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Mini Review

Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea: A New Kid on the Block

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Abstract

Around 29.5 million people in the United States over the age of 30 years suffer from mild to severe Obstructive Sleep Apnea. Positive Airway Pressure (PAP) remains the mainstay of treatment of OSA. Despite being the gold standard treatment for many years, the compliance rate for the PAP devise remains low. Other modes of treatment such as the use of Mandibular Devices, surgery for relieving the obstruction, and weight reduction surgeries carry high morbidity and mortality. The new evolving Upper Airway Stimulation therapy – Hypoglossal Nerve stimulation opens new and alternate pathways of treatment approach to OSA. This opinion-minireview explores two new devices, the INSIGHT MEDICAL SYSTEMS DEVICE, and the eXciteOSA device.

Keywords: Positive Airway Pressure (PAP); Obstructive Sleep Apnea (OSA); Mortality

Introduction

Obstructive sleep apnea (OSA) is one of the clinical conditions affecting millions of people with high prevalence and accounts for the significant increase in morbidity. It is the repetitive collapse of the upper airway, either partially or entirely during the sleep. OSA forms a part of the spectrum of Sleep-disordered breathing. Since the advent of sleep medicine, OSA has remained the most prevalent and deadly sleep disorder [1].

Despite the understanding and advancement of this disease, it remains underdiagnosed, with only 40% of patients with OSA are being diagnosed. The annual economic burden in the United States from undiagnosed OSA accounts for $149.6 billion, with $86.9 billion in lost productivity, $26.2 billion in motor vehicle accidents, and $6.5 billion in workplace accidents. With the association of OSA with multiple comorbidities, diagnosing and treating OSA could save $100.1 billion [2,3].

The mechanisms causing the obstruction are still not completely understood and ranges from upper airway anatomical disruption, muscle desynchrony, neuromuscular tone, and other factors such as obesity, congenital or acquired causes of obstruction. This can result in snoring, apnea, hypopnea, hypoventilation during different stages of sleep [4].

The symptoms associated with OSA can be snoring, witnessed and unwitnessed apneas, drooling, choking and suffocation sensation, dry mouth and sleep bruxism, daytime symptoms such as excessive daytime sleepiness, morning or nocturnal headache, disturbance in neurocognitive day to day functions [5].

Clinical symptoms of OSA include high blood pressure, obesity, increased mean neck circumference, retrognathia, high arched palate, macroglossia, erythema, and edema of uvula due to snoring tonsillar pillar hypertrophy, and elevated Mallampati score.

Untreated OSA is associated with increased mortality and morbidity associated with obesity, insulin resistance, glucose intolerance, and cardiovascular diseases such as hypertension, stroke, heart failure, atrial fibrillation, arrhythmias, and pulmonary hypertension. In addition to physical illness, excessive daytime

sleepiness and neurocognitive disturbances can affect day-to-day function resulting in drowsy driving leading to accidents, sleepiness at work leading to job loss, and strained relationships.

The main principle behind the treatment and management relies on keeping the airway patent during sleep, thus reducing the symptoms. The treatment options include behavior modifications, PAP, and surgical management. Depending on the severity of symptoms and Apnea Index (AI), treatment options can be chosen. Positive Airway Pressure remains the ultimate treatment option for patients with OSA currently. However, positive airway pressure devices are often uncomfortable for patients who require to be mobile and for those who cannot tolerate devices during sleep leading to low compliance [3,6,7].

Besides the PAP devices, oral appliances and surgical intervention has been considered. Lately, there has been increasing interest in genioglossal muscle stimulation to help patients with mild to moderate OSA [8]. Hypoglossal nerve stimulation has made its way to clinical practice, but its applications have been limited due to expertise, cost, efficacy, and selection criteria. Recently, the daytime genioglossal muscle stimulation device has been approved for patients with mild OSA, which is cheaper and noninvasive. In this minireview, we will try to discuss the two new devices, their indication, and their efficacy which helps in improving OSA by genioglossal muscle stimulation or hypoglossal nerve stimulation. Though polysomnography is the gold standard for diagnosing obstructive sleep apnea, it doesn't provide anatomic details of airway obstruction. The Drug-induced Sleep endoscopy (DISE) procedure allows the evaluation of the dynamics of the upper airway. It is primarily used for patient selection for surgical procedures for OSA treatment. It can also be used to analyze the reasons for the failure of Positive Airway Pressure treatments. DISE is a fiber optic examination of the upper airway under drug-induced sedation [9]. During the procedure, the patient is kept supine, with the environment in the procedure room mimicking the patient's usual sleep environment. Controlled sedation is given using propofol or midazolam, or both. Once a required level of sedation is achieved, a flexible fiberoptic endoscope is inserted, and structures of the upper airway, nasal passage, velum, the base of tongue, epiglottis, and larynx are visualized. There is no universal scoring system [10]. The commonly used scoring system is the VOTE classification, which assesses the degree of obstruction at four levels- Velum, Oropharynx Lateral Walls, Tongue Base, and Epiglottis. Patients with mild OSA are noted to have obstruction most often at a single site, whereas patients with severe OSA have a blockage at multiple sites [11]. Based on the maneuvers during the procedure, such as chin lift-jaw thrust, also help in assessment for Mandibular Assist Device.

PAP remains the first-line treatment of choice for OSA. However, the constant need to use the device, fewer choices of mobility, and lack of compliance for using PAP, alternate treatment modes for OSA are currently being explored. The other treatment procedure for OSA is surgical procedures such as Uvulopalatopharyngoplasty (UPPP), tongue base resection, hyoid suspension, multilevel pharyngeal surgery, etc. [12].

The latest advancement in science has opened a new model of OSA management with the minimally invasive procedure and device usage – Hypoglossal Airway Stimulation or the Upper Airway Stimulation (UAS) procedure using the Inspire medical systems inc.

The hypoglossal nerve is a somatic motor efferent nerve that innervates the tongue muscles. Among its four branches, the meningeal, descending, hypothyroid and muscular; the muscular branch supplies all the intrinsic and extrinsic muscles except the palatoglossus, which receives its innervation from the Vagus nerve [13]. The extrinsic muscles assist in drawing the tongue forward, upward, and retraction the tongue. Genioglossus remains the critical phasic muscle in the pathogenesis of OSA. Stimulation of the genioglossus muscle results in depression and protrusion of the tongue. Thus, maintaining the patency of the upper airway and decreasing the upper airway collapsibility. Loss of this muscle activity results in collapse of the upper airway [10]. The absence of upper airway collapsibility during wakefulness is attributed to reducing airway muscle tone and changes in the neural drive [4,14].

Upper Airway Stimulation (UAS) is indicated in patients with mild to moderate OSA who cannot tolerate positive airway pressure therapy or have failed PAP therapy. The UAS is currently used in patients aged 22 years and above. UAS is contraindicated in patients with central sleep apnea, sleep hypoventilation, complete palatal collapse, or patients with BMI above 32kg/m^2.

The latest treatment modulations for OSA target the hypoglossal nerve stimulation to maintain upper airway patency. These devices

contain a sensor, implantable pulse generator, and stimulating electrodes. The sensor detects intercostal chest respiratory movements sends signals to the pulse generator in the subclavian muscle, which sends stimulus to the branches of the hypoglossal nerve resulting in protrusion of the tongue and opening of the upper airway. Selection of patient requires assessment of patient using DISE procedure. The implantation of the device requires a short surgical procedure under anesthesia. Studies conducted using INSPIRE MEDICAL SYSTEMS DEVICE showed changes in OSA severity with reductions in Apnea-Hypopnea Index and oxygen desaturation levels. Examination at baseline, one month, and follow-up after 12 months showed significant improvement in AHI score, Functional Outcome of Sleep Questionnaire (FOSQ), and Epworth sleepiness score. Adverse effects include post-surgical procedure effects such as discomfort at the implantation site requiring repetition of the implantation procedure (reported in 2 patients), throat discomfort, pain at the insertion site, short-lived muscle soreness. Loss of tongue sensation was reported in 18% of the patients, which recovered in less than 30 days post-procedure. No permanent sensation loss was reported [15]. The ADHERE registry is an international prospective observational study that collects UAS outcome details from patients and physicians. This study shows the durability and adherence to UAS are high. Female sex and lower baseline BMI predict better positive outcomes from UAS therapy [16]. Five-year outcomes post-UAS therapy show improvement of sleep quality, quality of life, better respiratory function, and less adverse severe events [10,17,18].

Continuous hypoglossal nerve stimulation

The INSPIRE medical device requires stimulation from respiratory movements. The aura6000 system by ImThera Inc. consists of a silicone cuff with six independent electrodes inserted around the hypoglossal nerve, connected to the Implanted Pulse Generator and sensor. The IPG is implanted in the pectoral pocket subcutaneously. Stimulation was titrated 3- or 4-weeks post-surgery, and patients were followed with scheduled visits. A decrease in daytime sleepiness was observed at three months and continued to decrease until 12 months of the study. Fatigue Subjective Scale and Epworth sleepiness scale show reduction at three months until after 12 months of the study [6]. Adverse events most often were technical, either requiring replacement or repair. Loss of tongue sensation was observed in two patients who recovered without sequelae. The cyclical stimulation of the hypoglossal nerve tends to cause the minor repair to the nerve fiber. Patients in the study found the treatment comfortable despite the required charging duration of one hour. The aura6000 is currently in the clinical trials phase III.

Bilateral hypoglossal nerve stimulation

The Genio system consists of a disposable external activation unit that can be worn on the chin at night and removed in the morning, a stimulation unit implanted in the submental region over the genioglossus muscle, and electrodes inserted on the right and left hypoglossal nerve branches. The BLAST OSA study participants required four months for stimulation therapy tolerance. The study showed high treatment compliance with minimal adverse events. The main advantages of the Genio system are bilateral stimulation, minimal implanted components, predetermined rates, and cycle duration [8].

The eXciteOSA

A prospective cohort study was conducted at Queens Hospital, UK, on 75 patients with primary snoring or mild OSA using the eXciteOSA device[14]. The eXciteOSA device consists of a mouthpiece that fits the tongue, a control unit that attaches to the agent, and a phone application that helps to manage the functions of the device. The eXciteOSA device delivers neuromuscular electrical stimulation to the intrinsic and extrinsic muscles, increasing the muscle tone and thus preventing excessive relaxation [14]. This device consists of having biphasic pulses at 20Hz for 10 seconds, followed by 20 seconds rest, for a total of 20 minutes. The principle of the eXciteOSA device is the fast-to-slow fiber transition by electrical stimulation, which increases the endurance of the genioglossus, thus causing a reduction in the number of obstructive respiratory events. There is a decrease in snoring time, and a decrease of AHI has been noted to be statistically significant[14]. The eXciteOSA device has the advantage of requiring only daytime usage, thus potentially improving patient compliance to therapy [14]. It has been observed that the use of the eXciteOSA device resulted in mean adherence of 83% [19]. Since the eXciteOSA enables daytime therapy, it has demonstrated better patient and bed partner sleep quality [19].

Conclusion

Hypoglossal nerve stimulation is the emerging therapy for OSA. Patient-centric treatment plans can be devised with the

help of emerging devices, making therapy compliance better and preventing morbidity. The hypoglossal nerve stimulation is currently being studied towards its usage to treat other significant conditions associated with OSA, especially in patients with Downs syndrome and OSA. Advancement in technology does provide some hope, but at the same time, caution needs to be undertaken to prevent inappropriate use and abuse. Patient selection and being aware of proper indication and contraindication would help benefit the selective group of patients. The verdict is not out yet but

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