Therapy for Obstructive Sleep Apnea

Subjects: Respiratory System

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Obstructive sleep apnea (OSA) is one of the most common sleep problems defined by cessation or decreased airflow despite breathing efforts. It is known to be related to multiple adverse health consequences. Positive airway pressure (PAP) is considered an effective treatment that is widely used. Various modes of PAP and other emerging treatment options are now available.

Keywords: patient-centered ; obstructive sleep apnea ; patient preference ; phenotypes ; OSA ; personalized care

1. Introduction

Obstructive sleep apnea (OSA) is one of the most common sleep problems. OSA prevalence in the general population ranges from 9–38% [1], with a significant economic burden with undiagnosed sleep apnea costing USD 149.6 billion in the United States. This includes USD 89.6 in lost productivity and USD 26.2 billion in vehicular motor accidents (MVA). Patients with untreated OSA have a 243% higher risk of MVA than individuals without OSA [2].

The prevalence of OSA continues to increase substantially, likely related to the rising obesity prevalence. OSA can occur in both genders and increases in advanced age [3]. OSA is characterized by a decreased or complete pause in airflow despite the effort to breathe during sleep, resulting in intermittent hypoxemia. The diagnosis of OSA can be made either at home with home-sleep apnea testing or in-laboratory overnight sleep testing with in-laboratory polysomnography (PSG). The latter test provides more details, but is more expensive, time-consuming, and requires a sleep technician to monitor. Common complaints among patients with OSA include excessive daytime sleepiness, nocturia, fatigue, witness apnea, and morning headaches [4]. The cause of OSA has been reported to be muscle relaxation during sleep, leading to repetitive upper airway collapse and decreased blood oxygenation.

Several risk factors have been reported to be associated with OSA, for example, older age, male gender, obesity, large neck size, and craniofacial morphology. Various adverse outcomes are associated with OSA, including motor vehicle accidents, metabolic syndrome, neuropsychiatric dysfunction, cancer, cardiovascular diseases, cerebrovascular morbidity, and mortality [5]. Without treatment, OSA can cause a substantial economic burden on the healthcare system [6].

Understanding pathophysiology and different OSA endophenotypes will facilitate selecting the proper treatment. A structural or physiological pathways approach can be taken in managing patients with OSA. Structural or anatomical impairment in OSA includes the main risk factors, obesity and craniofacial anomalies, such as bilateral mandibular hypoplasia and craniofacial microsomia [7]. Obesity and a large neck circumference are well-known OSA risks because of an increase in neck adipose tissue leading to a high propensity of pharyngeal collapse [8]. Muscles that can lead to airway collapse include (1) tongue muscles (genioglossus), (2) muscles affecting the position of the hyoid bone (sternohyoid and geniohyoid), (3) muscles of the soft palates (levator veli palatini and tensor veli palatini) [9]. Patient evaluation is, therefore, essential to identify these abnormalities. In OSA populations with anatomical problems, intensive lifestyle modifications, hypoglossal nerve electrical stimulation, myofunctional therapy, oral appliance therapy, pharmacological treatment, and surgical correction such as a tonsillectomy or bariatric surgery should be considered [10]. On many occasions, OSA is classified based on its physiological phenotypes, including collapsibility, over loop gain (instability of ventilatory control system), low and high arousal threshold, airway dilator muscle responsiveness, and overnight rostral fluid shift [11].

2. Interventions for OSA

The initial treatment for OSA prior to the 1980s was a tracheostomy, which bypasses the impeded site of the upper airway, and unobstructed breathing occurs. However, this procedure has potential peri/postoperative complications, including mucous plugging, infection, tube dislodgement, disfigurement, communication challenges, and displacement [12].

In 1981, continuous positive airway pressure (CPAP) therapy was introduced by Collin Sullivan as an OSA treatment that provides a pneumatic splint for the nasopharyngeal airway to prevent airway collapse and improve oxygenation [13]. The 2015 American Academy of Sleep Medicine guidelines recommends using oral devices in cases where CPAP is contraindicated or alternative therapy is needed [2]. Despite the evolution of OSA treatment, PAP remains the preferred treatment with the most significant evidence of AHI and symptom reduction. Many other different PAP options are now available based on the mode of positive air pressure delivery and setting, such as auto-titrating positive airway pressure (APAP) and bi-level positive airway pressure (BIPAP) [14]. The individual must wear them regularly during sleep to avoid apneic events. However, many patients cannot tolerate PAP machines, resulting in poor adherence [15]. To improve adherence, advances have been made to monitor and track compliance and identify the challenge as leaks and residual apnea, with the data being downloaded via a smart card or cloud base [16]. Moreover, to maximize the benefits, the insurance providers are now mandating compliance of at least 4 h of usage for 70% of the night during the first month for continued device coverage [17].

Treatment for OSA should be tailored and offered to each patient so that each one will be able to receive the best treatment option. In general, CPAP is recommended as the first-line treatment for adult OSA. In patients with OSA who cannot tolerate the fixed pressure from the CPAP, APAP can be used. In patients who require a higher pressure than the maximal pressure of the CPAP machine to eliminate the apnea/hypopnea event, BIPAP is needed. For OSA with other comorbidities such as obesity hypoventilation syndrome, BIPAP may be considered for better hypercapnia improvement. Mandibular advancement devices can be an effective treatment, especially in those with small upper airway lumen and mild–moderate positional OSA [18]. Moreover, positional therapy may be used as an alternative treatment for mild positional OSA [19]. Inferior turbinate reduction and septoplasty have been shown to facilitate the OSA treatment in a patient with inferior turbinate hypertrophy and deviated nasal septum septoplasty, respectively. Maxillary/mandibular advancement can be considered in patients with maxillary/mandibular hypoplasia. For those with poor upper airway muscle function, nerve stimulation and myofunctional therapy can help increase muscle function. Hypoglossal nerve stimulation is found to be useful in patients with moderate to severe OSA who have no complete concentric collapse of the airway [20]. Recently, the electrical stimulation device to strengthen the tongue muscle tone has been shown to reduce AHI in mild OSA [21]. Pharmacotherapy may be added in those with high loop gain phenotypes to help decrease the plant and/or controller gain. Sedatives such as trazodone and eszopiclone have been found to be able to reduce AHI in patients with a low arousal threshold phenotype [22]. Unlike adults, adenotonsillectomy is considered the first-line therapy for pediatric OSA due to the risk of facial growth alteration from PAP mask usage [23][24]. In pediatric cases with high-arched palate or maxillary constriction, rapid maxillary expansion can be an alternative treatment [25].

Treatment for OSA may not be a one-size-fits-all problem due to the diversity of OSA. Therefore, many surgical interventions act as a salvage treatment after PAP treatment intolerance/failure, particularly in patients with surgically correctable abnormalities. This includes nasal polypectomy, adenoidectomy, tonsillectomy, uvulopalatopharyngoplasty, glossectomy, tongue base reduction, mandibular advancement, genioglossal advancement, hyoid myotomy suspension, maxillomandibular advancement, and bariatric surgery. Adenotonsillectomy in the pediatric population with OSA showed trivial results [26]. A recent meta-analysis by Bonetti et al. concluded that patients with pre-existing temporomandibular joints could be treated for OSA with mandibular advancement devices and will not experience a significant exacerbation of symptoms [27], disregarding TMJ disorders as a contraindication for MAD in OSA management. The most recent nonanatomic surgical option, hypoglossal nerve stimulator implantation, showed a surgical response in 75% of participants in a 5-year clinical trial. A surgical response in this trial was defined by the decrease in the apnea-hypopnea index (AHI) by more than 50% from the baseline and less than 20 events per hour [28]. Other therapeutic methods can also be considered an alternative or adjunctive treatment in mild–moderate OSA, such as oral appliances for patients with malocclusion, myofunction therapy [29], weight loss, and behavioral change, expiratory positive airway pressure (EPAP) therapy to help in preventing airway collapse during sleep. AHI increases with a supine position in more than half of the patients with OSA [30]. Therefore, positional therapy has been implemented as an additional treatment [19]. A recent meta-analysis concluded that treatment with trial and definitive MAD improved PSG parameters, with a statistically significant decrease in AHI (11.46 ± 9.65, $p < 0.0001$) and ODI (9.10 ± 8.47, $p < 0.0016$) with the definitive device [31]. Oral appliances can, therefore, be used as cheap and easy-to-use alternatives for OSA in the future [32]. Details are shown in **Table 1**.

Table 1. Surgical and Non-surgical Intervention of OSA.

Non-Surgical Intervention	Surgical Treatment
• CPAP, BIPAP, APAP • EPAP • Lifestyle modifications (weight loss, exercise) • Myofunctional therapy • Oral appliances • Pharmacological treatment	• Hypoglossal nerve stimulation • Genioglossal stimulation • Surgical correction of anatomical abnormalities (tonsillectomy, nasal polypectomy, adenoidectomy, uvulopalatopharyngoplasty, glossectomy, tongue base reduction, mandibular advancement, genioglossal advancement, hyoid myotomy suspension, maxillomandibular advancement) • Bariatric surgery • Tracheostomy

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