the MAD devices, in particular, they reported excellent compliance (question 1 and 2) as well as no pain or similar symptoms while wearing the appliance (Table **3**).

4. DISCUSSION

Patients'compliance is the main concern for the treatment of subjects affected by OSAS. Numerous patients discontinue treatment over the years, due to the low adherence with the CPAP appliance; consequently, finding the appropriate therapy for the patients is as important as choosing the alternative therapy in order to keep the patient in the treatment loop [42]. In this regard, we included in the present study, subjects with the previous diagnosis of moderate to severe OSAS who had interrupted the treatment with CPAP, afterwards they were treated with MADs in our clinic in order to provide continuity to the therapy. By these restrictive study criteria, we were able to investigate and compare the potential differences in the treatment effectiveness between MAD and CPAP appliances in the same patients.

According to the present findings, all functional parameters showed a significant enhancement after the treatment with CPAP but, interestingly, the values of AHI, SAO2, CT90, the number of apnea and hypopnea episodes were almost maintained even during treatment with MAD appliance. Our findings are in agreement with the previous studies that have investigated the effectiveness of treatment performed with MAD and CPAP appliances [43]. Data synthesis from previous RCT studies suggested a reduction in the frequency of the respiratory disorders from 80% to 28% with the usage of MAD devices and from 74 to 94% with CPAP therapy. Also, despite CPAP is more effective than MAD devices for reducing sleep apnea events, several studies suggested similar outcomes between the two treatments in terms of reduction of symptoms and cardiovascular health [44 - 46]. A recent well-conducted systematic review with meta-analysis [41] reported that the greater effectiveness of the CPAP therapy over MAD appliance suggested by previous clinical trials is strictly dependent on the severity of the OSAS of the included subjects. In this regard, CPAP causes an improvement of approximately three times than that estimated with MAD, meanwhile, the absolute difference between the two treatment approaches is significantly lower when patients with mild average baseline AHI are included. Therefore, MADs are recommended in patients with mild-to-moderate OSAS as they can better tolerate it, although they may be slightly less performing than CPAP [41]. This is also in agreement with the present study since all subjects included reported positive response (good tolerance) using MADs, according to the questionnaire provided. Since MADs significantly reduce the AHI compared with no treatment, this therapeutic option could also be a valid alternative for those subjects who are affected by severe OSAS and refused the CPAP, despite its effectiveness can be lower compared to subjects with mild to moderate disease.

According to previous evidence [31, 43 - 48], both treatments were effective in reducing ESS, with CPAP having only a small, additional effect over MADs, especially when trials reported similar baseline characteristics and the AHI was mild to moderate. In the present study, we obtained a similar finding for the ESS score, confirming a significant decrease in the sleepless phenomenon when subjects are treated respectively with the CPAP or MAD. However, most of the studies assessing the effects on daytime sleepiness and daily functions have been performed involving CPAP and not MAD and further studies are needed to better elucidate this important aspect.

One of the most important limitations of the available literature on the OSAS is that data from CPAP or MAD appliances are mainly obtained from short-term observational time since compliance tailed-off overtime [48]. Despite MAD can be better tolerated than CPAP, the limited longer-term studies suggested that patients' compliance diminishes with time even if this appliance is less invasive than CPAP [32, 48]. In the present study, we reported data from polysomnographic examination and patients' compliance after 1 year of treatment with MAD. All patients reported good experience with these appliances and considered the therapy with MAD a sort of "acceptable compromise" between the health benefits and some discomfort. Thus, our findings seem to encourage the usage of MAD as an alternative treatment in those patients refusing CPAP, however, further studies with a greater sample size and longer follow-up evaluation are required.

From a socio-economical perspective, it is important to underline that to date, the CPAP is delivered by the NHS since OSAS is recognized as a serious disease with severe short and/or long-term consequences. Considering the documented effectiveness of treatment with MAD and that it can represent a valid alternative to the CPAP in the long-term management of this pathology, we suggested to include these appliances in the NHS health-care delivery plan.

CONCLUSION

The present study would confirm that long-term therapy with MAD could be considered a valid alternative in those patients who refused or interrupted the therapy with CPAP. In this regard, all polysomnographic parameters and ESS values assessed after x of therapy with CPAP were maintained after x therapy with CPAP.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the ethics committee of School of Dentistry, University of Catania, Italy (protocol n. 14/19).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

All patients signed an appropriate informed consent for being recruited in a prospective clinical study.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is available from the corresponding author [G.F] upon request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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