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Research Article



# Preliminary Results of a New Mandibular Advancement Device: Orthoapnea NOA

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## Abstract

**Study Objectives:** Mandibular advancement devices (MAD) are indicated for the treatment of mild to moderate obstructive sleep apnea (OSA) patients, and for severe OSA patients who cannot tolerate continuous positive airway pressure (CPAP). The objective of this study is to evaluate the efficacy of the NOA Ortho-apnea Mandibular Device.

**Methods:** The study was a prospective study, in which 31 patients were evaluated in two clinical conditions (without MAD in situ versus with MAD in situ). A new custom-made titratable MAD was used.

**Results:** A pretreatment polygraphy was performed with a mean Apnea-Hypopnea Index (AHI) value of 27 SD 16.6 events per hour and a post-treatment polygraph with a mean AHI result of 6.6 SD 5.0 events per hour. All subjects showed improvement in AHI with zero exceptions. The use of the device represents an average reduction of 20.4 events per hour, which represents a 75.55% reduction in AHI.

**Conclusions:** The device has proved to have a significant effect on AHI, oxygen saturation, the Epworth test and secondary results of sleep studies. The vertical control of the device design has a significant effect on the effectiveness and comfort of the device.

**Keywords:** Mandibular advance device; Efficacy; Obstructive sleep apnea; OrthoApnea NOA.

## Declarations

1. The authors declare no competing interests.
2. Ethical approval and informed consent: All subjects gave written informed consent in accordance with the Declaration of Helsinki prior to initiating treatment.

## Introduction

Obstructive Sleep Apnea Syndrome (OSA) is a respiratory disorder that occurs during sleep and is characterized by repeated obstructions throughout the night of the upper airway due to relaxation of the soft tissues of the base of the tongue. Severity is measured with the Sleep Apnea-Hypopnea Index (AHI), which refers to the number of obstructions of more than 10 seconds per hour. OSA is a risk factor for a series of diseases such as cerebrovascular accidents, high blood pressure and neuropsychiatric disorders, among others. In addition, the risk of traffic accidents, occupational and domestic accidents increases due to daytime hypersomnolence that appears as a symptom of OSA.

Heinzer´s studies/study published in 2015 [1], with a population sample of 2, 121 people (1024 men with a mean age of 56 and 1097 women with a mean age of 58) show the high prevalence of OSA, 83.8% in men and 60.8% in women, for any type of apnea and severity. However, if only moderate and severe apnea are taken into account, the values are 49.7% in men and 23.4% in women [1]. The diagnosis is made by a conventional polysomnography

(PSG) which is a relatively expensive, laborious and technically complex technique that is not available in all centers. So, different studies have validated polygraphy (PG) as an alternative method to diagnose OSA.

Mandibular advancement devices (MAD) are indicated for the treatment of mild to moderate OSA patients, and for severe OSA patients who cannot tolerate continuous positive airway pressure (CPAP) [2]. MADs work to reposition and maintain the jaw in a forward position during sleep, pulling the tongue forward in its insertion in the genial tubercles of the mandibular symphysis, increasing the basal muscle activity of the genioglossus [3]. At the same time they stabilize the jaw and hyoid bone to avoid jaw opening and tongue retaining [4]. The efficacy of a MAD is determined by the advancement of the mandible, soft palate and tongue, which improves upper airway patency during sleep by increasing the upper airway and decreasing collapsibility, therefore preventing collapse during sleep [5]. MADs are often considered to be a more acceptable treatment option than CPAP [6].

Recent articles demonstrate that the mandibular anatomy, position and dynamics are important factors in the pathophysiology of OSA, as well as the design of MAD treatment. Garcia, et al. [7] demonstrated how the great variability in mandibular morphology influences the displacement of the mandible by analyzing three key points of the mandible: the apophysis geni process in the mental symphysis, the edge of the lower incisor and the goniac angle, which may explain why there are patients more prone to OSA. Mayoral, et al. [8] demonstrated how gradually increasing the vertical position of the jaw using George gauges of 2, 5, 8 and 11mm, reduces the total advancement range by approximately 0.3 mm for each mm of opening in addition to positioning the mandible further back due to posterior rotation. Bruno, et al. [9] analyzed the rotational translation in the mandible induced by MAD and showed the variability in mandibular dynamics with different devices.

All of this highlights the importance of analyzing the mandibular anatomy and dynamics of each OSA patient for the manufacturing of a customized MAD. It is important that these devices take into account this variability among individuals instead of designing them with the same mechanism for all subjects. This can help to find optimal jaw positions for OSA treatment. Limitation and control of mandibular movements with MAD, particularly opening, have shown to be more effective in the treatment of OSA, particularly in positional OSA. There are devices that incorporate this limitation and control in their design [10-12] and others that use attachments such as elastics [13, 14]. The objective of this study is to evaluate the efficacy of the NOA Ortho-apnea Mandibular Device. This device, used for the treatment of OSA, is customized according to the craneo-mandibular anatomy and the mandibular movement pattern of each patient, as presented by Bataller [10]. For its manufacture, a study of the mandibular kinematics is carried out to determine the relationship between mouth opening and mandible advancement. The device includes two cams, one on each side, to make the jaw move forward. The kinematics of each patient's jaw is taken into account to ensure that the jaw does not move backwards at any time when opening the mouth.

## Material and Methods

### Study design

The study was a prospective study, in which all patients were evaluated in two clinical conditions (without MAD in situ versus with MAD in situ). The data of this study were collected at a private practice in Madrid, Spain. The procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

### Participants

Patients with OSA eligible for MAD treatment were invited to participate in this study with the following inclusion and exclusion criteria. The inclusion criteria for participation were:

1) Age between 30 and 70,

2) AHI greater than 10 events/hours of sleep,

3) An Epworth >10.

Exclusion criteria were:

1) BMI > 40,

2) Use of medication that could influence respiration or sleep,

3) Morphological reversible upper airway abnormalities (e.g., enlarged tonsils),

4) Untreated periodontal problems,

5) Dental pain,

6) Severe temporomandibular disorders and

7) Lack of retention for an MAD or less than 5 teeth per arch.

### Mandibular advancement device (MAD)

A custom-made titratable MAD (NOA, Orthoapnea, Málaga, Spain) was used. This device consists of an upper splint, joined to the maxilla, and a lower split, joined to the mandible, that are connected to a personalized mechanism. The titration system consists of a set of four lower splints configured with an advanced sequence of SP+1mm, SP+2mm and SP +2.5mm. The starting position (SP) is set in the bite advancement position prescribed by the doctor. The advancement mechanism consists of a couple of followers in the upper splint and a couple of cams in the lower splints. These parts are designed according to the maxilla-mandibular anatomy and mandibular kinematics of each patient, as described by Bataller, et al. [10]. The contact between the cam and the follower produces the mandibular advancement (Figure 1).

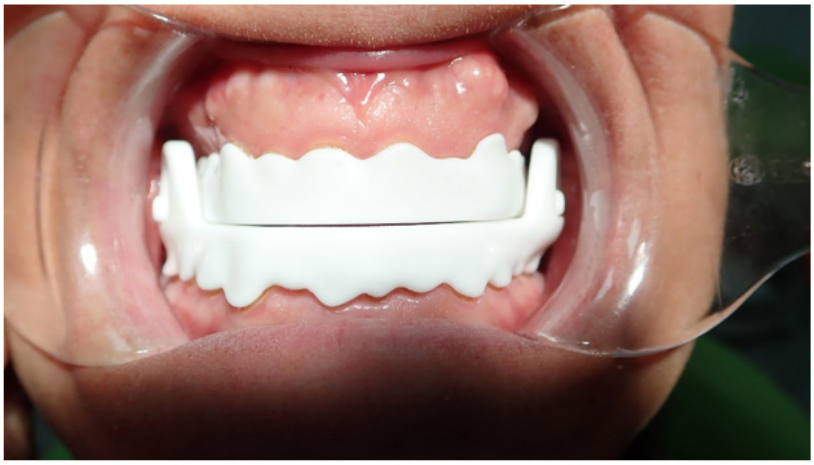

**Figure 1:** OrthoApnea NOA Devices.

The MAD was adjusted individually and advancement was titrated in a private dental clinic in Madrid using a standardized titration protocol. After assessment of the maximum retrusion and maximum protrusion using a construction bite with a George Gauge instrument (Great Lakes Orthodontic Laboratories in Tonawanda, New York), the MAD was set at 67% of the maximal advancement at the baseline. During each consecutive visit, the MAD was evaluated on OSA symptoms and advanced following the standardized titration protocol +1mm + 2mm and +2.5mm if OSA symptoms were not relieved or reduced to an acceptable level. If side effects appeared and were not acceptable for the participant (e.g., muscular pain resulting in difficulty wearing the appliance during sleep), the advancement was adjusted backwards to-1mm. Patients were instructed to wear the MAD every night upon delivery. After a habituation period of six to eight weeks, patients underwent Home Sleep Test (HST) recordings wearing the MAD.

## Home sleep test (HST)

Two ambulatory recordings were performed at home, using a ResMed machine (ApneaLinkTM Plus, version 9.00, ResMed), one for the baseline and another one for the outcome with the MAD. The following channels were recorded: thoracic respiratory effort, airflow (oronasal cannula) and oximetry. The body position was determined by means of a position sensor that could differentiate the upright, left side, right side, prone, and supine positions. The analysis was performed by a trained sleep physician certified by the Spanish society of sleep medicine. The HST recordings were scored manually, and respiratory, oximetry and positional outcome variables were obtained by a single and calibrated respiratory technician, following the criteria of the American Academy of Sleep Medicine [15].

## Epworth sleepiness scale (ESS)

The Epworth Sleepiness Scale (ESS) is a screening tool and questionnaire, validated in adults, consisting of eight questions. The questions are based on eight different situations in which patients can fall asleep. Situations are, for example, sitting and reading, watching television, talking with someone else, after eating, etc. Answers are rated from 0 to 3, where 0 is no chance of dozing off and 3 is high chance of dozing. The eight values are added together, which can give a total score of 0 to 24. Patients are sleepy when the ESS score is higher than 10. The higher the ESS value, the higher the subjective average for that person's daytime sleepiness.

## Side-effects

The questionnaire regarding possible side-effects included questions during MAD treatment. Patients were asked to indicate whether or not and which side-effects occurred:

1) Dry mouth sensation,

2) Increased salivation at night,

3) Muscle pain,

4) Sounds at the temporomandibular joint,

5) Changes in dental occlusion (no change, slight change or permanent significant changes),

6) Overall satisfaction with the treatment (very satisfied, somewhat satisfied or dissatisfied).

## Outcome variables

The primary outcome variables for this study were for the primary aim: AHI. Secondary outcome variables were the oxygen desaturation index, excessive daytime sleepiness, self-reported adherence, and side-effects.

## Statistical analysis

A group of 31 subjects were studied. A polygraphy was performed with and without the device in the mouth. The difference between the AHI without and with a MAD was calculated and a comparison was made by means of T-tests for the data with normal distribution.

These data are presented as mean ± SD. Furthermore, in some cases the maximum and minimum measured values are also presented. All statistical tests are compared with a 95% confidence interval. P-value results below 0.05 are considered statistically significant (Figure 2).

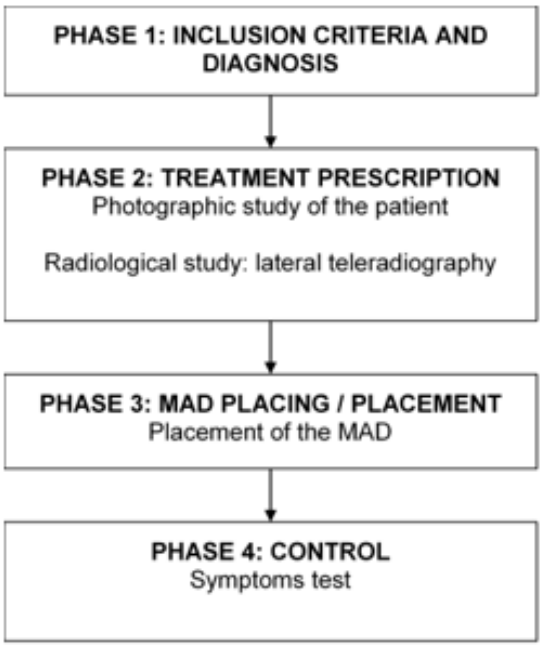


**Figure 2:** Phases of the Clinical Study.

## Results

The AHI is available for 31 patients (28 men and 3 women). The mean age of men is 52 SD 9.75 with a maximum age of 75 and a minimum age of 30. The mean age of women is 48 SD 8.72 with a maximum and minimum age of 54 and 38 respectively. Overall, the mean age is 52 SD 9.63 with a maximum age of 75 and a minimum age of 30. The mean body mass index of the patients was 28.8 (SD, 4.1; range, 22–37) kg / m2. For this study, the mean position after the titration procedure of the MAD was 70% (range, 60% - 90%) of the maximum protrusion. This corresponds to a mean protrusion value of 7.5 mm (SD, 1.0; range, 5mm- 9mm).

A pretreatment polygraphy was performed with a mean AHI value of 27SD 16.6 events per hour and a post-treatment polygraph with a mean AHI result of 6.6SD 5.0 events per hour (Z = 1.96; P = > 0.0001). All subjects showed improvement in AHI with zero exceptions. The use of the device represents an average reduction of 19.58 events per hour, which represents a 71% reduction in AHI. (Table 1) shows the AHI values before and after the treatment, as well as the reduction percentage of AHI in each of the subjects.

**Table 1:** AHI pretreatment, Post-treatment and Percentage of AHI Reduction in each of the Subjects.

| | AHI Pre | AHI Post | % Decrement |
|---|---|---|---|
| **1** | 17,3 | 3,8 | 78% |
| **2** | 32,6 | 4,6 | 86% |
| **3** | 45,3 | 8,6 | 81% |
| **4** | 14,5 | 1,8 | 88% |
| **5** | 14,9 | 1,9 | 87% |
| **6** | 35 | 7,6 | 78% |
| **7** | 14,2 | 3,5 | 75% |
| **8** | 12,1 | 3,4 | 72% |
| **9** | 63,1 | 14 | 78% |
| **10** | 22,7 | 4,9 | 78% |
| **11** | 49,3 | 12,4 | 75% |
| **12** | 14,8 | 3,2 | 78% |

| | | | |
|---|---|---|---|
| **13** | 22,4 | 8,6 | 62% |
| **14** | 51,4 | 16,4 | 68% |
| **15** | 8,3 | 1,6 | 81% |

| | AHI Pre | AHI Post | % Decrement |
|---|---|---|---|
| 16 | 39,9 | 22,2 | 44% |
| 17 | 45,2 | 4,2 | 91% |
| 18 | 24,8 | 15,3 | 38% |
| 19 | 12,5 | 3,1 | 75% |
| 20 | 20 | 6,5 | 68% |
| 21 | 17,4 | 2,8 | 84% |
| 22 | 47,3 | 6,3 | 87% |
| 23 | 11,8 | 3,9 | 67% |
| 24 | 17,8 | 1,9 | 89% |
| 25 | 12,8 | 5,4 | 58% |
| 26 | 11,8 | 5,2 | 56% |
| 27 | 6,4 | 2,1 | 67% |
| 28 | 35,9 | 7,5 | 79% |
| 29 | 46,8 | 7,8 | 83% |
| 30 | 58 | 12 | 79% |
| 31 | 11,2 | 2,3 | 79% |

These AHI values show that in 67.7% of patients (21) there is a reduction of more than 75% of the events per hour. On the other hand, there is a reduction of events per hour close to 50% in 93.5% of patients (29). Grouping the results considering the severity of AHI, in the pretreatment 12 patients (38.7%) have mild apnea, 7 moderate apnea (22.6%) and 12 severe apnea (38.7%). Once the control test was carried out, 16 patients (51.6%) did not have OSA, 12 had mild sleep apnea (38.7%) and 3 had moderate sleep apnea (9.7%). The values also show that none of the MAD patients have severe sleep apnea. (Figure 3) shows the number of patients grouped according to the severity degree of OSA. The results for the diagnosis without MAD are in blue and the results for the diagnosis with MAD are in green.

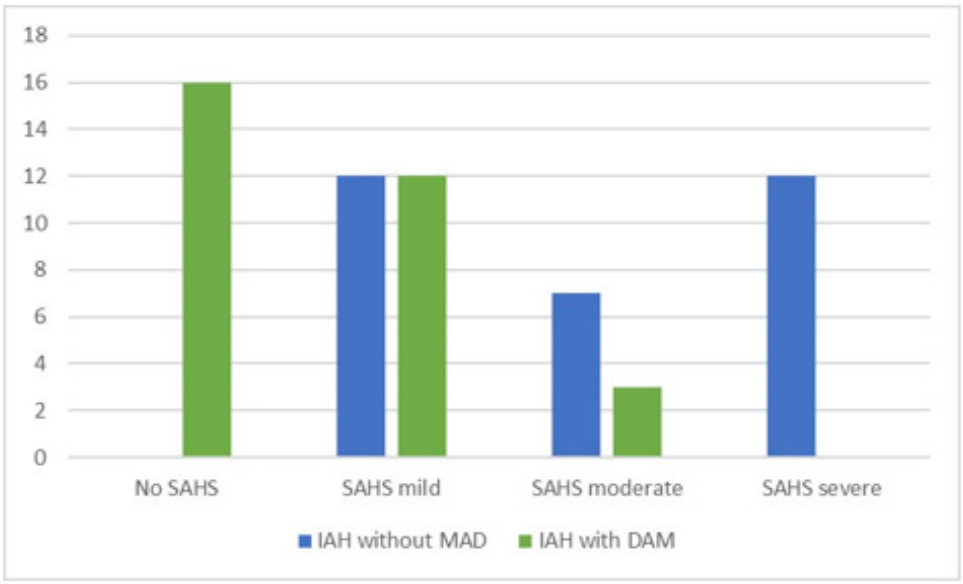


**Figure 3:** Patients Grouped According to the Severity Degree of SAHS with and without MAD.

Oxygen saturation has been analyzed in pre and post treatment diagnostic tests. According to the values obtained, the mean oxygen saturation level is 91% without MAD and 93% with MAD. On the other hand, the time that patients spend with oxygen saturation below 90% has also been analyzed. In the diagnosis without MAD, patients spend a mean value of 60.7 minutes (SD 64.8) with an oxygen saturation level lower than 90%, with a maximum value of 262 minutes and a minimum value of 0 minutes. In the diagnosis with MAD, the mean of the values obtained is 23.3 minutes (SD 26.7) with a maximum value of 114 and a minimum of 0 minutes. These results are shown in (Figure 4), where the vertical line represents the range and the point represents the mean for the analyses with and without MAD. It is observed that, when using MAD, this time decreases more than 50% in 67.7% of patients and more than 75% in 32.3% of patients.

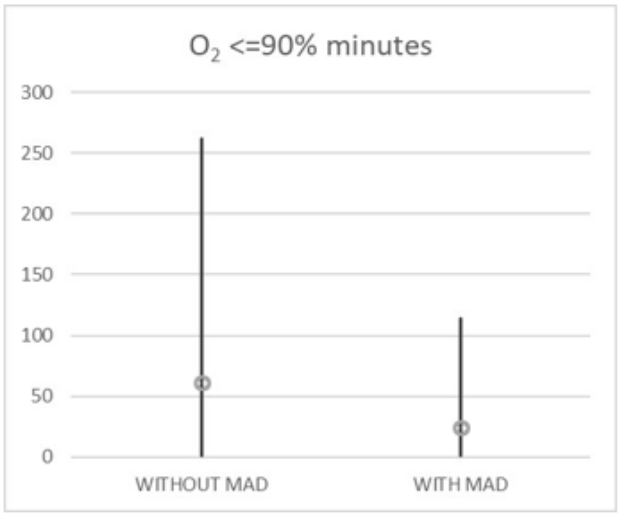


**Figure 4:** Range of Values (vertical line) and Mean Value (point) of Time in Minutes with Oxygen Saturation below 90% without and with MAD.

The values show that there is a reduction of 58% of time with a saturation level below 90%.

In the case of daytime sleepiness in patients, the improvement in the Epworth test score has been studied. In the study without MAD, the mean value is 13 (SD 1.83) with a maximum value of 16 and a minimum of 10. The results obtained with MAD are a mean value of 6.6 (SD 2.9) with a maximum of 12 and a minimum of 1. In general, an improvement of 7.5 points (SD 3.4) is achieved, which represents an improvement of 58% compared to the score without MAD. In 32.3% of patients (10) the Epworth score is reduced by 75% and in 67.7% (21) it is reduced by more than 50%. (Table 2) shows these results.

**Table 2:** Maximum, Minimum, Mean, Median and Standard Deviation Values for the Epworth Test without and with MAD.

| | WITHOUT MAD | WITH MAD |
|---|---|---|
| Maximum | 16 | 12 |
| Minimum | 10 | 1 |
| Mean | 12,81 | 5,26 |
| Median | 12 | 5 |
| Standard deviation | 1,83 | 2,90 |

Finally, some factors related to adaptation to the MAD have been analyzed. The findings are that 9% (3) of the patients notice an increase in salivation, 13% (4) experience a dry mouth sensation and 6% (2) experience an increase in muscle tension. None of the patients had temporomandibular join (TMJ) sounds or occlusion changes. These results are shown in (Figure 5). Regarding patients´ general satisfaction, 93.5% of the subjects (29) feel very satisfied with the treatment and 6% (2) are satisfied.

## Discussion

This study evaluates the efficacy of a new MAD model that limits and controls the vertical opening of the jaw and maintains its advancement during sleep. The results of the 31 patients treated show a significant reduction in AHI, an improvement in the mean saturation levels and a reduction in time with a saturation level below 90%, as well as an improvement in the Epworth test, few adverse effects and a good evaluation by the patients. The AHI went from 27 (SD 16.6) events per hour without MAD to 6.6 (SD 5.0) events per hour with MAD. The reduction in AHI was higher than 75% of events per hour in 67.7% of patients (21) and 50% in 93.5% of patients (29). Finally, it is observed that none of the patients with MAD present severe apnea. The mean oxygen saturation level

was 91% without MAD and 93% with MAD and a mean of 60.7 minutes (SD 64.8) with a saturation level below 90% without MAD and a mean of 23.3 minutes (SD 26.7) with MAD, which means a significant reduction in desaturation time below 90% and a higher level of mean saturation.

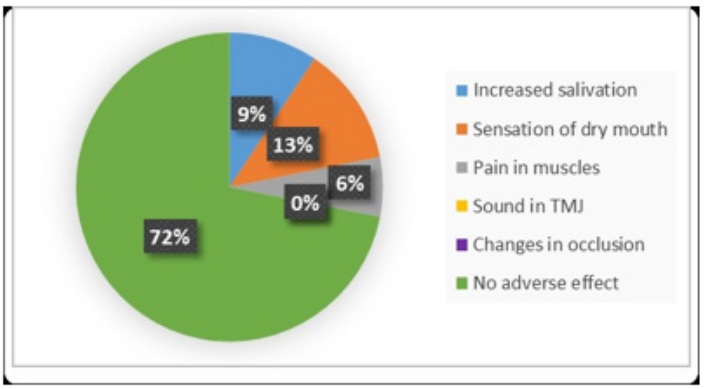


**Figure 5:** Adverse Effects when using the MAD.

The treatment success rate in this analysis (93.5% >50%; 67.7%>75%; 52% AHI<5), is consistent with previous studies [13, 16, 17]. To improve sensitivity and clinical relevance, we performed analyses using three different AHI thresholds:

1. Reduction >50% of AHI;
2. Reduction > 75% AHI [13];
3. AHI <5. A 50% reduction in the AHI was achieved in 91% of participants compared to 67% in the Attali study [17].

The reduction in AHI >75% in this study was 67.7% of patients, similar to Milano (67.39%) using vertical elastics [13]. The AHI findings were consistent with the maintenance of good OSA control, reduction in ESS, and quality of life. An AHI <5/h used to evaluate efficacy of CPAP [41] was achieved by 52% of patients during mandibular reposition device (MRD) therapy, compared to 30% achieved by Attali [17]. In this study, 93.5% of patients had an AHI <15/h, which has shown association with/which has been associated with reduction in the risk of new-onset hypertension [18].

Studies of other devices on the market show a reduction in AHI for 40-60% of cases. This study shows better results for the Ortho-Apnea NOA device, with a 97% response to treatment. Analyzing the results of the reduction in AHI achieved with the NOA device, it is observed that in 90% of the cases (28 out of 31) the AHI value is in a range between no apnea and mild apnea (0> AHI> 15). Furthermore, in 51.5% of the cases (16 out of 31) its value is reduced below 5, for which it is considered that there is no apnea.

The results of this study show good clinical effectiveness and minimal adverse effects, with 94% of the patients being very satisfied. The Epworth test score has a value of 13 without MAD and 6.6 with MAD, which represents an improvement of 58%. Similarly, in the Atalli study, 81% of patients with MAD had an ESS score <10, going from 11 at the baseline to 7 with MAD. Finally, some adaptation factors related to MAD have been analyzed and mild transient adverse effects have been observed such as increased salivation 9% (3 subjects), dry mouth sensation 13% (4 subjects) and increased muscle tension 6% (2 subjects). In no case were there TMJ sounds or occlusion changes. Regarding general patient satisfaction, 93.5% of the subjects (29 subjects) are very satisfied with the treatment and 6% (2 subjects) are satisfied.

The device bases its action on maintaining both the jaw and the ioid/hyoid bone in a forward position during sleep, avoiding the backward rotation of the jaw and the receding of the tongue towards the airways [19]. In this way, it is possible to mechanically open the airways, avoid closure and act as a retainer of the jaw and tongue [20]. Kurtulmus, et al. [3] pointed out that the action of a MAD is based on stabilizing the jaw, tongue and hyoid bone to avoid collapse during sleep. One of the strengths of the design of a MAD is the stabilization of the jaw and the control of mouth opening during sleep [13, 14]. Devices that incorporate a mechanism for limiting or controlling mouth opening have shown greater efficacy than those devices that do not. Milano, with the use of elastics, increased the effectiveness of a device from 36% to 67% [13]. The control of jaw movements during sleep while wearing a MAD has proved to be important, as uncontrolled mouth opening could cause posterior rotation of the jaw leading to more posterior positions, narrowing the upper airway and increasing resistance of the jaw to air flow [7, 21]. The design of the NOA device [10, 11] is focused on this particular point, positioning the jaw in an advanced position and ensuring that when the patient sleeps, the device maintains that position at any time, limiting and controlling mouth opening. We believe that this is one of the key points in the effectiveness of this device and the results obtained in this study.

The facial biotype plays an important role in the pathophysiology of OSA as well as the outcome of MAD treatment [7, 22, 23]. Studies

have shown that certain mandibular morphologies (retrognathia, dolichofacial growth pattern) predispose to OSA [23]. Other studies find associations between mandibular morphology and the probability of a positive response to MAD treatment [22, 24]. A recent study on mandibular kinematics has helped to explain the reason for these findings with the analysis of mandibular kinematics and the prediction of mandibular movement and their differences among subjects [7]. These authors conclude that the prediction of the movement of different mandibular points by means of the mathematical model presented in this work could allow greater customization in the design of mandibular advancement devices. The design of these devices should include an individual analysis of the patient's anatomy [10, 11] to obtain a personalized and more effective design. The NOA device meets these customization requirements based on the individual analysis of each patient's anatomy and, for this reason, we believe that this can be another key element in the good results obtained in this study. These results demonstrate that the Ortho-Apnea NOA device has a very good efficacy in reducing apnea events and that there is an improvement when using the device.

This study has the limitation derived from the subjective measures obtained from the patients' questionnaires, since it was not possible to objectively measure some variables of the study. Another limitation is the one-year follow-up and the unknown long-term effectiveness of the device.

## Conflict of Interest

No Conflicts of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

## Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Informed Consent

Informed consent was obtained from all individual participants included in the study.

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