

# Oral appliances for the treatment of obstructive sleep apnea in patients with low C-PAP compliance: a long-term case series

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**Objectives:** To assess the effectiveness of mandibular advancement devices (MADs) for the treatment of obstructive sleep apnea syndrome (OSAS) over a long-term follow-up in patients non-compliant with continuous positive airway pressure (CPAP) and to identify potential predictive factors of response to MADs.

**Methods:** Fifteen OSAS patients were enrolled. Apnea-hypopnea index (AHI) and daytime sleepiness were assessed at baseline and at the end of follow-up. Potential baseline predictors of treatment effectiveness were assessed.

**Results:** AHI and Epworth Sleepiness Scale (ESS) scores improved significantly with MADs. Sixty per cent of patients were 'responders', of whom 33% were 'full responders'. Sixty-seven per cent of patients showed total compliance. No correlations between the potential predictors and the response to MAD therapy were found.

**Discussion:** Effectiveness of MAD therapy was shown over a long-term follow-up in OSAS patients with low compliance to CPAP. Efforts to identify predictive success factors fell short.

**Keywords:** AHI, Compliance, C-PAP, Epworth, Mandibular advancement devices, Oral appliances, OSAS, PSG

## Introduction

Population-based studies suggest that 4–17% of men and 2–9% of women aged more than 50 years suffer from symptomatic obstructive sleep apnea syndrome (OSAS), which is associated with clinical, psychological and social impairment, and is currently viewed as a major risk factor for a number of medical disorders.<sup>1,2</sup> Both anatomic and neurological factors are involved in the development of obstruction of the upper airway in OSAS.<sup>3,4</sup> The severity of disease is classified by using sleep-time polysomnography (PSG), which allows rating the apnea-hypopnea index (AHI, calculated by dividing the number of events by the number of hours of sleep).<sup>3,5</sup>

Clinical evidence suggested that continuous positive airway pressure (CPAP) is the most effective

therapy to reduce symptoms as well as cardiovascular and metabolic complications of OSAS, but it should be borne in mind that the choice of the treatment modality and its effectiveness are conditioned by the type and the site of airway obstruction. To this aim, the use of sleep nose endoscopy may be a promising strategy to perform a reliable differential diagnosis of the causes and location of the obstruction and, consequently, to allow a tailored treatment.<sup>6,7</sup> Indeed, whilst CPAP is the standard of reference between treatments, it must be pointed out that the search for alternatives should be driven by the need to find some more tolerable and less invasive approaches and, importantly, also by the need for identifying anatomy-based treatment approaches.

Custom-made mandibular advancement devices (MADs) are an effective treatment option for snoring, upper airway resistance syndrome and OSAS. Literature data supported their effectiveness and oral appliance therapy is recommended for patients with

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sleep-related breathing disorders.<sup>8–12</sup> Practice parameters for the treatment of OSAS with MADs suggested that although not as effective as CPAP, oral devices are indicated for use in patients with mild to moderate OSAS who prefer them to CPAP, who do not respond to CPAP, or are not appropriate candidates for CPAP.<sup>10</sup> MADs are also recommended as a second-line treatment for severe OSAS patients not compliant with CPAP.<sup>10</sup> All these subjects may continue with their devices for many years, although the treatment needs to be followed up in terms of safety (e.g. absence of dental or articular side-effects) and effectiveness.

Based on these premises, the need to identify better the indications for MAD treatment as well as to provide long term data on MAD effectiveness and safety seems to emerge. In this study, a selected population of OSA patients with low CPAP compliance and who had MAD treatment indications based on sleep nose endoscopy was recruited, with the twofold aim to: (1) evaluate long-term effectiveness of MAD treatment, and (2) identify potential baseline predictive factors of positive treatment outcome.

## Methods

### Study participants

A sample of consecutive patients with moderate-to-severe OSAS and with a history of non-compliance to CPAP (<4 hour per night within the first week of treatment) was included in the study. Patients aged between 30 and 70 years were included if they had an AHI  $\geq 15$  at the time of registration. Hypopnea was defined as a flow limitation of 50% or more for more than 10 seconds associated with at least a 3% oxygen saturation drop.

Exclusion criteria included the following: impossibility for the patient to wear an MAD due to periodontal conditions, pre-existing temporomandibular joint pathology, class III patients, neurological or psychiatric disorders, morbid obesity defined by body mass index (BMI)  $>40$ .

### Study design

Potential participants to the study were screened on the basis of the sleep-endoscopy's identification of the anatomical indications for MAD therapy, according to the protocol described below.

At baseline, patients affected by OSAS with low-CPAP compliance, completed the Italian version (validated in 2002) of the Epworth Sleepiness Scale (ESS)<sup>13</sup> and they underwent home sleep-time polygraphy. The device used was a portable diagnostic system (Embletta® X100), which is highly sensitive

and specific in quantifying the AHI and differentiating obstructive events.<sup>14–16</sup>

After the diagnosis of moderate or severe OSAS and the confirmation of non-compliance with CPAP, all patients were evaluated by sleep endoscopy (SE) to assess the potential benefit of MAD placement. During SE, the mandibular traction maneuver was carried out with a customized device designed ad-hoc for such examination. The patients in which SE showed that a limited (50% of maximum protrusion) traction of the mandible solved the obstruction were treated by MADs. The underlying concept of this approach was that, if the obstruction did not solve with such a mandibular advancement, the expected effects of MAD treatment should not be beneficial and that other (or concurrent) factors should determine airways obstruction.

The selected patients underwent lateral skull tele-radiography, dental X-rays, dental impressions and maximum protrusion measurement. For each patient, the BMI and the history of previous surgeries to treat disorders of the upper airways (i.e. septoplasty, turbinoplasty, septoturbinoplasty, tonsillectomy, uvulopalatopharyngoplasty – UPPP, hyoid myotomy and suspension) were recorded.

The devices were manufactured and provided to the patients. A custom-made Herbst telescopic appliance was adopted in the study. The safety of this device has been extensively studied in the literature, especially with regard to its impact on the level of temporomandibular joints and in orthodontic cases of class II malocclusion.<sup>17</sup> Such appliance allows patients to move the mandible laterally and vertically without disengaging the appliance. Also, if it is determined that the initial position does not provide the anticipated relief of the condition, the mandible can easily be moved forward by a telescopic advancing mechanism in 1/4 mm increments by making one turn of the protrusion collar.

The advantage of the Herbst appliance is that it does not encroach on tongue space and allows for quick and easy mandibular protrusive adjustability. This is accomplished through simple manipulation of the rod/sleeve plunger mechanism. Vertical opening is up to 5 mm and there is limited freedom of movement for the mandible in a lateral direction. Bilateral interarch elastics are recommended to keep the jaw closed during sleep.

After a mean follow-up span of  $36.8 \pm 15.36$  months, all patients again fulfilled the ESS and underwent the same home-recorded polygraphy with the MADs *in situ*. According to literature criteria, patients were defined as 'responders' when AHI decreased by over

50%, and ‘full responders’ when the AHI decrease was greater than 50% with AHI<10 at the end of the study.<sup>18,19</sup> For all patients, data about the compliance with MADs were recorded.

Other data obtained through portable polygraphy, such as oxygen desaturation level or sleep posture, were not taken into consideration: the first one because redundant and less important than AHI for the aim of the study, the second one for its intrinsic variability.

**Statistical analyses**

Descriptive baseline and follow-up data were presented for each patient. Also, statistical analyses were conducted with the twofold aim to: (1) assess the treatment effectiveness over time, and (2) identify potential baseline predictors of effectiveness.

Numerical continuous variables were expressed as means±standard deviation and nominal variables were described by the absolute and relative (%) frequency.

For all statistical procedures, AHI score was the main outcome variable. The pre-treatment and follow-up AHI scores were compared by using a parametric test to detect significant treatment-related effects. Then, percentage change in the AHI scores was used as the dependent variable in a regression analysis aiming to identify predictors of treatment effectiveness among parametric data (i.e. pre-treatment AHI scores, pre-treatment ESS scores, BMI). Percentage changes in the AHI scores were then used to dichotomize a new variable, namely, improved patients with more than 50% decrease in AHI score versus patients with less than 50% change in AHI score. The presence of at least a 50% improvement was adopted as the dependent variable to be predicted by the dichotomic study variables (i.e. patients’ compliance to MAD [yes/no], patients’ satisfaction [yes/no], past surgical procedures). Also, two new dichotomic variables were created to split patients into those with high-low pre-treatment AHI and ESS, namely, ‘high’ values were those over the median score for the variable, ‘low’ values were those under the median score for the variable.

For both the parametric and dichotomic variables, single variable regression analysis was performed first, with the aim to screen among the potential predictors of the outcome variable. Predictors which were significantly related with treatment outcome at the single variable analysis, if existing, were then entered a multiple variable regression analysis in the attempt to build up a predictive multifactorial model.

For all statistical analyses, the level of significance was set at *P*<0.05. All statistical procedures were

performed with the Statistical Package for the Social Sciences (SPSS 19.0; SPSS Inc., Chicago, IL, USA).

**Results**

*Population*

From a population of 45 OSAS patients with low CPAP compliance attending the Institute of Otolaryngology of the University of Padova, Italy during the period from July to December 2007, a total of 15 patients (10 with severe and five with moderate OSA; 13 males; mean age 54±6 years) were included based on the study criteria. Considering the small proportion of women included, results were pooled for men and women. On average these patients were overweight and middle-aged. Demographic data as well as the history of previous surgeries are described in Table 1. The study has not been undermined by drop outs.

*Treatment outcome*

Apnoic events improved significantly with the MAD compared to baseline, with an average AHI reduction of 53±30% (*P*<0.05) (Fig. 1). Patients with moderate OSAS exhibited an average decrease in AHI of 50±25%, from 22±3.5 to 11.3±7.2 (*P*<0.05). In severe OSAS patients, average AHI decreased by 65±16%, from 48.8±11 to 16.1±7.3 (*P*<0.05).

At the individual level, all patients except one showed an improvement in their AHI score at the follow-up PSG, thus confirming that sleep endoscopy-based selection of participants was an effective screening approach to the inclusion of patients who may benefit from MADs. The only non-improved subject totalized the same AHI score as at baseline. A total of nine out of 15 (60%) of patients were classified as responders (six severe sufferers and three moderate), of which five out of 15 (33%) were full responders. There were no cases of pathology aggravation as defined by an increase of more than 10 points in the AHI index.

There was a significant reduction in subjective daytime sleepiness with an average ESS reduction of

**Table 1 Baseline data on study population**

	All (range)
No. of patients	15
Sex	13(M)/2(F)
Age	54±6 (34–68)
BMI	26±2 (23–29)
AHI	40.5±16
ESS	9.6±4.9
Septoplasty	1
Turbinoplasty	3
Septoturbinoplasty	8
Tonsillectomy	3
UPPP	3
Hyoid myotomy	3

Note: BMI, body mass index; AHI, apnea hypopnea index; ESS, Epworth sleepiness scale; UPPP, uvulopalatopharyngoplasty.

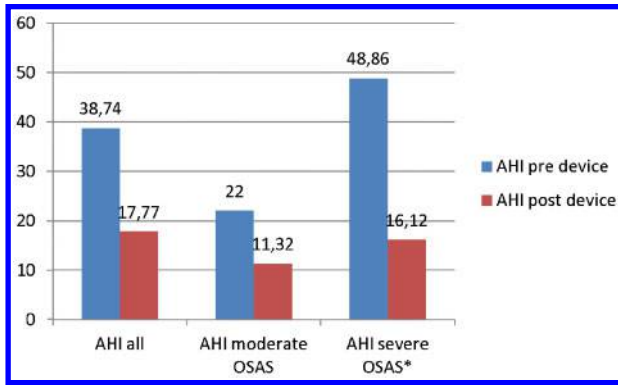


Figure 1 Respiratory events.

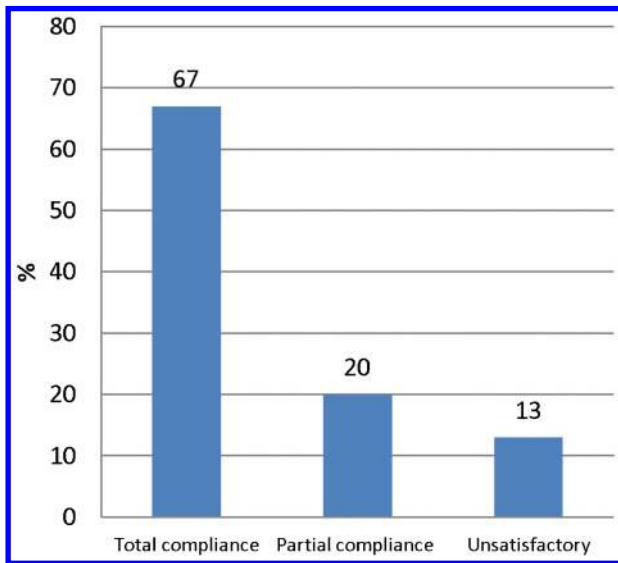


Figure 2 Treatment observance. Total compliance: patient wore MAD every night of the week all night. Partial compliance: patient wore MAD for at least 4 nights per week and for at least 4 hour per night. Unsatisfactory: patient wore the MAD for less than 4 nights per week for at least 4 hour per night.

54±37%. The average ESS score fell from 10.2±2.9 at baseline to 5.2±3.2 ( $P<0.05$ ). Observance of treatment was high (Fig. 2), with 67% of patients with total compliance (MADs worn every night of the week all night) and 20% of patients with partial compliance (MADs worn for at least 4 nights per week and for at least 4 hour per night). Only two patients had an observance that was unsatisfactory (MADs worn less than 4 hour per night and less than 4 days per week).

Data at the individual level are presented in Table 2.

*Predictors of treatment effectiveness*

Single variable regression analyses showed that none of the parametric and dichotomic predictors were actually related with treatment outcomes, thus indicating that neither baseline daytime sleepiness (ESS), morphometric criteria (BMI), and respiratory findings (AHI) nor a history of previous surgeries and patients’ satisfaction and compliance with MAD treatment were significant predictors of treatment improvement (Tables 3 and 4). Due to the absence of any significant correlations at the single variable level, the multiple variable regression analyses were not performed.

**Discussion**

CPAP is the treatment of choice in most subjects with severe OSAS, but patients’ failure to adhere to the therapy regimen due to poor compliance represents a major limitation to the widespread adoption of such approach. Oral devices designed for mandible advancement have potential advantages over CPAP in that they are unobtrusive, make no noise, do not need a power source and are potentially less costly. When directly compared in randomized trials, oral appliances are generally preferred by patients over CPAP.<sup>20,21</sup> Of course, MAD treatment should be

Table 2 Data at the individual level

Name	Age	Pre-BMI	Pre-AHI	Post-AHI	Δ AHI	Δ% AHI	Pre-ESS	Post-ESS	Δ ESS	Δ% ESS	Compliance
Z.D.	62	23	61	32	29	47.54098	5	3	-2	40	2
P.A.	49	NR	22.1	15	-7.1	32.1267	NR	NR	NR	NR	2
M.R.	53	29	36	36	0	0	15	15	0	0	0
C.A.	60	25	18.5	6.8	-11.7	63.24324	2	NR	NR	NR	1
C.L.	47	25.4	35	13.1	-21.9	62.57143	10	2	-8	80	2
P.F.	66	24	32	9.7	-22.3	69.6875	3	0	-3	100	1
P.R.	42	23.3	61	11.7	-49.3	80.81967	10	2	-8	80	2
S.G.	51	29	45	45	0	0	NR	NR	NR	NR	0
D.L.	66	25.4	40.3	33.1	-7.2	17.866	8	1	-7	87.5	2
B.M.	47	26.5	20.6	5.6	-15	72.81553	19	5	-14	73.68421	2
R.T.	62	29.3	52.6	10.1	-42.5	80.79848	12	8	-4	33.33333	2
T.M.	68	22.5	26.1	19.5	-6.6	25.28736	15	12	-3	20	2
R.G.	47	27	35	9.3	-25.7	73.42857	6	4	-2	33.33333	1
C.G.	34	25.3	74	10	-64	86.48649	9	0	-9	100	2
P.M.	NR	NR	22	9.7	-12.3	55.90909	11	11	0	0	2

Note: NR: Not Reported.  
Compliance: 2=total, 1=partial, 0=unsatisfactory.

**Table 3 Single variable regression analysis. Predictors of %AHI improvement**

Predictors	Correlation with %AHI improvement	P value
Baseline AHI scores	0.306	0.267
Baseline ESS scores	-0.320	0.287
BMI	-0.254	0.402

based on specific indications, in order to maximize their effectiveness and to tailor therapy of such a multifaceted disease.<sup>22</sup>

The present investigation was performed as a long-term case series study on a super-selected population of moderate-to-severe OSA patients with a history of non-compliance to CPAP. Patients were recruited on the basis of sleep nose endoscopy's indications to MAD treatment.

The underlying hypothesis that patients' selection was appropriate was confirmed by the fact that treatment with MADs showed a good effectiveness, with a significant improvement of the apnea-hypopnea index and daytime sleepiness. The full response rate (AHI reduction greater than 50% with AHI<10) was about 33%, and the positive response rate based on a 50% AHI reduction was 60%. Importantly, all except one patients reported a decrease in their AHI scores with respect to baseline values, so suggesting that SE is an interesting approach to visualize the site of anatomical obstruction, as to identify potential MAD responders.

In the researches of Salamanca *et al.*<sup>23</sup> the most significant finding at SE was that oropharyngeal obstruction widely prevails on the other areas. Furthermore, they preferred the combination of oropharyngeal surgery (with or without tonsillectomy) plus MADs as treatment of choice when the mandibular traction maneuver was effective only at the hypopharyngeal level. Based on that finding, it can be hypothesized that multisegmental obstruction could explain the lack of success for the unique patient of our study who was unresponsive to MAD therapy).

**Table 4 Single variable regression analysis. Predictors of more than 50%AHI improvement**

Predictors	Correlation with AHI improved	P value
High AHI scores	-0.167	0.553
High ESS scores	0.051	0.867
Compliance with MAD	0.113	0.688
Satisfaction with MAD	0.272	0.326
Septoplasty	0.218	0.435
Turbinoplasty	0.068	0.810
Septoturbinoplasty	0.055	0.847
Tonsillectomy	0.068	0.810
UPPP	0.068	0.810

Our findings also showed a post-treatment reduction in ESS.<sup>18,24,25</sup> The AHI reduction was more marked in patients with severe OSAS than in subjects with moderate OSAS, even if it must be pointed out that this observation needs to be confirmed on large-sized samples.

No relevant side effects were reported, in line with literature data on the use of such devices.<sup>26</sup> Regarding treatment tolerance, only two of the 15 patients showed a non-compliance with the MAD; 67% of the patients wore the device every night of every week; this result is comparable with the mean of 68% of patients across seven studies reviewed by Ferguson *et al.*,<sup>18</sup> while Vecchierini *et al.*<sup>19</sup> reported a good tolerance in the 80% of the subjects.

In our super-selected population of OSAS patients, efforts to identify predictive factors for treatment improvement fell short, since regression analyses did not detect any significant predictors: pre-treatment AHI, ESS, BMI, compliance and satisfaction with MAD, history of previous surgeries showed no correlation with the percentage of improvement in the apnea-hypopnea index. This might be due to the study sample size and to heterogeneity of surgeries and patients conditions prior to use of the device, and must be viewed as a remark of the need for improving knowledge on the predictive factors at the individual level. On the other hand, it can also be viewed as a confirmation of the fact that potential participants' screening with SE influenced drastically the treatment planning phases and represented the unique factor that may identify potential MAD responders. Thus, the usefulness of SE to screen for patients that may have anatomical benefits from MAD treatment has to be assessed in future investigations attempting to refine further the indications of approaching OSAS patients by using such devices. A possible strategy to perform such an investigation might be the design of controlled studies, also including patients without potential SE-based indications for MAD treatment.

This study adds to the scarce literature on the outcomes of oral appliance (OA) therapy in OSAS over a long-term observation period. Indeed, most of the literature studies have a short-term follow-up ranging from 45 days to 3 months, with only a few

studies on longer observation periods, namely, follow-up of more than one year.

Of course, to address limitations of the present investigation, future studies on enlarged samples and with multiple observation points are needed to confirm these pilot data. Notwithstanding that, importantly, this study also pointed out the fact that, in this population of OSAS patients with CPAP low-compliance, the high long-term MAD effectiveness may primarily depend on an accurate diagnosis and patient selection based on sleep nose endoscopy. Considering that, it is recommended that future studies on OSAS treatment take into careful accounts for the differential diagnoses with respect to the anatomical site of obstruction before proceeding with MAD treatments.

## Conclusions

This investigation showed the effectiveness of MAD therapy in the long-term follow-up, both in moderate and in severe OSAS with CPAP low compliance. More research is needed to define potential predictive factors of positive treatment outcome, possibly based on sleep nose endoscopy-diagnosed OSAS, in order to provide patients with the appropriate tailored treatment.

## Disclaimer statements

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**Conflicts of interest** No conflicts of interest declared.

**Ethics approval** The research has been conducted in full accordance with ethical principles.

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