Title: SEVERE OBSTRUCTIVE SLEEP APNEA TREATMENT WITH ORAL APPLIANCE: THE IMPACT ON OBSTRUCTIVE, CENTRAL AND MIXED EVENTS

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Abstract:

**Purpose** Evaluate the effectiveness of two types of oral appliance (OA) in the treatment of severe obstructive sleep apnea syndrome (OSAS) and their impact on the reduction of obstructive, central and mixed apneas.

**Methods** Forty-eight patients suffering from severe OSAS with a history of nonadherence to positive airway pressure therapy were treated with OA (lingual orthosis and combined orthosis). Polysomnography exams were performed before and after treatment. Computed tomography and cephalometric radiography were requested for all patients to evaluate the titrated position of the OA and the airspace obtained. Statistical tests used the Minitab, version 17, program. The level of statistical significance was 5%.

**Results** Before treatment the mean AHI was 56.3 ± 19.1 events/hour. It decreased to 8.1 ± 5.2 after the OA titration (p < 0.001). There was a significant reduction in obstructive events from 43.0 ± 20.2 events/hour to 7.1 ± 4.6 events/hour (p < 0.001). The reduction in central events after OA treatment was also significant (from 5.1 ± 9.3 events/hour to 0.8 ± 1.9 events/hour p ≤ 0.001) whereas mixed events decreased from 6.4 ± 9.5 events/hour to 0.1 ± 0.3 events/hour (p ≤ 0.001). The minimum oxygen saturation also showed significant improvement after treatment (p ≤ 0.001). There was no statistically significant difference between both OA with respect to central events (p = 0.22) or mixed events (p = 0.98).

**Conclusion** The treatment was effective in reducing obstructive events which were evaluated through the AHI and minimum oxygen saturation. The oral appliances also normalized central and mixed events among patients with severe OSAS.

**Key-words** Oral appliances, Obstructive sleep apnea, Sleep disordered breathing, Orthotic Devices
Introduction

Sleep-related breathing disorders are divided into four main categories: central sleep apnea (CSA), obstructive sleep apnea (OSA), hypoventilation disorders related to sleep and hypoxemia disorders related to sleep [1].

CSA is a disorder characterized by repetitive cessation or reduction of both the airflow and the respiratory effort during sleep [2]. When symptomatic it is called central sleep apnea syndrome (CSAS) and appears to be more prevalent among elderly people, males or persons who present certain medical or neurological comorbidities [3, 4].

Unlike CSA, OSA is characterized by a respiratory effort against a closed upper airway, showing that patients with OSA have anatomical or functional deficits in the upper airway [5]. When associated with clinical signs and symptoms such as excessive daytime sleepiness, cognitive impairment, decreased quality of life and increased cardiovascular morbidity, it is called obstructive sleep apnea syndrome (OSAS) [6-8].

In clinical practice patients, rarely present pure OSAS, and most of them exhibit some central and/ or mixed events. The coexistence of more than one type of apnea disorders indicates more complex underlying disorders than just the increased upper airway resistance. In fact, unstable respiratory control has been implicated in the pathogenesis of both central and obstructive sleep apnea [5].

The treatment of sleep-related breathing disorder is mainly based on greater ventilation during sleep with positive airway pressure (PAP) devices [9]. Medication is rarely used, but patients suffering from CSAS may need it [1]. Oral appliances (OAs) are recommended only for OSAS treatment. The literature points out three major groups of intraoral appliances: the soft palate elevators, tongue-retaining devices and mandibular advancement devices. The latter category is by far the most currently used type of oral appliance [10]. According to the American Academy of Dental Sleep Medicine (AADSM) the term ‘oral appliances’ refers to mandibular advancement devices (MADs), since these are the most effective and widely used devices in clinical practice. Nevertheless, such definition will be reviewed and revised as new methods and evidences become available [11].

Although OAs are indicated only for treatment of obstructive sleep apnea, a study published in 1991 showed two cases of patients with central apnea treated with OAs [12]. The pathophysiology of central sleep apnea syndrome is not fully understood,
but the obstruction of the upper airway might be a possible correlated cause [13]. The relationship between central sleep apnea and partial obstruction of the upper airways was suggested in a study in which not only did CPAP improve respiratory events during sleep but also eliminated central sleep apnea events in patients who had narrow upper airways. However, CPAP did not present positive effects on central apnea patients with brainstem lesions [14].

Innovations related to OAs and the OSA treatments have been discussed in the literature [15, 16]. This novel type of oral appliance (the lingual orthosis proposed by Caram) was first described in the literature in 2013 and it was designed to prevent the obstruction of the oropharynx through a tongue control mechanism [16]. The appliance can be used in combination with or as an alternative to the conventional MADs and it was developed to address limitations of mandibular advancement devices, such as the occurrence of temporomandibular disorders, teeth absence, severe periodontal problem, patients with extensive prostheses, patients newly discharged from orthodontic appliances, young patients (less than 19 years old) [15]. Although observed side effects include: difficulty in swallowing, gagging, vomiting and injury to the mucosa, the lingual orthosis has shown satisfactory results in cases of OSAS and has improved obstructive, mixed and central events [15,16].

Lingual control devices may have a mechanism similar to the lingual retainers, such as neutralizing genioglossus muscle activity [17]. In addition, a lingual control mechanism based on proprioceptive information acquired with tongue surface receptors can help patients to maintain a tongue position preventing oropharyngeal obstruction and, consequently, preventing OSA [15].

The aim of this study was to evaluate the effectiveness of the OAs using Caram’s lingual and combined orthoses in the treatment of OSAS and its impact on the reduction of the obstructive, central and mixed apneas among patients suffering from severe OSAS.
Material and Methods

Participants

Forty-eight patients referred by sleep specialists for dental clinic specialized in the treatment of OSAS with OAs were recruited for the study. All selected patients had a history of nonadherence to PAP. To be included in the study the patient had to present a diagnosis of severe obstructive sleep apnea-hypopnea syndrome (AHI above 30 events/hour) with central and/or mixed components. No cutoff values were established for the minimum number of central or mixed apneas for patients to be included in the research. The main complaints were: snoring, daytime sleepiness and mood swings. The sample presented severe OSAS (AHI above 30 events/hour), with central and/or mixed components. These individuals were referred by sleep medicine centers in the city of Belo Horizonte, southeastern Brazil. Informed consent forms were obtained from all the participants.

Research instruments

- Polysomnography

The diagnosis of OSAS was accomplished through a polysomnography (PSG) exam performed in a sleep laboratory. Polysomnography included electroencephalography recording, right and left electro-oculogram, electromyography of the genioglossus and tibialis anterior muscle, electrocardiogram and oxygen saturation measured by a finger pulse oximeter. The respiratory variables were recorded, including the nasal air flow by means of a thermistor and a pressure nasal cannula. Respiratory effort was measured using a respiratory inductance plethysmography. Snoring was recorded by a microphone and body position was monitored using a piezoelectric sensor.

Polysomnographic recordings were scored according to the guidelines of the American Academy of Sleep Medicine [18]. Obstructive apnea was defined as a ≥10-second cessation of airflow on the pressure nasal cannula, associated with an oronasal thermal sensor. Hypopnea was defined as a ≥50% reduction in airflow, or a reduction of
airflow <50% on the nasal pressure cannula accompanied by a decrease ≥3% in oxygen 
saturation (SpO2) or an arousal. Central apnea was defined by the absence of respiratory 
effort throughout the entire period of absent airflow; and mixed apnea was defined by 
the onset of the respiratory event with no airflow and no respiratory effort during the 
first half of the event and, at the second half of the event, the absence of airflow 
persisted even after a resumption of inspiratory effort. The minimum SpO2 (SpO2 
 nadir) was also recorded [18].

All patients were subjected to two full night polysomnography recordings: the 
first PSG was performed to diagnose sleep-related breathing disorders, it was the 
baseline recording. Once the OA was optimally titrated resulting in symptoms 
resolution or the titration had achieved individual tolerance, the patient was referred to 
the sleep laboratory for polysomnography monitoring with the OA in situ. These exams 
allowed the therapeutic effect of the titrated OA to be objectively assessed by 
comparing the PSG results.

Complete response to the treatment (treatment success) was defined by an AHI 
cut-off values of < 5/h or < 10/h. Sleep and respiratory parameters were recorded during 
sleep at baseline and the follow-up visit using PSG recordings which were manually 
scored according to the American Academy of Sleep Medicine (AASM) guidelines 
[18]. The therapy was considered suboptimal when AHI decreased < 50% and/or patient 
presented persistent symptoms.

- Oral appliance

The treatment for controlling obstructive apnea was performed by OA using the 
lingual orthosis proposed by Caram [16]. This technique is applied through two devices: 
the first is designated as ‘lingual orthosis’ or ‘spring’ and it consists of a jaw fitting 
single plate in which is attached an acrylic lingual control device (Figure 1). The second 
device consists of an acrylic block, articulated by means of helical vestibular arcs, 
providing mandibular advancement associated with direct mechanical action on the 
tongue [16]. This OA is designated as ‘combined orthosis’ (Figure 2).

The combined orthosis was used to enhance the spring action through the 
protrusion mechanism and stabilization of the jaw. The patients were not randomly 
allocated to the treatment with lingual orthosis or combined orthosis. If the patient had a
history of temporomandibular disorders (TMD) or if there was no minimum number of
teeth for retention of the combined mandibular advancement device, the patient was
referred to treatment with the lingual orthosis. Thirty-six patients were treated with the
combined orthosis and twelve with the lingual orthosis. During titration, the mandibular
advancement and the lingual control device were adjusted according to the sleep dentist
criteria in order to provide the best risk-benefit ratio.

The oral appliance titration protocol consists of an initial mandibular
advancement set to advance the mandible between 50% to 70% of the patient’s
maximum protrusion. After two weeks, if the patient presents no signs or symptoms
related to pain or discomfort, the appliance is titrated again until it reaches 80% of
maximum protrusion. Once this titration has been made and the patient adhered/adapted
to the OA treatment, a second phase is started which consists of attaching a spring to the
body of the oral device.

The titration of the spring is done weekly or according to the patient’s adaptation
(biweekly or monthly). Initially, a small spring is placed and juxtaposed to the palate,
and during the titration it undergoes a process of stretching in which it is directed
towards the base of the tongue. The device is composed of two wires (caliber 1.0 mm)
which are stretched (titrated) in a ratio of 1 to 2 mm during each dental appointment.
Approximately 2 months after the oral appliance has been fitted, the wires are fully
extended and are supporting the acrylic retainer which must be in close contact with the
base of the tongue. In most cases this position achieved by the combined orthosis is
sufficient to treat patients with mild and moderate OSAS in whom solely the
mandibular advancement has no effect or who presents persistent snoring even after the
mandibular advancement.

When treating cases of severe OSAS, after the wire caliber 1.0 mm is completely
distended, it is replaced by a wire caliber 1.2 mm. The titration process continues to be
gradually conducted aiming to place the acrylic retainer towards the oropharynx and
pressuring the base of the tongue. The titration limit is achieved when the wire caliber
1.2 mm is fully extended or according to the patient’s tolerance. During the treatment, a
monitoring polysomnography is requested by the dentist to check if the respiratory and
sleep parameters improved. The exam is requested when the patient reports no
symptoms related to the OSAS.
Imaging

In order to evaluate the titrated position of the OA and the airspace obtained using the OA both computed tomography and cephalometric radiography were requested for all patients (Figures 3 and 4). The images were requested after the oral appliances final adjustments aiming to evaluate the positioning of the spring in relation to the oropharynx tissues and avoid possible traumas to the tissues.

Statistical analysis

Statistical tests used univariate analysis by Minitab 17 © program. In order to verify the requirements for parametric or nonparametric statistics Anderson Darling test was used. The level of statistical significance was 5%. Mean and standard deviation were the measures used for data following normal distribution.

Comparisons between parametric and dependent continuous variables used paired t-test, and in cases of non-parametric data it was used the Wilcoxon test. Comparisons between parametric and independent continuous variables used the two-sample t-test, and non-parametric data was compared by Mann-Whitney test.

Results

Forty-eight patients took part in this study. The sample’s age varied from 21 to 84 years (mean ± SD age was 53.7 ± 10.8 years), being 6 women and 42 men. At least two months were required to achieve the optimal OA titration in 86% of participants; and 25% of the patients required additional titration after the first monitoring PSG. The mean total amount of mandibular advancement in the combined orthosis was 7.3 ± 2.1 mm. The time interval between fitting the OA and the monitoring PSG exam with the OA in situ was 5 ± 3 months.

When comparing the final AHI with the baseline parameters, all patients reduced their AHI by more than 50%, and the majority of them presented a complete response to the treatment (72.9% achieved an AHI <10/h and 35.4% achieved an AHI <5/h). Before treatment the mean AHI of the sample was 56.3 ± 19.1 events/ hour and it decreased to 8.1 ± 5.2 after the OA titration (p ≤0.001). There was a significant reduction in obstructive events from 43.0 ±20.2 events/ hour to 7.1 ±4.6 events/ hour (p ≤0.001).
The reduction of central events after OA treatment was also significant when compared to baseline events (from 5.1 ± 9.3 events/hour to 0.8 ± 1.9 events/hour; p < 0.001) whereas mixed events decreased from 6.4 ± 9.5 events/hour to 0.1 ± 0.3 events/hour (p < 0.001). The minimum oxygen saturation also showed significant improvement after OA treatment (71.0 ± 13.9 to 84.7 ± 4.9, p < 0.001). These results are summarized in Table 1.

The baseline AHI among patients who used lingual orthosis and combined orthosis was 57.4 ± 18.4 events/hour and 53.0 ± 21.8 events/hour, respectively. After treatment, a significant reduction in the AHI was observed among patients with lingual orthosis (8.4 ± 5.5 events/hour) and with the combined device (7.0 ± 4.2 events/hour; p = 0.42). Table 2 shows that there was no statistically significant difference between both devices with respect to the AHI <5 and AHI <10 (p > 0.05).

Central events decreased from 3.8 ± 6.7 to 0.5 ± 1.3 events/hour among patients using lingual orthosis and among patients using the combined orthosis it decreased from 5.6 ± 10.0 to 0.9 ± 2.0 events/hour. There was no statistically significant difference between both OAs (p=0.22). With respect to mixed events, after treatment both orthosis showed significant improvements and there was no statistically significant difference between the two types of devices (p=0.98) (Table 2).

Treatment with both devices significantly improved minimum oxygen saturation from 71.0 ± 13.9 to 84.7 ± 4.9 (p < 0.001), but there was no statistically significant difference between the two types of devices (p > 0.05) (Table 1 and Table 2). In one case, the AHI was reduced from 64.5 events/hour to 19.5 events/hour, the central events increased from 0.2 to 2.8 events/hour and mixed events slightly decreased from 9.8 to 7.0 events/hour. In a single case, in which the AHI decreased from 66.4 to 16.8 events/hour, there was a simultaneous worsening in central apneas, which increased from 0.2 to 3.2 events/hour, and mixed apneas that increased from 0 to 1.8 events/hour.

Discussion

In this study, the sample consisted of patients noncompliant with CPAP who had severe OSA. The sample presented predominantly obstructive apnea events, but they also suffered from central and mixed apnea events. There was no control group, but the
main objective of the present research was to evaluate the short-term effectiveness of
the OA using Caram’s lingual orthosis and combined orthosis in patients with severe
OSA who dropped out the CPAP treatment. Treatment with these OAs aimed to
improve obstructive apneas, but the results also showed an equally effective control of
mixed and central events, as well as in the minimum oxygen saturation.

The phenotypes that have current treatment options for central sleep apnea are
upper airway collapsibility, chemoreflex activation level and sleep fragmentation
propensity [19]. We believe that the results of the present study using Caram’s lingual
and combined orthosis may have been achieved due to the patient’s collapsibility
phenotype.

Thirty-six patients used the combined orthosis which was composed of a lingual
control device associated with plaques embedded in the upper and lower arches for
mandibular advancement. The use of a combined orthosis aimed to potentiate the action
of the spring mechanism allowing the protrusion and stabilization of the mandible in
order to maintain a patent upper airway during sleep. Radiographs showed a greater
increase in the upper airway with the combined orthosis. However, the lingual orthosis
showed a higher number of patients with AHI <5 and AHI <10, although this difference
was not significant. After treatment both devices, lingual and combined orthoses,
significantly improved the AHI. Central and mixed events also improved significantly
with both OAs, with no statistically significant difference between them.

Mandibular advancement devices are the most widely used type of oral
appliance and those with greater scientific evidence of effectiveness, but as more
evidence becomes available, new devices may be considered in the treatment of OSAS.
Furthermore, clinical judgment (such as the individual requirements of patients that may
dictate alternative methods) must be respected. The definition established by AADSM
related to mandibular advancement appliances should serve as a clinically relevant
standard for the selection of oral appliances by sleep dental practitioners and as a guide
to facilitate development of the next generation of OAs design [11].

The intraoral devices with lingual controls used in this study were developed by
one of the authors (JMC) and were designed to prevent further slip of the tongue and the
consequent oropharynx obstruction. Devices using similar lingual control mechanisms
have already been discussed in the literature [15].
The OAs using Caram’s lingual technique have a lingual control accessory or "spring" that allows an activation to ensure complete resolution of obstructive respiratory events [16]. Adjustments in the spring depend on each case. It may be mild and limited up to the base of the tongue, or may be more vigorous and deep enough to reach the area of the epiglottis. Clinical success is evaluated by a lack or reduction of snoring and improvements in the sleep quality. Polysomnography is performed to objectively evaluate the OAs effectiveness. It is conducted after a positive report of the patient with respect to his symptomatology. The average period of treatment to achieve clinical success is 4 to 6 months.

In this study, some patients presented worsening in central and mixed events after the treatment. We realized that patients with mixed apneas tend to respond more easily to the obstructive apnea control, even in the few cases in which the central events worsen. By analyzing the possible causes of this worsening we could not find any explanation related to the clinical aspects of OAs. All OAs were checked a week before the PSG examination.

Treatment-emergent central sleep apnea has been described especially after the positive airway pressure (PAP) therapy. Moreover, it is important to be aware that central apneas may also arise from treatment with OAs [20]. However, these devices have been used with reasonable success in patients with complex sleep apnea who are intolerant to PAP. Residual AHI can occur with OAs requiring adjuvant therapy. Once OAs are less likely to induce hypocapnia but treatment of obstructions is less precise, ‘cocktails’ have been currently used and they include oral appliance + benzodiazepine or acetazolamide, or supplemental oxygen [19].

In our clinical practice, we observe that the polysomnography of patients with OSA often do not exhibit central and mixed events in the reports. We believe that this happens once scores of respiratory events in patients with sleep apnea have traditionally been directed to an obstructive phenotype, even with the update of the 2007 American Academy of Sleep Medicine guidelines, which has criteria for scoring central hypopneas and short sequences of periodic breathing / Cheyne-Stokes respiration [21].

The rules for scoring respiratory events state that central hypopneas should not be marked in the presence of flow limitation, although the obstruction is a common feature of central events [19]. Direct visualization of the upper airway often shows collapse at the nadir of the cycle, even in polysomnographic "central" disease [22].
Expiratory pharyngeal narrowing occurs during central hypopnea, supporting the concept that the presence of flow limitation alone cannot be used to distinguish obstructive and central hypopneas [23, 24].

We consider that a score of central and mixed events in polysomnography is important not only to evaluate baseline events in sleep-related breathing disorders, but it should also be taken into consideration when analyzing the criteria used to estimate therapies success.

In the present study, there was a 100% response rate, which means that no patient discontinued the treatment. The side effects and possible treatment abandonment/ non-adherence were not analyzed. However, the main complaints pointed out by the patients related to the treatment were recorded and divided into 4 categories:

A) Swallowing difficulty. We understand that the swallowing physiology includes lifting the back of the tongue, which suffers a movement limitation due to the spring retainer. However, the tongue is a functional and elastic muscle capable of adapting to this restriction and it can develop alternative movements. After 2 weeks using the oral appliance, nearly 90% of the patients reported they were not having trouble swallowing (dysphagia). B) Gagging. This initial tongue restriction may cause an accumulation of saliva and it can trigger eventual gagging. In the present study, this side effect was rarely reported; C) Vomiting. It may emerge from a physiological cause such as an exaggerated gag reflex related to the appliance being placed deep into the throat and often happens just after fitting the oral appliance. This side effect is reported by nearly 80% of patients.

Furthermore, sometimes it is necessary to place the spring in a position far below the oropharynx and the deeper the appliance is placed, the more the patient may use the vomiting as a defense mechanism. All the side effects mentioned before may occur when initially fitting the oral appliance but they are transitory events; D) Injury to the mucosa. Although it is not supposed to happen, the spring may traumatize the tongue, palate and/or the throat tissues if the device itself or the appliance titration is incorrectly conducted. Therefore, it is of paramount importance an image (cephalometric radiograph) to verify the spring positioning.

Moreover, by analyzing the computed tomography and the cephalometric radiography the dentist can conduct a more detailed adjustment/titration, providing a perfect juxtaposition of the spring and the tongue retainer. In several cases, the
cephalometric radiography demonstrated that the space in the oropharynx had been reduced by the action of the spring. However, the result on PSG parameters did not worsen, probably due to the action of the spring preventing the tongue and soft palate falling back against the posterior pharyngeal wall, and thereby preserving the airway patency.

The present study has some limitations. Some patients underwent the baseline and after-treatment polysomnography in different sleep laboratories. However, the laboratories used the same polysomnographic parameters and the same guidelines of the American Academy of Sleep Medicine (AASM) for the elaboration of the reports, allowing the parameters standardization and comparison of results.

Furthermore, there was no control group and the participants were not randomized, therefore it is not possible to state whether the analyzed appliances improve treatment beyond mandibular advancement alone. Nevertheless, the main objective of the present study was to evaluate the efficacy of the lingual and combined orthoses in patients with severe OSAS who dropped out CPAP treatment and required mandatory treatment. Further studies, such as randomized clinical trials, should be conducted to compare this novel appliance to the existing mandibular advancement devices which have already proven their efficacy by the scientific evidence.

Conclusions

It was observed that treatments using Caram’s lingual and combined OAs were effective in reducing obstructive events which were evaluated through the AHI and minimum oxygen saturation. It was also observed a significant effectiveness in normalizing central and mixed events among patients with severe OSAS.

More studies are needed to better understand and clarify the relationship between obstructive, central and mixed events and the impact of OAs on sleep-related breathing disorders.

Funding

No funding was received for this research.
**Conflict 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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    appliance for the treatment of obstructive sleep apnea and snoring: a report of


Fig. 1 Caram’s lingual orthosis

Fig. 2 Caram’s combined orthosis

Fig. 3 (a) Baseline: the sagittal plane shows the close relationship between the soft palate and tongue. Note that both structures are in contact (white arrow) and oropharynx is narrow (black arrow), (b) The sagittal plane shows the change related to the soft palate and the tongue position when Caram’s lingual orthosis is in situ. It can be observed a space between both structures promoted by Caram’s lingual orthosis (white arrow), (c) The sagittal plane shows a change in the soft palate and tongue relationship after the lingual orthosis titration. It can be observed an increase in the oropharynx caliber (white arrow)

Fig. 4 (a) Baseline: the sagittal plane shows the soft palate and tongue in normal occlusion without the lingual orthosis, (b) shows the change related to the soft palate and the tongue position when Caram’s lingual orthosis is in situ, (c) The sagittal plane shows a change in the soft palate and tongue relationship when Caram’s combined orthosis is in situ. It can be observed an increase in the caliber of the oropharynx with both orthoses, but the increase was even higher when the combined orthosis was used.

Table 1 Polysomnographic respiratory parameters after lingual orthosis and combined orthosis titration

Table 2 Effects of lingual orthosis and combined orthosis on respiratory parameters
Table 1

<table>
<thead>
<tr>
<th></th>
<th>Baseline* (mean values)</th>
<th>After treatment* (mean values)</th>
<th>p</th>
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<tr>
<td>AHI</td>
<td>56.3 ±19.1</td>
<td>8.1 ±5.2</td>
<td>p ≤ 0.001</td>
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<tr>
<td>Obstructive events</td>
<td>43.0 ±20.2</td>
<td>7.1 ±4.6</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>Central events</td>
<td>5.1 ±9.3</td>
<td>0.8 ±1.9</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>Mixed events</td>
<td>6.4 ±9.5</td>
<td>0.1 ±0.3</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>Apnea</td>
<td>19.6 ±17.9</td>
<td>1.6 ±2.4</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>Hypopnea</td>
<td>23.1 ±17.9</td>
<td>5.5 ±4.3</td>
<td>p ≤ 0.001</td>
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<tr>
<td>SpO2</td>
<td>71.0 ±13.9</td>
<td>84.7 ±4.9</td>
<td>p ≤ 0.001</td>
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*Combine results for both oral appliances (combined orthosis and lingual orthosis)

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Combined orthosis* (n=36)</th>
<th>Lingual orthosis* (n=12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline AHI</td>
<td>57.4 ±18.4</td>
<td>53.0 ±21.8</td>
<td>0.49</td>
</tr>
<tr>
<td>AHI after treatment</td>
<td>8.4 ±5.5</td>
<td>7.0 ±4.2</td>
<td>0.42</td>
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<tr>
<td>Percentage of patients with AHI &lt; 5 (after treatment)</td>
<td>32.4</td>
<td>41.7</td>
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<tr>
<td>Percentage of patients with AHI &lt; 10 (after treatment)</td>
<td>70.3</td>
<td>75.0</td>
<td>0.53</td>
</tr>
<tr>
<td>Baseline obstructive events</td>
<td>42.5 ±19.0</td>
<td>44.8 ±23.4</td>
<td>0.73</td>
</tr>
<tr>
<td>Obstructive events (after treatment)</td>
<td>7.3 ±4.9</td>
<td>6.3 ±3.9</td>
<td>0.49</td>
</tr>
<tr>
<td>Baseline central events</td>
<td>5.6 ±10.0</td>
<td>3.8 ±6.7</td>
<td>0.45</td>
</tr>
<tr>
<td>Central events (after treatment)</td>
<td>0.9 ±2.0</td>
<td>0.5 ±1.3</td>
<td>0.22</td>
</tr>
<tr>
<td>Baseline mixed events</td>
<td>7.5 ±10.7</td>
<td>3.2 ±2.8</td>
<td>0.27</td>
</tr>
<tr>
<td>Mixed events (after treatment)</td>
<td>0.1 ±0.3</td>
<td>0.0 ±0.1</td>
<td>0.98</td>
</tr>
<tr>
<td>Baseline minimum oxygen saturation</td>
<td>70.9 ±15.1</td>
<td>71.3 ±9.5</td>
<td>0.51</td>
</tr>
<tr>
<td>Minimum oxygen saturation (after treatment)</td>
<td>84.7 ±4.6</td>
<td>84.9 ±5.9</td>
<td>0.53</td>
</tr>
</tbody>
</table>

*mean values