# 2013; 17: 385-391

# OSAS treatment with oral appliance: assessment of our experience through the use of a new device

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**Abstract.** – BACKGROUND: Obstructive sleep apnea syndrome (OSAS) is defined as repeated episodes of obstruction of the upper airway and oxygen desaturation of the arterial hemoglobin. OSAS is associated with loud snoring, excessive daytime sleepiness, cardiovascular and neurocognitive disease, increase risk of road accidents.

AIM: The aim of this study is to evaluate nonsurgical therapy for OSAS using a mandibular advancement device (MAD) that provides for lower jaw protrusion and for an adequate vertical opening, that allows for greater airflow.

MATERIALS AND METHODS: The device was assembled using the working principles of "Herbst-like" appliances and splints of neuromuscular deprogramming of the "Federici" type used for gnathologic treatments. We selected 17 males and 4 females, with an average age of 42 years, and an average BMI of 29. Eighteen patients were treated with our oral appliance, 1 patient was treated with the orthesis proposed by Schmidt-Nowara et al and 2 patients were treated with the oral appliance proposed by Johal and Battagel. All patients used the appliance for at least 6 months.

**RESULTS:** After treatment with the oral appliance, the posterior airway space increased (p = 0.0002); no statistically significant difference for the improvement degree of OSAS severity (p = 0.1085) was shown; an improvement was found in: AHI (p = 0.0028); Nadir O<sub>2</sub> (p = 0.0035); TO<sub>2</sub> < 90% (p = 0.0140); 2 patients presented with temporomandibular joint (TMJ) discomfort.

**CONCLUSIONS:** Our MAD has proved effective in improving the polysomnographic and radiographic parameters and assures good TMJ compliance.

Key Words:

Obstructive sleep apnea syndrome, Sleep disordered breathing, Mandibular advancement device, Oral appliance, Upper airway.

#### **Abbreviations**

OSA = obstructive sleep apnea

OSAS = obstructive sleep apnea syndrome

CPAP = continuous positive airway pressure

MAD = mandibular advancement device

TMJ = temporomandibular joint

BMI = body mass index

CT = computed tomography

PAS = posterior airway space

AHI = apnea/hypopnea index

Nadir  $O_2$  = Nadir oxygenation

 $TO_2 < 90\%$  = time spent with oxygenation less than

90%

CNS = central nervous system

#### Introduction

Over 25% of the adult population suffers from obstructive sleep apnea (OSA), and of these patients, approximately 10% have moderate to severe disease. If left untreated, mortality for severe OSA is 30% at 15 years<sup>1</sup>. Several studies have confirmed that OSA is more common in men than women<sup>2,3</sup>, which is probably due to the differences in fat distribution, airway height and collapsibility, neurochemical mechanisms and sex hormones. There are also differences between different ethnic groups. Among Asians, the risk of developing OSA seems to be more related to craniofacial morphology than to obesity, which is, instead, an important risk factor among Hispanics and American Indians<sup>4</sup>. The rate of road accidents attributable to sleep disorders is 1-3% in the USA, 10% in France and more than 30% in Australia<sup>5</sup>. Risk factors for developing OSA are age, male gender, structural variations (retrognathia, micrognathia, macroglossia, midfacial hypoplasia, trauma, oncological demolitions, radiotherapy, enlarged tonsils and obesity),

hormonal factors (androgens, polycystic ovary and menopause, although estrogens and progesterone have a protective role), acromegaly, Down's syndrome and hypothyroidism. Sleep apneas are considered risk factors for hypertension, ischemic heart disease and stroke. They are also associated with loud snoring at night, waking with a pause in breathing and excessive daytime sleepiness. This syndrome has an impact on the patient's neurocognitive function (memory loss, personality disorders and increased risk of car accidents)<sup>6</sup>. Appropriate treatment significantly improves the cardiopulmonary function and the clinical condition of the patient. Treatment can be surgical or nonsurgical, and it aims to re-establish normal airflow of the rhino-pharynx. More than 70% of OSA can be treated with nonsurgical therapy that is essentially based on two elements: the injection of air at positive pressure with the technique called continuous positive airway pressure (CPAP) and the use of an Oral Device, which is used to increase the tension of the pharyngeal wall and to advance the base of the tongue. Despite its efficacy in the treatment of obstructive sleep apnea syndrome (OSAS), CPAP is not fully accepted by patients. This factor leads to increased demand of the use of an oral device to reach or enhance the benefits possible with CPAP. Oral devices are appliances that are used during sleep to increase the upper airway's size through a mechanical action<sup>7</sup>. In this therapy, two types of appliances have proved to be effective: tongue retaining devices and the mandibular advancement device (MAD). The former provides a suction cup that moves the tongue into a more advanced position; it is mainly used when there is not a complete dentition<sup>8</sup>. There are several mandibular advancement devices reported in the literature 9-18, and they can be divided into two main types: "monobloc", which is an orthesis set up with only one element<sup>19-21</sup>, and "bibloc" 10,22-24, which is an orthesis set up with two elements<sup>25</sup>. These devices are well tolerated by patients, easy to use, non-invasive and removable, with mild and, overall, acceptable side effects<sup>23</sup>. We experienced some difficulties in the use of two oral devices mainly related to poor patient compliance and temporomandibular joint disorder (TMJ) problems with the "Monobloc" type and persistent airflow obstruction with the "Bibloc" type. To compensate for these complications, we designed, according to "Bibloc" typology, a mandibular advancement device that provides for an adequate vertical opening in ad-

dition to lower jaw protrusion. The described device is custom-made from a patient's dental impression to increase comfort and compliance. Other devices of similar design proposed in the literature have the disadvantage of creating a barrier to oro-pharyngeal airflow when jaw is in the closed position<sup>10,24,26</sup>. In comparison to these devices, the oral device we introduced offers a forced mouth opening that allows for greater airflow associated with mandibular protrusion, combining in a single device the benefits of the two orthesis typologies.

#### **Materials and Methods**

Between January 1, 2007 and December 31, 2009, we followed 74 patients with breathing diseases associated with sleep at our Center. We selected 21 of these patients, including 17 males and 4 females, aged between 19 and 72 years, with an average age of 42 years, and a body mass index (BMI) between 27 and 32, with an average BMI of 29. Eighteen of the 21 patients were treated with our oral appliance, 1 patient was treated with the orthesis proposed by Schmidt-Nowara et al<sup>19</sup> and 2 patients were treated with the oral appliance proposed by Johal and Battagel<sup>24</sup>. The selection criteria of the group were as follows: over 18 years; undergoing therapy with an oral appliance; completed clinical tests, such as CT, polysomnography, Rx teleradiography in lateral view and Helkimo analysis; and no use of CPAP therapy during the observation period. Polysomnography, teleradiography and the Helkimo analysis were performed before the application of the device and again with the oral device in place after a period of at least six months of use. With CT, we studied the nasopharyngeal and oropharyngeal airways, recording the values observed at the locations of the major constrictions on both sides. Using cephalometry we evaluated the PAS (posterior airway space). With polysomnography, we investigated the following parameters: AHI, Nadir oxygenation and time spent with oxygenation less than 90% (TO<sub>2</sub>) < 90%). By Helkimo analysis, we assessed the condition of the TMJ before and after treatment with the oral appliance.

## **Device Description**

The device is made up of two splints of acrylic resin that run both in the palatal and tongue direction towards the gum border of both upper and lower arches. Both splints included "Adams-like" retention hooks on the fourth and sixth molars. when in place, and a raised occlusal plane made of transparent resin. The retention hooks anchor the splint maximally and the occlusal plane facilitates the identification of interferences or precontacts between the two planes. The occlusal plane covers the apical surface of the teeth crowns on both the vestibular and lingual sides and is made in the sagittal plane with an angle of approximately 15°-20° in order to allow spontaneous mandibular protrusion when the mouth closes. The thickness of the two planes is approximately 8-10 mm at the molar level and 10-12 mm at the premolar level in order to achieve a frontal opening of approximately 15 mm to allow air to flow through the mouth. This plane extends from the molars to the distal canines' cusps. The two splints are stabilized by two telescopic "Herbst" hinges. To ensure the system's stability, the telescopic hinges are installed with two screws and soldered into the acrylic on metal peduncles, which are located at the most distal point of the upper arch and in the lower arch at the canine level. The hinges contain a piston-like mechanism. The mandibular protrusion position was determined with CT studies and by Telecrane in lateral views, a cast was made with a wax bite to record this position (Figures 1, 2, 3). At the beginning of the treatment, the two splints are applied but not secured by the hinges in order to guide and strengthen the occlusal plane. The splints are initially applied twice a day for just one hour at set time intervals, and the application time is gradually increased over approximately 15 days. Once the patient is completely adapted to the splints, the hinges are applied. The hinges can be adjusted to accommodate changes in jaw opening and protrusion by inserting preformed metal gauges, which range in size from 2 to 4 mm, according to the case needs (Figures 4, 5, 6).

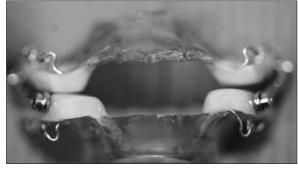


Figure 1. Oral device frontal view.



Figure 2. Oral device lateral view.

## Statistical Analysis

We performed descriptive analysis using the frequencies for qualitative variables, and we calculated the quantitative variables using the median and interquartile range. We used the non-parametric Wilcoxon signed ranks test to assess the existence of a statistical difference between the values before and after of: PAS, degree of OSAS severity calculated with polysomnography; AHI, Nadir  $O_2$  and  $TO_2 < 90\%$ . The significance level was set at p < 0.05. Analyses were performed using Stata 10 for Windows.

## Results

In our sample, there were 14 males and 4 females. The median age was 42.5 years (interquartile range = 17 years). The subjects who were analyzed had a BMI of 29 (interquartile range = 2). All patients used the appliance for at least 6 months. We found a statistically significant difference between PAS values before and after treatment (p = 0.0002); specifically,



**Figure 3.** Frontal opening.



Figure 4. Patient at the start of treatment.

post-treatment values were higher than pretreatment values in 17 patients, with values ranging from +5 mm and +1 mm (median pre = 6.5 mm, median post = 8.5 mm). In 1 patient, the values did not change. Regarding the polysomnographic evaluation of the degree of OSAS severity, we recorded an improvement in 13 patients, a worsening in 1 patient and no change in 4 patients. No statistically significant difference for these values (p = 0.1085) was shown. However, a statistical significant difference was found in the analysis of each of the polysomnographic indices:

- AHI decreased on the whole with median values of pre = 31.5 events/h and post = 12 events/h p = 0.0028; AHI decreased in 15 patients (values ranged from -54 and -3 events/h), increased in 2 patients (values between +2 and +25 events/h) and remained unchanged in 1 patient.
- Nadir O<sub>2</sub> improved in 15 patients, with values ranging from +33% and +3%. We recorded a



**Figure 5.** The occlusal plane covers the apical surface of the teeth crowns on both the vestibular and lingual sides.



Figure 6. Mandibular protrusion when the mouth closes.

- reduction of this value in 3 patients (values between -2% -18%). The values before and after treatment were statistically different (median pre = 78%, median post = 90% p = 0.0035).
- TO<sub>2</sub> < 90% decreased on the whole with median values of pre = 5.5% and post = 0% p = 0.0140; TO<sub>2</sub> < 90% decreased in 12 patients (values ranged between -2% and -37%), increased in 2 patients (values ranged between +7% and +9%) and remained unchanged at 0% in 4 patients. In 7 of the 12 patients who experienced some improvement, the O<sub>2</sub> saturation never fell below 90% (TO<sub>2</sub> < 90% = 0%) during the exam (Table I).

Regarding the assessment of TMJ compliance, based on the Helkimo analysis, 5 patients presented with joint discomfort after 6 months of therapy, with Ai no more than grade II and Di no more than grade I. However, it should be noted that 3 of these 5 patients suffered from joint disease before starting therapy.

The patient who used the device proposed by Schmidt-Nowara et al <sup>19</sup> reported an improvement on all polysomnographic parameters (PAS +2 mm, AHI –1 events/h, Nadir  $O_2$  +2%,  $TO_2$  < 90% –1%) and a worsening of the Helkimo analysis indices (Ai from 0 to II, Di from 0 to II) after 2 months of therapy. Of the 2 patients treated with the Johal oral appliance<sup>24</sup>, one reported an increase in the PAS (+1 mm) and no change in other polysomnographic parameters, whereas the PAS of the other patient increased (+2 mm), AHI decreased (–7 events/h), Nadir  $O_2$  increased (+3%) and  $TO_2$  < 90% decreased (–2%). In both patients, the Helkimo analysis indices remained unchanged.

**Table I.** Statistical evaluation of PAS, Degree of OSAS, AHI, Nadir  $O_2$  and  $TO_2 < 90\%$  values before and after treatment with the oral appliance.

	Variable	Median	Interquartile range	<i>p</i> -value
PAS	Before	6.5 mm	2.0	0.0002*
	After	8.5 mm	3.0	
Degree of OSAS	Before	2.5	3.0	0.1085
	After	1.0	1.0	
AHI	Before	31.5 events/h	31.0	0.0028*
	After	12.0 events/h	26.0	
Nadir O <sub>2</sub>	Before	78.0%	15.0	0.0035*
	After	90.0%	11.0	
TO <sub>2</sub> < 90%	Before	5.5%	16.0	0.0140*
	After	0.0%	7.0	

<sup>\*</sup>Significant value.

#### Discussion

Sleep apnea is defined as an intermittent ceasing of airflow from the upper airway while the patient is sleeping. Sleep apnea can be either central or obstructive. In central sleep apnea, neural impulses to all of the respiratory muscles stop temporarily. In obstructive sleep apnea (OSA), airflow is blocked by the occlusion of the oropharyngeal airway<sup>6</sup>. There are a number of factors that lead to the collapse of the airways and the occurrence of obstructive sleep apnea:

- Increase in upper airway resistance, which requires a greater inspiratory effort to maintain adequate ventilation. Structural alterations, present in the majority of OSA patients, predispose them to occlusion, including retrognathia, micrognathia, macroglossia, midface hypoplasia, trauma, cancer demolitions, radiotherapy, hypertrophic tonsils and obesity.
- Depression of respiratory centers, which manifests through a reduction of muscle activity that allows a regular airflow through the airway, as it happens during sleep. Alcohol is one important depressive influence on this muscle tone.
- Immature CNS<sup>27</sup>.

Obstructive sleep apnea syndrome (OSAS) is defined, pathophysiologically, as repeated episodes of partial or complete obstruction of the upper airway and oxygen desaturation of the arterial hemoglobin; the resulting progressive asphyxia provokes a brief awakening from sleep during which the airway opens and the airflow starts again. The aim of treatment is to re-establish the normal airflow of the rhino-pharynx, which can be achieved in different ways. Surgery allows the identification of one or more surgically workable sites. However, the

success rate is only approximately 40-60% because the clinical symptoms of OSA are not often attributable to a single anatomic abnormality<sup>1</sup>. Non-surgical therapy involves the use of CPAP or oral devices associated with weight loss, a reduction of smoking and of alcohol and drug consumption (sedatives, hypnotics, etc.), which can worsen the apneas. In this study, we evaluated non-surgical therapy for OSAS using a mandibular advancement device (MAD). The functioning of a MAD in the treatment of OSA is enabled by two mechanisms. One, direct, increases the airway's caliber and prevents its collapse due to the negative pressure that develops within it during inspiration; indeed, cephalometric studies of patients treated with MAD have shown an increase in the airway space behind the tongue and the soft palate, in addition to a change in uvula and tongue conformation<sup>26</sup>. The other mechanism is indirect; the MAD-induced stretch activates the neuromuscular reflexes of the airways, causing an increase in muscle tone, which in turn prevents the walls from collapsing<sup>26</sup>. Regarding the treatment of snoring, the MAD increases the size of the oropharynx and hypopharynx and can cause an increase in pharyngeal wall tension. Consequently, this tension can lead to a reduction of the turbulent flow that is usually the basis of snoring<sup>20</sup>. The MADs reported in the literature are the "monobloc" type 19-21 or the "bibloc" type<sup>10,22-24</sup>, described as follows:

• "Monobloc" devices have been tested by Schmidt-Nowara et al<sup>19</sup> and O'Sullivan et al<sup>20</sup>. These tests show that the use of these devices resulted in improved sleep quality and reduced daytime sleepiness, improvement in the frequency and intensity of snoring, significant AHI reduction and increased oxygen satura-

tion. These devices, however, have some drawbacks, including they only allow air to flow through a frontal orifice, appear cumbersome and block the lower jaw in a fixed position, which could cause long-term problems in the TMJ.

"Bibloc" devices 10,22-24 seem to be more flexible, are less cumbersome and place less stress on the TMJ. Bernold and Bondemark<sup>22</sup> investigated the effectiveness of a magnetic device, and after 6 months of treatment, the main symptoms of snoring and daytime sleepiness were significantly decreased, the hypopharyngeal airway space was increased and the contact between the tongue and soft palate was reduced significantly. Aarab et al<sup>23</sup> used a MAD consisting of two splints connected in the front by an adjustable screw mechanism that allows the adjustment of the protrusion position in the anterior and posterior directions. The splints are further supported by orthodontic elastics on either side; this MAD has significantly improved the AHI in patients with mild OSA, but it was not effective in reducing snoring. Johal and Battagel<sup>24</sup> has treated 37 patients with a Herbst-type mandibular advancement device with intermaxillary elastics to prevent jaw opening. 28 patients reported significant reduction or cessation in snoring, in apnea and in daytime sleepiness, 2 subjects did not tolerate the device and all patients reported a series of short-term problems: facial muscle discomfort, abnormal bite upon wakening, dry mouth and excessive salivation during the night. None of the subjects reported long-lasting discomfort of muscles in the face or the temporomandibular joint. Eveloff et al<sup>10</sup> tested another removable Herbst appliance, and he has achieved an improvement in the degree of OSA with a decrease of AHI. However, this improvement was not significantly correlated with the magnitude of change in any cephalometric parameter after mandibular advancement; only two parameters were statistically significant, one being the distance between the hyoid bone and the mandibular plane and the other being the posterior facial height.

In our caseload, we treated a patient with the orthesis proposed by Schmidt-Nowara et al<sup>19</sup>, but the patient compliance was poor; the patient stopped use within 2 months and has not completed the therapy. Despite the brevity of the therapy, we found a decrease in AHI, an increase of

Nadir O<sub>2</sub> and a worsening of the Helkimo analysis indices. Two patients were treated with the oral appliance proposed by Johal and Battagel<sup>24</sup>, which showed a good compliance, but the results were unsatisfactory. In fact, in one patient, all of the polysomnographic indices showed no change, and the second patient showed only small changes. The failure of previous cases has motivated us to design an oral appliance that would combine the advantages of both devices described here and that would maintain acceptable patient compliance.

Our device was custom-made from plaster models of each patient's dental arches. It was assembled using the working principles of "Herbstlike" appliances and splints of neuromuscular deprogramming of the "Federici" type used for gnathologic treatments. Distinctive features of this device include its full reversibility and the degree of mandibular advancement that can be modulated over time by inserting gauges on the telescopic hinge. Additionally, the occlusal plane applies a posterior functional support that does not stress the masticatory muscles, the mandibular protrusion is so gradual that it does not stress the TMJ. There are no occlusal alterations because the occlusal plane is locked in place by the splints and it is not equipped with restraints, such as elastics or magnets, so it does not make it difficult for the patient to open the mouth. In conclusion, compared to the other oral devices we have used, our MAD has proved more effective in improving the polysomnographic and radiographic parameters and assures better TMJ compliance. Indeed, only 2 of 18 patients showed TMJ discomfort ex novo (in both cases, not severe enough to stop the therapy) because they used the protocol that provides for a gradual adaptation to the device in addition to splints used for gnathologic therapy. Possible disadvantages of our appliance are dry mouth due to the forced opening of the mouth and muscular and TMJ discomfort during the early stages of adaptation.

#### References

- HOLTY JE, GUILLEMINAULT C. Maxillomandibular advancement for the treatment of obstructive sleep apnea: a systematic review and meta-analysis. Sleep Med Rev 2010; 14: 287-297.
- JORDAN AS, MCEVOY RD. Gender differences in sleep apnea: epidemiology, clinical presentation and pathogenic mechanisms. Sleep Med Rev 2003; 7: 377-389.

- LIN CM, DAVIDSON TM, ANCOLI-ISRAEL S. Gender differences in obstructive sleep apnea and treatment implications. Sleep Med Rev 2008; 12: 481-496.
- BARBÉ F, BARCELÓ A, MONTSERRAT JM. Sleep apnoea syndrome: a look at ethnicity, pathogeny and potential therapheutic approaches. Sleep Med Rev 2005; 9: 415-418.
- GEORGE CF. Sleep. 5: Driving and automobile crashes in patients with obstructive sleep apnoea/hypopnoea syndrome. Thorax 2004; 59: 804-807.
- PHILLIPSON EA. Apnea durante il sonno. Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J, Fauci AS. Harrison—Principi di Medicina Interna. McGraw-Hill, 2005, pp. 1774-1778
- AARAB G, LOBBEZOO F, HAMBURGER HL, NAEJE M. Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnea: A randomized, placebo-controlled trial. Respiration 2011; 81: 411-419.
- 8) Woodson BT. Non-pressure therapy for obstructive sleep apnea: surgery and oral appliances. Respir Care 2010; 55: 1314-1320.
- BONHAM PE, CURRIER GF, ORR WC, OTHMAN J, NANDA RS. The effect of a modified functional appliance on obstructive sleep apnea. Am J Orthod Dentofac Orthop 1988; 94: 384-392.
- EVELOFF SE, ROSENBERG CL, CARLISLE CC, MILLMAN RP. Efficacy of a Herbst mandibular advancement device in obstructive sleep apnea. Am J Respir Crit Care Med 1994; 149: 905-909.
- 11) FERGUSON KA, ONO T, LOWE AA, KEENAN SP, FLEETHAM JA. A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. Chest 1996; 109: 1269-1275.
- MENN SJ, LOUBE DI, MORGAN TD, MITLER MM, BERGER JS, ERMAN MK. The mandibular repositioning device: role in the treatment of obstructive sleep apnea. Sleep 1996; 19: 794-800.
- 13) MARKLUND M, SAHLIN C, STENLUND H, PERSSON M, FRANKLIN KA. Mandibular advancement device in patients with obstructive sleep apnea: long-term effects on apnea and sleep. Chest 2001; 1: 162-160
- 14) HANS MG, NELSON S, LUKS VG, LORKOVICH P, BAEK SJ. Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS). Am J Orthod Dentofacial Orthop 1997; 111: 562-570.
- 15) RAPHAELSON MA, ALPHER EJ, BAKKER KW, PERLSTROM JR. Oral appliance therapy for obstructive sleep

- apnea syndrome: progressive mandibular advancement during polysomnography. Cranio 1998; 16: 44-50.
- LAMONT J, BALDWIN DR, HAY KD, VEALE AG. Effect of two types of mandibular advancement splints on snoring and obstructive sleep apnoea. Eur J Orthod 1998; 20: 293-297.
- 17) BONDEMARK, L. Does 2 years' nocturnal treatment with a mandibular advancement splint in adult patients with snoring and OSAS cause a change in the posture of the mandible? Am J Orthod Dentofacial Orthop 1999; 6: 621-628.
- SCHÖNHOFER B, HOCHBAN W, VIEREGGE HJ, BRÜNIG H, KÖHLER D. Immediate intraoral adaptation of mandibular advancing appliances of thermoplastic material for the treatment of obstructive sleep apnea. Respiration 2000; 67: 83-88.
- SCHMIDT-NOWARA WW, MEADE TE, HAYS MB. Treatment of snoring and obstructive sleep apnea with a dental orthosis. Chest 1991; 99:1378-1385.
- 20) O'SULLIVAN RA, HILLMAN DR, MATELIAN R, PANTIN C, FINUCANE KE. Mandibular advancement splint: an appliance to treat snoring and obstructive sleep apnea. Am J Respir Crit Care Med 1995; 151: 194-198.
- COZZA P, POLIMENI A, BALLANTI F. A modified monobloc for the treatment of obstructive sleep apnoea in paediatric patients. Eur J Orthod 2004; 26: 523-530.
- Bernold M, Bondemark L. A magnetic appliance of snoring patients with and withouth OSA. Am J Orthod Dentofac Orthop 1998; 113: 144-155.
- 23) AARAB G, LOBBEZOO F, WICKS DJ, HAMBURGER HL, NAEUE M. Short-term effects of a mandibular advancement device on obstructive sleep apnoea: an open-label pilot trial. J Oral Rehabil 2005; 32: 564-570.
- 24) JOHAL A, BATTAGEL JM. An investigation into the changes in airway dimension and the efficacy of mandibular advancement appliances in subjects with obstructive sleep apnoea. Br J Orthod 1999; 26: 205-210.
- 25) Petituean T. Principles of mandibular advancement device applied to the therapeutic of snoring and sleep apnea syndrome. Sleep 2000; 15: 166-171.
- CLARK GT, SOHN JW, HONG CN. Treating obstructive sleep apnea and snoring: assessment of an anterior mandibular positioning device. J Am Dent Assoc 2000; 131: 765-771.
- 27) MORETTI C, FASSI C, BARBÀRA CS. Sviluppo e fisiopatologia delle vie aeree. Presented at "Bronchiolite e asma nel bambino: ambiente e comunicazione. La realtà basata sulle evidenze", Roma, Palazzo delle Esposizioni 23-24 Nov 2001.