Obstructive Sleep Apnea: An Overview

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Obstructive sleep apnea (OSA) is a sleep-related respiratory disorder characterized by intermittent episodes of upper airway collapse during sleep. The events are predominantly obstructive, with partial (hypopnea) or complete (apnea) occlusion of the upper airway (Fig. 1), resulting in reduced oxyhemoglobin saturation and sleep fragmentation [1].

The pathophysiology of OSA is multifactorial and includes reduction of the upper airways, resulting from both anatomical narrowing of the pharynx and functional alterations such as obesity (infiltration of fat in the neck region), maxillofacial injury or structural alterations [3, 4], increased pharyngeal collapsibility due to reduced neuromuscular compensation (decrease of the pharynx dilatory musculature response), lack of protective reflex of the pharynx during sleep [5], reduction of the awakening threshold, increase of the ventilatory response, decreased pulmonary volume and caudal traction of the pharynx, and fluid displacement to the neck

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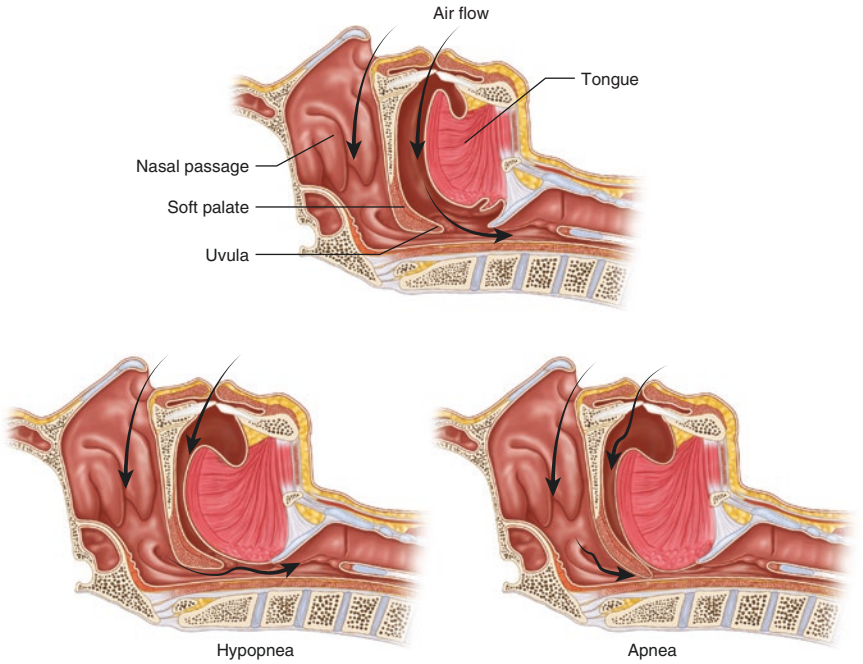

Fig. 1 Partial and complete upper airway obstruction, resulting in hypopnea and apnea, respectively. (Reprinted with permission from Somers et al. [2])

during the night [6–9]. Decreased upper airway size and increased resistance may result in snoring, a vibration of the soft palate, uvula, and/or pharyngeal walls.

OSA also has an individual variability regarding the clinical presentation of patients. The main risk factors are the male sex, age progression, obesity, craniofacial structure, and postmenopausal stage, and in the latter two factors the genetic and ethnic constitution may have a determining role.

OSA is considered an important public health problem, affecting about 5–15% of the general population, increasing linearly with age up to at least 60–65 years [10, 11]. The prevalence of OSA is alarmingly high and varies widely between studies, from 0.5 to 32.8%. This disparity is due to methodological differences and limitations with different samples (e.g., different ethnicities), inconsistencies in the techniques used to monitor sleep and breathing, and variability of diagnostic criteria for OSA. An epidemiological investigation conducted in the city of São Paulo found a prevalence of 32.8% of OSA in individuals between 20 and 80 years by polysomnography [12]. Epidemiological studies have shown an increase in prevalence ranging between 14% and 55% in the last two decades, affecting mainly middle-aged men [13].

In the current International Classification of Sleep Disorders (ICSD-3)[14], the diagnosis of OSA is defined by the presence of items A and B or C:

A. Presence of one or more of the following items:

   1. Complaint of drowsiness, non-repairing sleep, fatigue, or insomnia symptoms
   2. Awaken with breathing suspension, panting, or asphyxiation
   3. Bed partner or another observer report usual snoring, interruptions of breathing, or both during the patient's sleep
   4. Diagnosis of hypertension, mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes mellitus

B. Portable polysomnography or polygraph with:

   1. Five or more predominant obstructive events (Fig. 2): apnea, hypopnea, or RERA (respiratory effort-related arousal) per hour of sleep during polysomnography or per hour in monitoring

C. Portable polysomnography or polygraph with:

   1. Fifteen or more predominant obstructive events (apnea, hypopnea, or RERA) per hour of sleep during polysomnography or per hour at monitoring

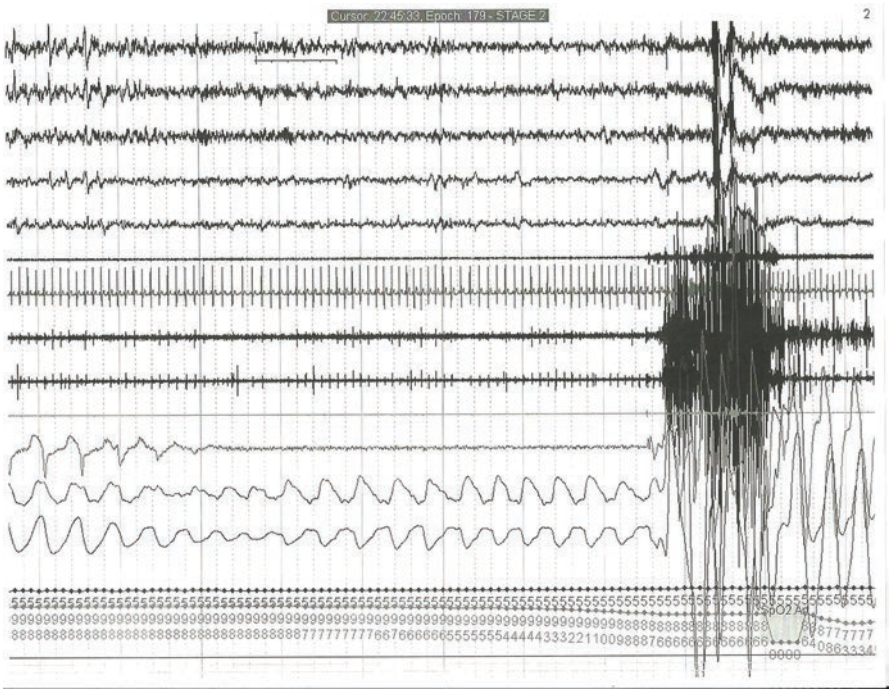

Fig. 2 Representation of an OSA event in a 30 seconds epoch seen in this window from a polysomnographic examination. (Image courtesy from Dr. Fernando Morgadinho Santos Coelho.)

1 General Treatments

Several treatments are available for OSA, but the choice should be based on severity, including symptoms, complications, and polysomnographic findings. In moderate to severe OSA, positive airway pressure (PAP) is the gold standard treatment. Other therapeutic modalities such as behavioral measures, positional therapy, and oral devices are available and involve an interdisciplinary approach. Surgical treatment in well-selected patients may be indicated.

Clinical and behavioral measures should be offered to all patients with OSA even in those treated with other therapies, such as PAP. Obesity is one of the main risk factors for OSA, so weight loss should be strongly recommended, and a nutritionist may be suggested. Studies with dietary intervention for weight loss along with prescription by a physical therapist for an active lifestyle are welcome in patients with OSA. In patients with mild OSA, the prescription of very low calorie together with lifestyle counseling showed an average weight reduction of 10.7 Kg, and for apnea-hypopnea index (AHI) of 4 events per hour, demonstrating that the greater the weight loss, the greater the decrease of AHI [15]. Another investigation assessed whether PAP influenced weight loss in patients with moderate and severe OSA [16]. For that, three types of intervention were instituted for 24 weeks: (i) use of PAP, (ii) management of weight loss, and (iii) combined intervention of PAP plus weight loss. The isolated PAP group did not present weight loss but presented a reduction of insulin resistance. The other two groups showed a significant weight reduction (~5 kg) in addition to decreased triglycerides and insulin resistance in the group with PAP plus weight loss [16]. This study showed that PAP can enhance metabolic improvement of weight loss.

In patients who do not respond to dietary intervention, bariatric surgery may be indicated. Weight loss through bariatric surgery showed a decrease in OSA in 83.6%–88.5% of patients, with an average reduction of the AHI of 34 n°/h, being the most effective gastric bypass [17]. However, even with considerable weight loss, many patients persist with residual OSA [18] and changes in OSA severity, decreasing it. Bariatric surgery may be an adjuvant in the treatment of OSA, except for the risks of perioperative complications due to OSA and recognition of the possibility of residual OSA.

Behavior measures should also be taken together along with OSA treatment. Alcohol, for example, aggravates OSA by having a dose-response effect [19]. Untreated OSA patients should avoid ingestion of alcohol because it leads to increased duration and frequency of apnea aggravating desaturation during sleep. In addition, other effects of alcohol include reducing sleep latency onset and the REM sleep stage.

Some medications may also aggravate OSA, such as benzodiazepines, benzodiazepine agonist receptors, opioids, and barbiturates, and should be avoided especially in those not under treatment. In cases where such medications are necessary, it is important that the monitoring is performed with adjustment in the prescribed treatment (e.g., increased PAP pressure, adequate mandibular advancement in the

case of the oral appliance, etc.). Attention should also be given to medications that increase weight and may aggravate OSA such as some antidepressants and antipsychotics.

2 Myofunctional Therapy

It is an alternative therapy indicated in the presence of orofacial myofunctional disorders associated with mild to moderate OSA associated or not with the use of PAP or intraoral device. Studies have demonstrated, in addition to the improvement of the orofacial myofunctional condition, the quality of life with reduction of the AHI and increased saturation of oxyhemoglobin [20]. When concomitant to CPAP theraphy, can improve CPAP adherence, reducing the require pressure. In many countries, myofunctional therapy is provided by speech therapists.

3 Oral Appliance

An oral appliance, or oral device, is like an orthodontic retainer, a noninvasive treatment, and the patient uses it only at sleep, to support the jaw in a forward position, therefore increasing the upper airway space. Research shows that oral appliance therapy is an effective treatment option for snoring and OSA. They are nocturnal oral devices that stabilize the upper airways and increase their diameters, inducing a decrease in the collapsibility of the pharynx. There are many types, such as maxillary expansion; mandibular advancement devices, which induce the advancement and distraction of the lower jaw; and tongue retaining devices that primarily keep the tongue from falling to the back of the upper airway (Fig. 3). They are made by dentists specializing in dental sleep medicine.

Therefore, the practical parameters of the American Academy of Sleep Medicine together with the American Academy of Sleep Dentistry stipulate that oral devices are not indicated for all OSA patients [23] and are indicated for primary snoring, upper airway resistance syndrome (please refer to chapter "Upper Airway Resistance Syndrome: An Overview"), mild OSA, moderate OSA, and severe OSA that are intolerant to PAP therapy. For example, patients with mild OSA showed no difference in the improvement of AHI between oral devices and PAP therapy [24]. However, in those with moderate or severe OSA, PAP was better in reducing AHI and hypoxemia compared to oral devices [24]. A moderate degree of evidence of the effect of the oral devices of the custom adjustable mandibular advancement type was observed in reducing the AHI, increasing oxygen saturation, decreasing nocturnal awakenings, and improving daytime sleepiness and quality of life compared to the condition before the use of the oral device. Therapeutic adherence to oral devices is generally higher, and its discontinuity is lower compared to PAP [25]. The most common adverse effects are dry mouth,

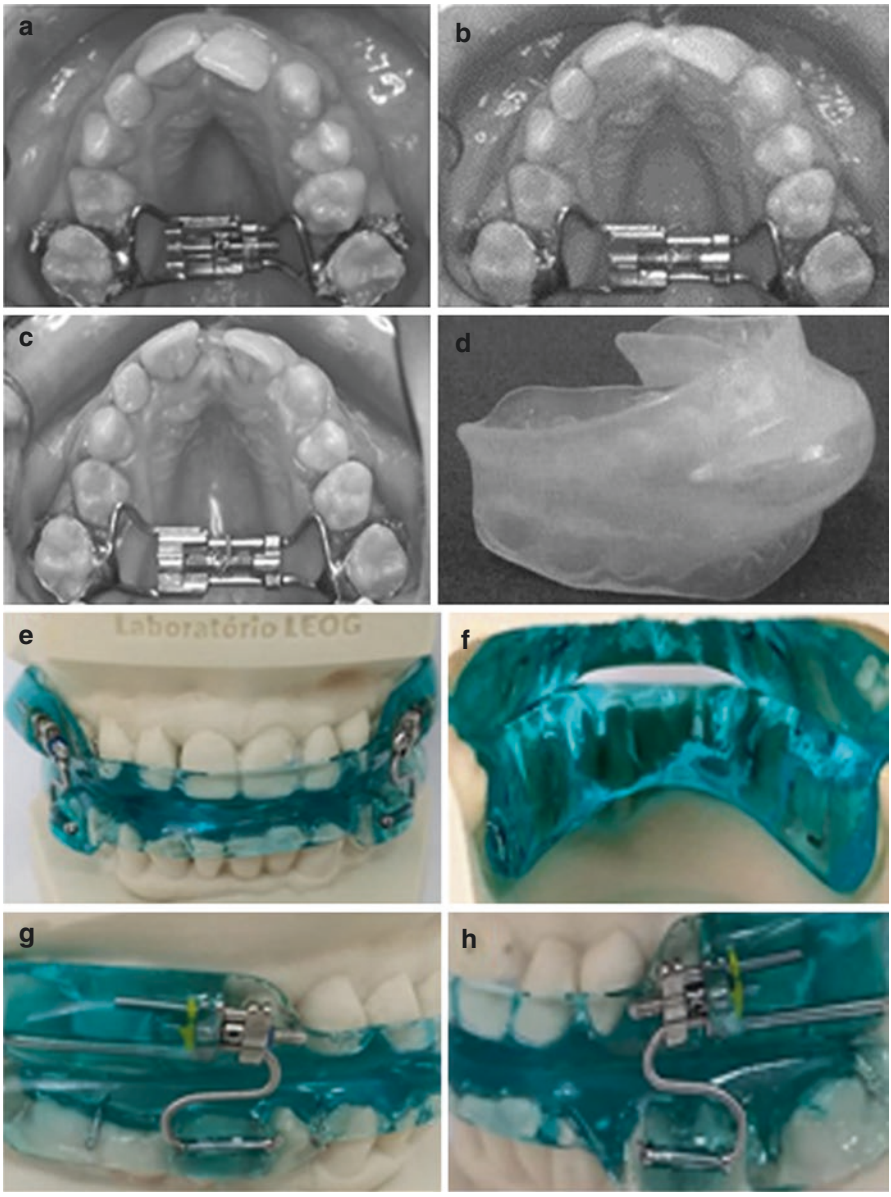

Fig. 3 Oral appliance devices: (**a**–**c**) Occlusal sequence of treatment with rapid maxillary expansion from crowding in the upper central incisors (**a**) to a wide space (**c**); (**e**, **f**) adjustable mandibular repositioning device, front view (**e**), from inside (**f**), right (**g**), and left (**h** sides; and **d**) tongue retaining device, designed to keep the tongue in an anterior position during sleep. This device secures the tongue by means of negative pressure in a soft plastic bulb. A flange, which fits between the lips and teeth, holds the device and tongue anteriorly in the oral cavity. (Reprinted with permission from: (**a**–**c**) Pirelli et al. [21]; (**d**) Higurashi et al. [22]; (**e**–**h**) (Image courtesy from Dr. Eliana Lottenberg Vago (original figure)))

excessive salivation, mandibular discomfort, increased sensitivity to teeth, dental mobility, and occlusal changes. Among the contraindications, we have periodontal disease, acute temporomandibular dysfunction, uncontrolled generalized convulsions, and limited mandibular advancement. Detection of oral device response predictors (positional apnea, BMI, younger patient), as well as accurate determination of the optimal degree of mandibular advancement, may improve the effectiveness of this treatment. It is important to perform follow-up PSG to assess the effectiveness of the oral devices because subjective reports of improvement may not be safe.

4 Surgical Treatment of OSA

The surgical treatment may be indicated with curative purpose, seeking to control the disease, and it may also be indicated as a supporting role, to facilitate adherence to the PAP or oral devices. Recently, studies on different OSA phenotypes started identifying different clusters to try to customize the treatment of OSA and also to understand why surgical treatment has distinct responses in "apparently similar" patients [26]. These different possibilities of responses from the surgical treatment must be presented to the patient at the time of the surgical indication, to suit their expectations within the treatment.

Different surgical modalities and techniques can be performed in the different levels of upper airways, both in the soft parts of the pharynx and in the facial skeleton, such as pharyngoplasty, maxillomandibular advancement and hypoglossal nerve stimulation.

The risks of surgical treatment should be considered, considering the patient's age, the severity of OSA, and the presence of comorbidities such as obesity, diabetes, hypertension, and cardiopathies. The risks of complications are higher in patients with OSA, and care should be taken with pre-anesthetic and anesthetic drugs, orotracheal intubation, extubating in the immediate postoperative period, upper airway edema, and medications prescribed in the postoperative period.

4.1 Nasal Surgeries

The most frequent procedures performed in the nose in the treatment of OSA are septoplasty and partial inferior turbinectomy. They aim to clear the nose to improve nasal breathing. Several studies have shown that nasal surgery, when performed in isolation, has little impact on the improvement of AHI, but there is evidence of improvement in the subjective quality of sleep and may help in the adaptation of PAP [27]. These procedures are often performed in association with other surgical procedures, especially pharyngeal surgeries.

4.2 Pharynx Surgeries

There are several surgical techniques performed in the pharynx, which clear the airway and decrease its collapsibility. Older techniques, such as uvulopalatopharyngoplasty [28], which were widely performed in the 1980s and 1990s, without any criteria for patient selection, have demonstrated over the years controversial results and high incidence of side effects and sequelae [29]. In recent decades, with the best knowledge of the pathophysiology of OSA and seeking to decrease the rates of adverse effects, new surgical techniques have emerged, which act more on the pharynx lateral walls, sparing the midline, such as lateral pharyngoplasty and expander pharyngoplasty, among others [30]. Recently, criteria for a better selection of patient candidates for surgical treatment have been valued, seeking better success rates. Friedman staging [31], which uses modified Mallampati, palatine tonsil size, and body mass index to classify patients, has been used in the selection of patients for the indication of pharyngeal surgeries.

Minimally invasive palatal procedures are different surgical modalities (soft palate radiofrequency, palatal implants, and sclerotherapy), which can be performed on an outpatient basis with local anesthesia and have as objectives the increase of the tonus and the stiffening of the soft palate leading to the improvement of the snoring. They are indicated in patients with primary snoring or mild OSA and, generally, in individuals with normotrophic or amygdalectomized palatine tonsils, with contraindication for use of oral device and history of intolerable PAP therapy [32]. The results are variable; usually, there is an improvement of snoring in the short term; however, the success rate decreases in the medium and long term.

In the hypopharynx, procedures performed at the base of the tongue are indicated in cases of suspected collapse in this region with increased volume of the base of the tongue, mainly increased lingual tonsil. When indicated, these procedures are often performed in association with other surgical procedures (multilevel surgeries).

4.3 Hypoglossal Nerve Stimulation

The genioglossus muscle, innervated by the hypoglossal nerve, is one of the main dilating pharynx muscles and is directly involved in the pathophysiology of OSA, contributing to prevent the pharynx from collapsing during sleep. In recent years, a new treatment modality has been proposed, in which a hypoglossal nerve stimulator is implanted unilaterally and is able to synchronize stimuli with respiratory effort, preventing the collapse of the pharynx that leads to respiratory events during sleep [33]. The results seem promising; however, it is a high-cost treatment, and more long-term studies are needed to better evaluate its results.

4.4 Skeletal Surgery

Several skeletal procedures are performed for the treatment of OSA, such as suspension of the hyoid bone, advancement of the genioglossus muscle, and maxillomandibular advancement. The first two are usually performed in association with other procedures in multilevel surgeries. Maxillomandibular advancement is a treatment that presents excellent results in the treatment of OSA [34] and is generally indicated for patients with accentuated OSA who were unable to adapt the CPAP or in patients with other grades of OSA who present significant skeletal abnormalities.

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