ARTIGO DE REVISÃO

Obstructive sleep apnea: lessons on clinic and surgery
Apnéia obstrutiva do sono: lições na clínica e na cirurgia

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Introdução: A síndrome da apnéia obstrutiva do sono (SAOS) é uma doença crônica e progressiva com alta morbimortalidade cardiovascular. A SAOS afeta 2-4% da população masculina entre 30 e 69 anos, e 1-2% da população feminina na mesma faixa etária, constituindo um problema de saúde pública. Fisiopatologia: A SAOS ocorre por associação de alterações anatômicas e um aumento na complacência da musculatura durante a passagem do ar. A musculatura das vias aéreas superiores relaxa durante o sono, causando uma redução das forças de dilatação das mesmas e episódios repetidos de obstrução. Cada obstrução é acompanhada por despertares e redução da saturação de oxigênio arterial, causando ativação aguda do sistema nervoso autônomo simpático com alterações cardiorrespiratórias. Aspectos Clínicos: Os sintomas da SAOS são noturnos e diurnos. Durante o sono, há a presença de roncos, pausas respiratórias, sono agitado, despertares e noctúria. Enquanto acordado, o paciente apresenta sintomas de sonolência diurna excessiva, dor de cabeça matinal, queda da função intelectual, sintomas depressivos, impotência sexual e distúrbios de personalidade. Os pacientes com SAOS são frequentemente homens, de meia-idade, com sobre peso, pescoço curto, com alterações anatômicas das vias aéreas superiores. O diagnóstico definitivo é realizado por meio do estudo do sono através da polissonografia. Tratamento: O tratamento clínico inclui medidas comportamentais, como perda de peso, abstinência de álcool, sedativos, assim como o uso de dispositivos intra-órais removíveis ou pressão positiva contínua das vias aéreas (CPAP). Os tratamentos cirúrgicos visam aumentar o diâmetro das vias aéreas superiores e variam desde a uvulopalatofaringoplastia ao avanço maxilo-mandibular.
continuous positive airways pressure (CPAP). Surgical treatments aim at increasing UA and varies from Uvulopalatopharyngoplasty to maxillo-mandibular advance.

**Keywords** Apnea; Snoring; Pharynx; Muscles; Surgery, Oral.

**Introduction**
One of the common complaints made to health professionals concerning sleep habits is the presence of snoring. Although it is known that snoring brings harms only to the social life of these individuals, the patient that presents respiratory alterations associated with snoring necessitates specialized medical attention, since the complications inherent to these alterations, principally cardiovascular, are innumerable and already well documented. Obstructive sleep apnea is the stoppage of air movement through the upper air passages, in the presence of respiratory effort, with a minimum duration of 10 seconds, hypopneas, constitute a reduction in the passage of air in the referred area in this same period of time. These respiratory events occur innumerable times and exclusively during sleep, determining symptoms and signs that characterize obstructive sleep apnea syndrome.

Respiratory pauses can result from lack of neurological stimulus for respiration, thus called central apnea or by obstructive factors in the upper air passages, where respiratory effort is present, called obstructive apnea, or by association of the two situations, denominated mixed apnea. Obstructive sleep apnea, a common disorder that affects about 2-4% of men and 1.2% of women of adult age (approximately 30 to 69 years), is characterized by recurrent and intermittent episodes of obstruction of the upper air passages during sleep, provoking hypoxemia and frequent sleep interruptions.

**Physiopathology**
Obstructive sleep apnea syndrome represents a complex alteration of the upper air passages, whose principal event corresponds to intermittent collapse of their walls in inspiration during sleep.

Studies by means of fibroscopy, cineradiography, dynamic magnetic resonance and acoustic manometry clearly evidence that the location of the obstruction of the upper air passages is in the pharynx, extending from the rhinopharynx to the hypopharynx, including also the supra-glottis. These areas of obstruction can occur at isolated points or in multiple areas, which is most common, varying according to the patient. In the etiology of obstructive sleep apnea syndrome, Sher posits two fundamental components to consider: Firstly, anatomical and physical alterations that diminish the air space of the pharynx, by means of accumulation of soft parts or skeletal disproportions, bring about an increase in the resistance of the upper air passages, and consequently, elevate the negative intra-thoracic pressure to secure normal air flow volume. This increase in negative intra-thoracic pressure creates a suction mechanism that applies downward traction to the tracheobronchial tree and as a result there is lengthening and narrowing of the oropharyngeal isthmus. On the other hand, the narrowing of the upper air passages provokes a vacuum effect according to Bemüllle’s principle, following which it exists in a partial vacuum in more external margins of a moving fluid column. The rapider the flow, the greater the partial vacuum; and the less the diameter of the air column, the rapider the flow. In this context, when the upper air passage is narrowed, the vacuum increases, resulting in collapse of the air passage. These aerodynamic principles explain how a smaller air passage accelerates the air flow velocity, creating a negative air pressure that brings about collapse.

Abnormalities in bone structures at the oropharyngeal level are observed commonly in patients with obstructive sleep apnea syndrome. The most frequent is the retro-positioned mandible, restricting the oropharyngeal space. In relation to the soft tissues, the reduction in the diameter of the superior air passage, can occur by increase in the volume of pharyngeal walls, of the tongue, or tonsils, of the soft palate, blood vessels and the lymphatic and fat tissues. Besides the physical and spatial disproportions of the upper air passages, the permeability of the pharynx depends on equilibrium between intra-pharyngeal suction pressure and forces external to its walls determined by activity of dilating muscles of the upper air passages. The muscles of the pharynx produce active opening and closing movements and their effectiveness depends on their tonus and coordination of their contraction with the diaphragm. It is known that besides the anatomical alterations of the upper air passages, patients who are carriers of obstructive sleep apnea syndrome also present a greater tendency toward collapse by presenting greater complacency of this air passage. The complacency, expressed as the change in volume or transversal area per pressure unit, is an indicator that the air passages can be deformed and that complacency can be augmented by various factors.

The pressure at which the upper air passages collapse is called the critical pressure, which is markedly negative in normal individuals and positive in those with a severe degree of obstructive sleep apnea. Structural alterations in fibers of pharyngeal muscles have been described in patients with obstructive sleep apnea syndrome and in animals. Smirne et al. reference histological and histochemical studies of the median constrictor muscle of the pharynx, demonstrating that apneic individuals have an abnormal distribution of muscle fibers, with reduction in fibers of types I and II-b and an increase and hypertrophy of II-a fibers. Some authors studying palatopharyngeal muscle of 11 patients uvulopalatopharyngoplastized, resultant from apnea, presented an increase in the proportion of conjunctive tissue in comparison with the control group and alterations that suggest a process.
of denervation and degeneration in these patients. In a histological study of the soft palate of carriers of obstructive sleep apnea, found hypertrophy of mucosal glands, edema of the lamina propria, atrophy of musculature and desmyelinization of peripheral nerve fibers. Researchers reported a significant reduction in the proportion of muscle and non-significant difference in relation to fat tissue between snoring patients and the control group. In a histological study of the distal region of the soft palate and uvula of 34 patients that were submitted to uvulopalatopharyngoplasty concluded that the proportion of muscle, adipose tissue, blood vessels and glands are similar between the control group and the patients with apnea. However, the proportion of connective tissue was significantly greater in patients with moderate and severe apnea.

**Clinical Aspects**

The clinical picture of patients who are carriers of obstructive sleep apnea syndrome can be divided into nocturnal and daytime symptoms. Nocturnal symptoms are characterized principally by snoring, which is a product of vibration of the uvula, of the soft palate, pharyngeal walls, epiglottis and tongue, respiratory pauses, in general, referenced by the spouse; agitated sleep, with multiple sleep interruptions, nocturia and excessive sweating. Yet the daytime symptoms are principally, excessive somnolence, neurocognitive deficits, personality alterations, reduction of libido, irritability, depressive symptoms, anxiety and morning headache. Some authors, such as White, already cite criteria that suggest the presence of obstructive sleep apnea syndrome, enumerated in Table 1. The classification of the obstructive sleep apnea syndrome severity level must be made based on polysomnographic indices, on intensity of symptoms, impact on social functions and the presence of cardiovascular manifestations (Table 2).

**Treatment**

The treatment of obstructive sleep apnea must be individualized, with each patient evaluated and treated in a singular manner. This treatment can be clinical or surgical. Clinical treatment is accomplished from several forms, such as weight loss, which brings improvements as much in snoring as in respiratory pattern of the patient; obesity alters the architecture of the upper air passages, reducing the diameter of the air column. Lifestyle modification, especially weight loss, sleep hygiene and exercise, are often recommended. These could help by relieving pressure on the upper airway, and increasing muscle tone in the airway. However, the review found no trials to assess the effects of these strategies, and more research is needed. Some authors have identified 26 studies assessing the effects of 21 drugs in the treatment of sleep apnea. Drug therapy has been proposed as an alternative to CPAP in some patients with mild to moderate sleep apnoea and could be of value in patients intolerant of CPAP. Most of these studies have involved only a small number of participants and for many the design has been poorly reported. In one such study, topical fluticasone in patients with coexistent rhinitis and OSA reduced apnoea. Nasal lubrication to reduce surface tension in the airway was shown to reduce AHI, but the compound tested is not suitable for long-term use. Paroxetine, physostigmine, mirtazapine and acetazolamide have been shown to reduce the frequency of apnoeas, but the symptomatic response remains uncertain. Paroxetine had no impact on symptoms in an unselected group of patients. Results are only available for physostigmine and mirtazapine from studies with single night protocols. Acetazolamide was poorly tolerated by patients who tried to take it in the long term. Protriptyline (no longer available in some countries) led to a symptomatic improvement in two trials but no change in the frequency of apnoeas. Individual patients had more complete responses to particular drugs. It is likely that better matching of drugs to patients according to the dominant mechanism of their OSA will lead to better results and this also needs further study. The use of continuous positive airways pressure (CPAP) or bilevel positive pressure airway (BIPAP), which are devices that provide continuous positive pressure in the upper air passages, present high efficacy in control of apneas, employs a noninvasive device that can have its use interrupted at any moment; but many patients do not tolerate its use as a result of irritating symptoms and its necessity of daily application, even during travel. The removal oral appliances are options for patients not able to surgery and that don’t tolerate the CPAP therapy. It increase de upper airway lumen during sleep by protrusion of the mandible and tongue, increase the upper airway muscle tone. Several studies have demonstrated that this appliance are effective in controlling symptoms of OSAS, nocturnal breathing disturbance, oxygenation and sleep disturbance in patients with only snoring or with mild sleep apnoea. Rodriguez et al shows a significant association between 5-year survival and increasing adherence with PAP treatment in patients with OSAHS that is independent of other covariates. Cardio vascular disease was the main cause of death, and positive airway pressure use groups, arterial hypertension, and forced expiratory volume in 1 second percent predicted were the variables that best predicted death before the start of treatment. The evidence demonstrates significant benefit in sleepiness and health status with CPAP when compared to sham CPAP, dummy pill or conservative management, and in respiratory disturbances when compared with oral appliances. There is stronger evidence of effectiveness in symptomatic patients with moderate and severe apnoea and hypopnoea indices (AHI). When compared with use of an oral appliance symptoms did not show a significant difference, but additional data are required. Preference data did not show a consistent difference and could reflect differences in appliance tolerability, order effects and withdrawal of participants. People who respond to both CPAP and oral appliances are more likely to prefer an oral appliance, but study withdrawal favoured CPAP.
evidence supports the use of CPAP as first-line treatment for people with high AHI and moderate-to-severe sleepiness associated with obstructive sleep apnoea. Some patients offered CPAP might not accept it or struggle to continue with therapy. Where this is so, patients should be provided with alternative options. Recommendations should be seen in the context of the uncertain long-term effects of the treatment options available, and patients should be offered support in adhering with treatment given the potential risks of under-treatment of sleep-disordered breathing.

Surgical treatment — according to the consensus of the Brazilian Sleep Society in the year 2000, by a meta-analysis of more than 280 works in which patients were monitored for at least three years, and utilizing articles with series greater than 10 patients — concluded that it is necessary to evaluate and treat all of the upper air passages of patients with apnea, from the nose to the larynx.

Surgeries performed in soft parts, as much for snoring as for apnea, present obesity as a limiting factor, with the body mass index being above 28 kg/m² one of the parameters related to lack of success.

Uvulopalatopharyngoplasty, a procedure with the removal of palateine tonsils, remodeling of the soft palate, associated or not with genioglossus advance and or median glossectomy, showed success for the treatment of light and moderate apnea in 40% of cases, although, in the long term, it showed no practical success in the respiratory pattern of patients with severe apnea. Nevertheless, Friedman in 2004, proposed a classification of disease stages that evaluated and associated: the position of the palate, the size of the tonsil and the body mass index of the individual (Table 3 and Figure 1); such classification has been utilized by the author as a predictive factor of the success of surgical treatment and in his study, patients classified with Friedman I — in other words, with soft palate slightly lowered, tonsil enlarged and weight within normality — had a success rate of 80.6 with uvulopalatopharyngoplasty, showing that this procedure has its indications, but only in selected cases. And in 2008 the same author performed a meta-analysis and conclude that the multi-level surgery has the efficacy of the 66.4% and the overall complication rate was 14.6%. 62

Maxillomandibular advance, a surgery realized with osteotomies, anteriorizing the mandible and maxilla by up to 12 mm, presents high indices of success; about 90% of patients submitted to this procedure will present respiratory patterns less than 20, a fact that becomes more evident in the above-50 age group.

Several comparative studies concerning the treatment of severe apnea with maxillo-mandibular advance were employed by varied research groups and is plotted in the Table 4. Smatt et al. reported that 85% of their patients with severe obstructive sleep apnea, submitted to and mandibular maxillary advance presented a respiratory disturbance index within normality two years after the procedure.

There are now a small number of trials assessing different surgical techniques with inactive and active control treatments. The studies assembled in the review do not provide evidence to support the use of surgery in sleep apnoea/hypopnoea syndrome, as overall significant benefit has not been demonstrated. The participants recruited to the studies had mixed levels of AHI, but tended to suffer from moderate daytime sleepiness where this was measured. Short-term outcomes are unlikely to consistently identify suitable candidates for surgery. Long-term follow-up of patients who undergo surgical correction of upper airway obstruction is required. This would help to determine whether surgery is a curative intervention, or whether there is a tendency for the signs and symptoms of sleep apnoea to re-assert themselves, prompting patients to seek further treatment for sleep apnoea.

Complications

According to the specialized literature, crises of apnea, associated with recurrent sleep interruptions in patients who are carriers of sleep apnea syndrome, can provoke serious complications, principally related to the cardiovascular system. There is increasing evidence that OSAHS is associated with hypertension, myocardial ischaemia, an increased risk for developing stroke as well as with metabolic derangement and impaired glucose tolerance.

In patients without cardiovascular disease OSAHS is associated with an increased incidence of both systolic and diastolic dysfunction and left ventricular hypertrophy.

Some authors reported that obstructive sleep apnea is an independent risk factor for cerebral vascular accident and must be treated in every patient who is a victim of this event, and further noted that individuals with a respiratory disturbance index greater than 20 present a mortality rate, resultant from cerebral vascular diseases, significantly greater than those who present a respiratory disturbance index less than 20, a fact that becomes more evident in the above-50 age group.

Studies related that cerebral vascular accident is among the principal causes of death in the Unites States, having well known risk factors with arterial hypertension, tobacco use, dyslipidemia and diabetes, but their studies evidenced that about 50% of victims of cerebral vascular accident were carriers of obstructive sleep apnea syndrome, suggesting a cause and effect relationship in this pathology.

Authors described that arterial hypertension is observed in 50% of patients who are carriers of obstructive sleep apnea syndrome and that 35% of carriers of essential arterial hypertension, for which a definitive cause has not been found, also are carriers of obstructive sleep apnea syndrome, suggesting that this population may be carriers of non-diagnosed apnea.

Peppard et al. accompanied 709 patients who were carriers of obstructive sleep apnea syndrome for a minimum period of 4 years and concluded that obstructive sleep apnea is an independent risk factor for the development of arterial hypertension. Subsequent studies reveal that treatment of obstructive sleep apnea syndrome is essential in these patients, reducing pressor levels substantially.

Some authors observed that each additional apnea event per hour increases that risk of developing arterial hypertension by about 1% in carriers of the syndrome and that each 10% decrease in blood oxygen saturation increases the risk of developing...
arterial hypertension in approximately 13% of these individuals. Obstructive sleep apnea syndrome with the independent risk factor for arterial hypertension, and added that diastolic pressure suffers the influence of apnea crises to the greatest degree, elevating with greater intensity during physical activity in this group of patients.

The mechanism by which repeated apnea crises provoke arterial hypertension remains under investigation, although it is known that it is related to one on the activity of the sympathetic nervous system, with functional lesions of vascular endothelium and of metabolic abnormalities that are known as risk factors for arterial hypertension, such as intolerance to glucose, resistance to insulin and that, in general, are present in apnea patients. Studies suggested that the use of CPAP reduces arterial pressure indices of apnea patients during sleep and that beta blockers are the most effective drugs in the control of arterial hypertension of obstructive sleep apnea syndrome carriers, indicated for adrenergic discharge as a cause of hypertension.

Cardiac arrhythmia, another important cause of cerebral vascular accident, is a disturbance of electrical conduction of the heart that is frequently present in carriers of obstructive sleep apnea syndrome. In a study of 400 obstructive sleep apnea syndrome -carrier patients demonstrated that 48% of these individuals were carriers of cardiac arrhythmia, documented principally during sleep, which did not correlate with the severity of apnea. Authors submitted 45 carriers of obstructive sleep apnea to cardiac monitoring, holter for 18 hours, finding disturbances of cardiac rhythm in 35 patients, of which eight presented disturbances that could cause cerebral vascular accident. They reported also that the use of nasal CPAP is capable of abolishing disturbances of cardiac rhythm in the majority of obstructive sleep apnea syndrome carriers.

In a study reviewing the literature, suggested that one of the factors that contributes to increased incidence of coronary and cerebrovascular diseases and in carriers of obstructive sleep apnea syndrome is hypercoagulability. They concluded in their study that such individuals present an elevated level of fibrinogen, increase in the platelet aggregation capacity and reduction of fibrinolytic capacity, alterations reversible with the use of CPAP. Román et al. cited in their studies that one of the causes of vascular dementia is subcortical ischemia, an alteration that can occur with pathology based on obstructive sleep apnea syndrome, resultant from intermittent periods of cerebral hypoxia present in this syndrome.

In a study with 23 obstructive sleep apnea syndrome-carrier patients, concluded that they present alterations in the cognitive system, such as attention deficit, reduction in capability of visual learning and limitation of planning capacity. These alterations are partially corrected with the use of CPAP.

The relation between obstructive sleep apnea syndrome and automobile accidents has already been well clarified and, according to data from the Ministry of Health, about 300,000 automobile accidents occur annually in Brazil, with more than 27,000 deaths per year, constituting a principal cause of death in the age range between 15 and 44 years. According to data from the literature, approximately 60% of truck drivers in Brazil presented some degree of daytime somnolence while accomplishing their activities; and the risk of an auto accident in carriers of obstructive sleep apnea, in Brazil, is from four to seven times greater than that of the general population, while North American studies report that about 16 to 20% of such accidents are related to excessive somnolence.

Concluding Remark
Obstructive sleep apnea syndrome is a pathology of high incidence that afflicts the population in its productive phase and causes important complications, often irreversible, to humans. Although its etiology still is not totally elucidated, it is known to be multi-factorial, which justifies more detailed studies, from which more efficacious and less invasive new treatments can arise.

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