Obstructive Sleep Apnea- A Comprehensive Review of Risk Factors, Pathogenesis and Management

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Abstract

Sleep is a blessing to humans. Good quality of sleep helps people live and enjoy their lives. Obstructive sleep apnea, widespread sleep disorder accompanied by disturbance or complete absence of sleep along with difficulty in breathing, choking sensation and loud snoring. Chronic obstructive sleep apnea may lead to systemic side effects especially on cardiovascular system and other vital body organs. The exact etiology is unknown, but various factors may lead to this condition. The diagnosis is made by multiple methods. Treatment is also multimodal and depends on the type and severity. This review article is written in order to provide an insight to the risk factors, pathogenesis and management of obstructive sleep apnea. Special emphasis is made on the dentist's role, duties and responsibilities in the analysis and treatment of this clinical condition.

Keywords: Sleep Apnea, Obstructive, Sleep, Dentists

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Introduction

All of our troubles fade away with a good night's sleep andeach day is put to rest with a good night's sleep. Sleep refreshes the weary laborer and restores the minds of those who have been hurt. "In life's buffet, sleep is the healthiest meal"[1]. Sleep is an essential part of human life. Several biological pathways are activated during sleep whenever humans lay their bodies to bed. The tissues of the person's body regenerate and revive themselves so that the bodies are ready for action and go about normal tasks the next day. Despite many metabolic diseases, disorders of sleep are quite prevalent nowadays. Sleep-disrupted breathing, which includes apneas, hypopneas, and oxygen desaturations, is common in asymptomatic people and gets worse as they get older. Among sleep disorders obstructive sleep apnea is the commonest of them.

There are two divisions of Sleep Apnea(SA). Central sleep apnea and obstructive sleep apnea. Central sleep apnea (CSA) is characterised by a lack of desire to breathe when sleeping as a result of insufficient breathing and perfusion on a regular basis. Such night time respiratory anomalies can result in serious sickness as well as an increased risk of severe cardiovascular outcomes[2].

OSA is a frequently reported condition characterized by the collapse of oropharyngeal muscles repeatedly while sleeping, resulting in temporary hypoxia and arousals from sleep. OSA is a prevalent situation that is distinguished from other sleep disorders by repeated bouts of obstructive, complete absence or decrease in the airflow for at least 10-30

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seconds or longer during sleep, as well as daytime tiredness or decreased cardiopulmonary function[3]. OSA is very common in adults, especially in mild to moderate forms. Its incidence has risen over the last 25 years, owing in part to the incidence of obesity in civilized countries. The implications of OSA can differ significantly amongst patients on a case-by-case basis.

Classification

There are many classification systems for OSA but the most popular is “The Apnea-Hypopnea Index (AHI)”,(Table 1) which measures numeral value of apnea along with hypopnea measures in an hour of sleep, and is used to further classify OSA. As a result, it is classified as

- Mild ($5 \leq$ AHI < 15),
- Moderate ($15 \leq$ AHI < 30), or
- Severe ($30 \leq$ AHI)[4]

Risk Factors

Although exact etiology is unknown but various factors may contribute to the development and exacerbation of the disease. Risk factors vary according to the populations examined, assessment periods and how OSA breathing episodes are defined, however they can range from minor to major age range in certain demographic groupings (e.g., adult man). Obstructive sleep apnea is a complicated chronic illness that is influenced by a variety of circumstances[5]. (Fig. 1) As more evidence accumulates, it appears that this illness has substantial hereditary origins. Familial factors are thought to account for about 40% of the variance in the apnea-hypopnea index (AHI). The OSA phenotype is most likely caused by a combination of genetic variables related to craniofacial development, fat mass accumulation, and neurological regulation of the upper airway muscles. The dangers of OSA in the overall population are well established and include hypertension, coronary artery disease, stroke, pulmonary hypertension, sudden cardiac death, and deep vein thrombosis, to name a few that significantly impact on preoperative survival. Although particular genes that regulate OSA development have yet to be identified, current mouse research suggests that multiple genetic systems may be essential[6]. Male sex, larger body mass, and older age are the "big three" risk factors for OSA. This has been known for decades. However, in the last 25 years, the relationships between these risk variables, as well as their combinations, have indeed been better documented. For instance, OSA has been discovered in women in quite majority; Although fatness may be substantially a more hazardous feature especially for young people, The relationship between gender and OSA, however, lessens as patient becomes old, although frequency among elderly lady's approaches those of males[7].

The majority of research found a strong link between OSA and hypertension, particularly resistant hypertension. Heart failure, coronary artery disease (cardiac ischemia), arrhythmias, and ischemic stroke were among the findings that supported OSA's independent role in generating CV disorders.

OSA is a multifaceted condition. However, some degree of anatomical damage of the upper airway is required. As a result, it's only natural that the majority of OSA treatments focus on resolving the anatomical issue. Studies on imaging in persons with OSA, major pharyngeal anatomical anomalies have been found to be 64-66%. A small pharyngeal airway, increased airway length, and particular pharyngeal lumen geometries, for example, have all been linked to the risk of pharyngeal collapse during sleeping. One or more sites in the upper airway can collapse. The dilator muscles, such as the genioglossus, soft palate, lateral pharyngeal walls, and the epiglottis, are pharyngeal structures that can contribute to airway crowding and collapse. Obesity is a significant risk factor for heart disease. In the clinic, neck circumference is frequently assessed and has been used to predict OSA risk. Some of the characteristics linked to OSA risk and severity include cranial-facial morphology, the position of the hyoid bone, airway surface tension, tongue scalloping, and tongue fat.

Whereas these methods have provided insight into the pathophysiology of OSA, they have two drawbacks for clinical use: 1) the expensive expense of imaging procedures, and 2) awake static imaging provides limited information into the features of a dynamic structure that closes involuntarily during sleep.

Patients undergoing elective surgery had a substantially greater rate of sleep apnea. Sedation and anaesthesia have been demonstrated to promote upper airway collapsibility, increasing the risk of problems in these individuals after surgery. Furthermore, the majority of sleep apnea sufferers go undetected, putting them at danger during the perioperative period. It's critical to recognise these patients so that proper action can be performed quickly.

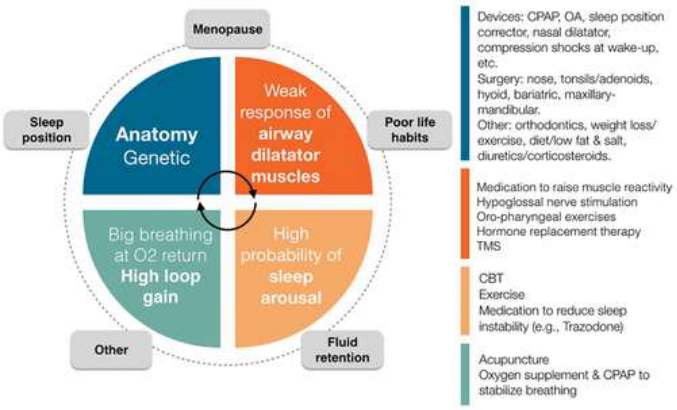

Fig. 1 Obstructive sleep apnea susceptibility variables, with varied dominance depending on patient attributes and instances of therapy objectives (not exclusive to each factor). CPAP stands for positive end-expiratory pressure; OA stands for oral appliance; TMS stands for transcranial magnetic stimulation[7].

Pathogenesis

OSA occurs when neck muscles relax and restricts the airway during sleep. Forceful inhalation against a blocked upper airway causes negative intra-pleural pressure in people with OSA. Hypoxia and hypercapnia become more severe as the apnea persists. Hypoxia also produces systemic and pulmonary vasoconstriction as a result of sympathetic nervous system activity[8]. A cruel sequence of hypoxia-reoxygenation develops during the apnea/hypopnea-recovery period, generating homocysteine, cysteine, and free radicals, leading to oxidative stress. Systemic inflammation is triggered by recurrent hypoxia, which causes changes in transmural, intrathoracic, and cardiac pressures. Coronary arteries are damaged by vascular endothelial cell (VEC) injury, which can lead to coronary artery disease (CAD) or cardiac ischemia[9]. Reduced Nitric Oxide (NO) expression causes damage to VECs [dysfunction in endothelial NO synthase (eNOS), also called "eNOS uncoupling"] with superoxide (O2) generation boosted[10]. Drager et al. discovered that hypoxia in adipose tissue occurs at the cellular level, resulting in lipolysis, macrophage infiltration with chronic inflammation, endoplasmic reticulum strain, and mitochondrial harm. Cardiometabolic dysfunction might result from such alterations, which are accompanied by a drop in adiponectin and raised levels of leptin[11].

Sign and Symptoms

Patients may complain of the following symptoms

- Insomnia (disturbance in sleep),
- snorting,
- breathing cessation while sleeping.
- extreme daytime sleep
- noisy snores
- Sleep-related episodes of halted breath ing have been seen.
- Awakenings that include gasping or coughing
- development of xerostomia or burning sensation in mouth
- difficult to focus in daily activities
- temper swings like despair or anger
- High blood pressure
- Decreased libido[12]

Effects of OSA

Long-term and chronic OSA has significant effects on the human body. It has a significant effect on the cardiac and metabolic functions of an individual's body. OSA may lead to hypertension in susceptible individuals. Not only high blood pressure, but it has also been associated with ischemic stroke myocardial infarction, heart failure, and arrhythmias[13]. Because of how common but under-diagnosed OSA is, much research is needed to fully comprehend its impact on the human body. Modifications in the cardiovascular system (CVS) are caused by injury to the vascular endothelial cells (VECs) and other processes seen in OSA. OSA can harm a patient's general functionality, particularly in light of the current focus on detecting and reducing cardiac-related mortality[14].

Obstructive sleep apnea is prevalent, and it's linked to daytime sleepiness, as well as an increased likelihood of automobile accidents and heart disease[15]. In patients with COVID-19, the occurrence of OSA should be considered as a potential cause for adverse outcomes (such as ICU hospitalization, assisted ventilation, or death). OSA may facilitate SARS-CoV-2 infection, and once infected, it may lead to a higher prevalence of cardiovascular problems such as arrhythmias and cardiac ischemia, and hypercoagulability conditions, resulting in a poor clinical outcome[16].

Some drugs and general anesthesia might cause obstructive sleep apnea.

Sedatives, narcotic analgesics, and general anesthetics press the oropharynx, that leads to worsening of obstructive sleep apnea. It may contribute to common eye problems like glaucoma[17].

Prof. Gilles Lavigne and colleagues had made a publication, related to etiology, diagnosis and therapy related to sleep problems in dentistry patients in 1999[18]. OSA may cause mouth breathing which may lead to xerostomia, dental caries, gingivitis, periodontitis, and oral ulcers. Patients with TMJ disorders may also predispose to OSA. Bruxism has also been reported in patients with OSA 19. - Fig 2. demonstrates the possible complications of OSA.

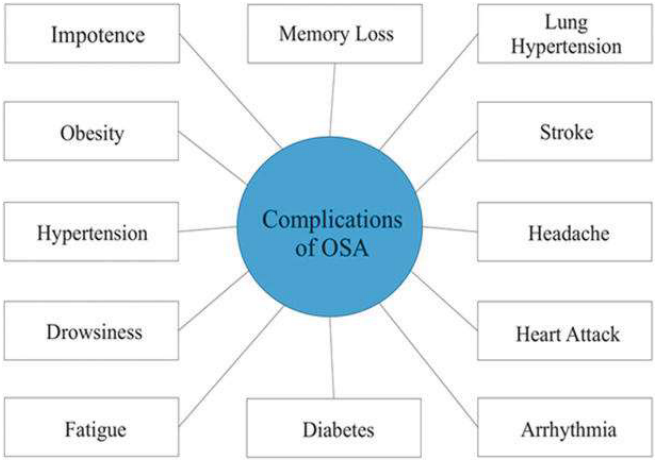

Fig 2. Demonstrating the possible complications of OSA[20].

Diagnosis

Treatment of any disorder is based on appropriate history, diagnosis and treatment. Polysomnography, limited channel testing, split-night testing, and oximetry are utilised to diagnose OSA, as well as the history and physical examination. The most common method for determining if a person has OSA is nocturnal attended polysomnography, which requires an overnight stay in a sleep facility. It may be assisted with electroencephalography (EEG), electrooculography (EOG), electromyography (EMG), and physiological variables like sleep positioning, respiratory activity, oxygen saturation, blood pressure, and ECG[21].

Several surveys such as the STOP, Berlin, Epworth sleepiness scale, STOP-BANG survey, and Pittsburg sleep quality index, were created and validated to assess for OSA high risk (in children). The STOP questionnaire is the most widely used of these, with a sensitivity of 72 percent and an increase to 83.6 percent when BMI, age, neck circumference, and gender are included (STOP-BANG questionnaire)[22]. When indicated, preoperative polysomnography is recommended by the American Society of Anesthesiologists (ASA)[12] despite the

fact that it may be the most less expensive method of detecting OSA. Clinical approaches that could be used preoperatively to predict severe OSA with a fair degree of precision are possible, but no one prediction tool acts as an optimal prior test. The most reliable questionnaires were the Berlin questionnaire and the Sleep Disorders Questionnaire, whereas the most efficient diagnostic models were morphometry and combined clinical-cephalometry.

Treatment

Individuals with sleep-related respiratory issues have a better quality of life and have a higher rate of morbidity and mortality. For choosing and arranging obstructive sleep apnea (OSA) therapies, a thorough assessment is required. A sleep physician diagnoses OSA and other sleep-disordered breathing problems. OSA is handled by a multidisciplinary team through courteous interprofessional collaboration[21]. (Fig. 3,4,5).

The treatment for OSA patients can be divided into:

Active treatments that patients apply themselves and other treatment strategies which are broken down into two parts.

1) Non-invasive: (oropharyngeal exercises in general and specific, CPAP, OA, food control, and cognitive and behavioral treatment)

2) Invasive: Nasal operations, upper airway surgical procedure, maxillary/mandibular surgery, and weight loss surgery for obesity, as well as hypoglossal nerve stimulation in more severe cases) are all examples of surgical procedures.

For mild cases patient should be evaluated by sleep physician. Sleep doctor evaluates medication and alcohol usage, degree of activity, and the existence of appropriate situation, for example; overweight, depression or anxiety, diabetes, hypertension, and metabolic syndrome. Following that, the sleep doctor recommends individuals different sleep related investigations then makes therapy recommendations depending on their medical condition and test results[22]. Easy, efficient, and cost-effective TIMT training can be done at home.

Behavioral therapy focuses on variables which could support the development of OSA. Most OSA advised to stop alcohol and sedatives. In some people, losing weight can improve airway patency by reducing apneic episodes and snoring. Preventing the supine posture during sleep may assist to prevent the development of insomnia and respiratory issues in some people.

Many noninvasive methods are introduced which help patients For example threshold inspiratory muscle training (TIMT) which is an easy, efficient, and cost-effective can be done at home. Although the effect of any specific medication is not proven, and the effectiveness related to potential drug treatments and its effects for OSA has yet to be determined[23].

The Dentist's Role

A dental sleep medicine dentist's main responsibilities include screening for OSA risk factors, providing sleep hygiene and health education to avoid OSA, prescribing OA treatment when necessary, and referring patients to a sleep specialist for objective assessment of successful dosage. Treatment includes first consultation with a sleep medicine specialist. Dentists should rule out additional illnesses that are associated with OSA, including insomnia, headaches, or gastroesophageal reflux disease while treating sleep bruxism and temporomandibular disorder/pain[25]. Therefore, the dentist's job entails

1) Checking sufferers for OSA risk variables (e.g., retrognathia, high arched palate, enlarged tonsils or tongue, enlarged tori, high Mallampati score, poor sleep, supine sleep position, obesity, hypertension, morning headache, or orofacial pain, bruxism);.

2) Making necessary referrals to competent health professionals, and

3) Offering oral appliance therapy with regular dental and sleep medical follow-up. Anatomic, behavioral, demographic, and neurophysiologic variables, in conjunction with smart devices and clinician experience, can impact dental prosthesis success in controlling OSA. As a result, OSA management should be customized for each individual[26].

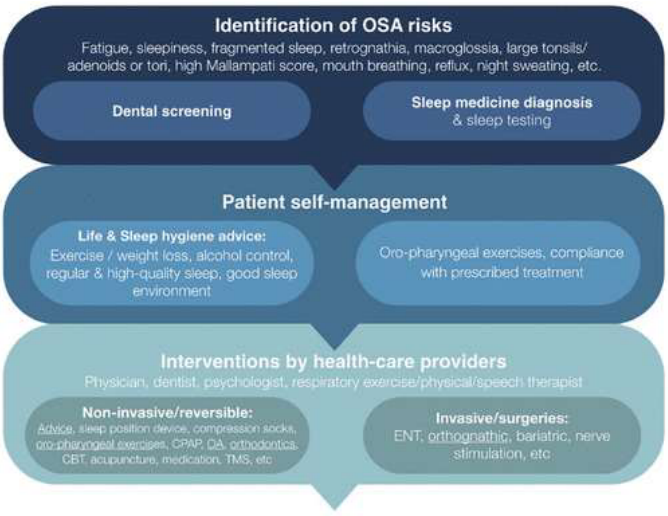

Fig 3. Proposed dental management clinical method as per OSA severity index. TMS (transcranial magnetic stimulation); CBT (cognitive behavioral therapy); CPAP (continuous positive airway pressure); ENT (ear, nose, and throat); OA (oral appliance); ENT (ear, nose, and throat);[23]

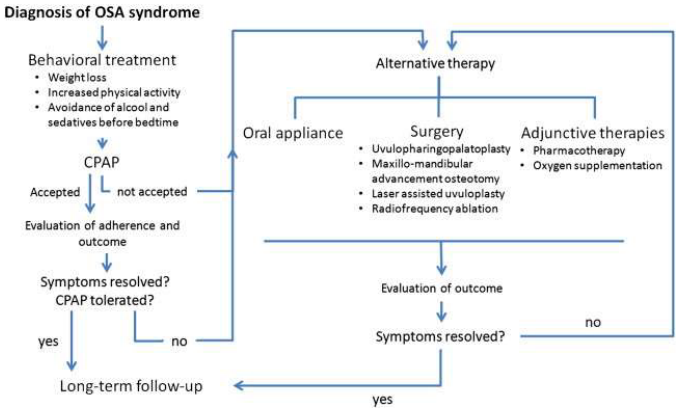

Fig 4. Flow chart showing diagnosis and treatment options for OSA patients[24]

Dental Follow Ups

For OA, dental follow-ups are scheduled every 2 to 4 weeks, then every 6 and 12 months, and finally every year. Comfort, efficacy, adverse effects (e.g., tooth displacement, temporomandibular complaints, tooth clenching or grinding with headache or pain exacerbation), and subjective response/benefit to therapy are all evaluated. OA dental follow-ups begin at the dentist's office. When a subjective perception of effective modulation (progress in patient symptomatology) is acquired, a reference to a sleep physician should be made to assess improvement in objective indexes using a PSG or a home sleep test. Relief in clinical features like weariness or drowsiness may suggest a more consistent sleep architecture, but it does not always mean that apnea and oxygen desaturation, which are thought to be the source of OSA's comorbidity, have improved.

Non-surgical Treatments for Adult OSA

Continuous Positive Airway Pressure

Nasal continuous positive airway pressure (CPAP) will be the primary nonsurgical method in which oropharynx is kept open which facilitates while sleeping. In moderate-to-severe OSA, proper frequent use of CPAP successfully lowers sleepy complaints and enhances life quality measurements. In most cases, CPAP has shown 75% success in moderate to severe cases[27].

Oral Appliances

Dental prostheses are only worn at night and at workplace to widen the airway by shifting the tongue (forward) or the jaw (backward). The appliance's stimulation of oropharyngeal relaxing muscles may result in reduction of airway non permeability, which may help to maintain airway patency when sleeping, while the enlargement of oropharyngeal airway is the primary factor which prevents airway blockade[28]. Many oral appliances were designed and in use to treat this clinical modality. Among them tongue-retaining devices and orthodontic or mandibular progressing appliances

are frequently used appliances. OAs and CPAP, are comparable in terms of clinical and associated consequences. When CPAP is unsuccessful, many individuals manage dental prostheses (OAs) well. Majority patients preferred oral appliances to surgery. The combination of CPAP and oral appliances had success rate of 40 - 80%. Long-term OA use necessitates continuous monitoring for dental and bone abnormalities[28].

The Tongue-retaining Appliance

The tongue-retaining appliance is a tailor soft acrylic appliance with an anterior plastic bulb that covers the upper and lower teeth. The tongue is held in the forward direction within the bulb by negative suction pressure. It stabilises the mandible and hyoid bone by pushing the tongue forward through its connection to the genial tubercle, avoiding tongue retrolapse. Such appliances open up the throat and reduce snore and apnea by reversing pharyngeal blockage at both the oropharyngeal and hypopharyngeal levels. Tongue posture stabilizers and soft palate trainers are rarely utilised[29].

Factors Affecting Efficiency of Oral Appliances

The patient's age, marital status, avoidance from recreational drugs such as caffeine and alcohol, weight gain across a 12-month period, reduction of BMI upto 25%, obesity, early magnitude of the AHI scores (5-15), supine sleeping posture, sufferer's acceptance and confidence are all variables that impact the sleep disorder's reaction to oral devices[30].

Complications of Oral Appliances

Complications depend upon the type of oral appliance. Patients may report dental malocclusion, TMJ pain and TMJ dislocation. Excessive salivation, tongue dryness, tooth soreness, posterior open bite, and insomnia are some of the other negative effects. However, these side effects were typically moderate and disappeared with device adjustment[31]. Limited lateral flexibility during jaw motions is one of the drawbacks of oral appliances. Recalls are required every two weeks, one month, and then every six months. The appliances are held in position through residual teeth and apply pressures over dentition that are practically orthodontic in nature. They can also become loose, deformed or may break, necessitating regular repair.

Mini-implant Assisted Rapid Maxillary Expansion

Rapid maxillary expansion (RME) is considered to be an effective therapy for OSA in children with maxillary contraction, as per recent studies. By expanding the nasal cavity, the maxillary skeletal expander (MSE) can considerably improve ventilation through the nasal airway. Mini-implant-assisted rapid maxillary expansion (MARME) has been a common therapeutic option for elderly patients since it reduces or eliminates unpleasant dental side effects. The MSE is a special MARME device because it uses four mini-implants in the posterior region of the palate with bicortical engagements of the palatal and nasal cortical bone layers. Nonsurgical MARME in young individuals is now achievable and anticipated, according to new research. In many individuals, MARME appears to reduce upper airway obstruction while also being an appropriate treatment for maxillary transverse insufficiency. As a consequence, MARME may be a viable treatment alternative for people who suffer from OSA.[31].

Surgical Treatments for Adult OSA Uvulopalatopharyngoplasty

Among the most appropriate treatment therapies for OSA is uvulopalatopharyngoplasty (UPPP), which involves the removal of the tonsils, uvula, and posterior velum. UPPP has been described in a number of ways. As UPPP does not reliably produce AHI normalisation, the AASM does not recommend it as a stand-alone treatment for treating moderate to severe OSA[32].

Tracheostomy

In 1980s, tracheostomies were the most common surgical technique for treating OSA patients when traditional medicinal therapies failed. Even though tracheostomy has the advantage of significantly relieving OSA by bypassing upper airway blockages, it is considered to be the last surgical procedure for treatment of OSA. Individuals who already have rejected medical treatment, are not suitable for soft tissue surgery, and/or have declined maxillomandibular advancement (MMA) surgery are the ideal options for tracheostomy[33].

Maxillomandibular Advancement Surgery

MMA surgery has a documented consierable success rate which makes it a very appropriate therapeutic modality. Modified MMA is an effective therapy for moderate-to-severe OSA since it has no negative effects on facial appearance or dental occlusion. Surgical-orthodontic collaboration is necessary for better results. Early improvement can be achieved using a surgery-first approach[34].

Staged or Phasic Surgical Protocol for OSA

The soft palate, lateral pharyngeal wall, base of the tongue, and hypopharynx are now well recognised as possible locations for upper airway blockage in Patients with OSA. The surgical therapy for Phase I is decided by the amount of obstruction established during the presurgical evaluation. For phase I failures, the MMA advanced osteotomy is employed in phase II surgical reconstruction[35].

Hypoglossal Nerve Stimulation

In the age of neurostimulation, hypoglossal nerve stimulation may be used as a treatment for OSA patients. The ultimate success of hypoglossal nerve stimulation appears to be greatest in patients with a low BMI, an AHI of less than 50, and a palatal collapse pattern that is anteroposterior[35].

Treatment type	Measure used
Conservative	Lose weight, sleep in lateral position, avoid alcohol
Medical	Use nasal continuous airway pressure, auto-continuous positive airway pressure, bilevel positive airway pressure
	Use oral appliances
	Give medication
	Treat associated diseases, e.g., hypothyroidism, acromegaly, allergic rhinitis
Surgical	Tracheostomy
	Nasal procedure, e.g., turbinectomy, polypectomy, septoplasty
	Uvulopalatopharyngoplasty
	Laser assisted uvulopalatoplasty
	Maxilla-mandibular advancement
Experimental	Pharyngeal pacing
	Radio-frequency ablation
	Rapid maxillary expansion

OSA: Obstructive sleep apnea

Fig 5. Showing surgical options for OSA patients

Future Studies

Modern dental prostheses enable for more lateral jaw movement, improved dental coverage, and higher retention. Removable (titratable) devices enable the dentist to gradually increase the degree of mandibular protrusion in order to produce the highest available therapeutic outcome. Users experience increased rates of dental prosthetic treatment compliance, that can be verified scientifically with an intraoral regulatory device. Several studies are presently being conducted to compare the effects of adjustable oral appliances vs. CPAP in the treatment of OSA. Snoring, choking, weariness, or excessive daytime sleepiness are all signs that can be used to screen for OSA. Yearly polysomnography may be recommended for screening OSA in suspected individuals, as it is preferable to over-diagnose even a worrisome illness than to under-diagnose it. Future study is needed to see if polysomnography can be used as a screening tool for OSA and improve cardiovascular outcomes.

Furthermore, to investigate the relationship of endocrine variables to obstructive sleep apnea syndrome in a thorough manner, case-control studies are required. A small number of mortality studies have revealed that people with obstructive sleep ap-

nea syndrome have a worse chance of survival, probably due to vascular disease.

Conclusion

Despite advances in the understanding of OSA, there are still open concerns and issues with regards to OSA treatments. Multidisciplinary teams of dentists, orthodontists, and oral-maxillofacial surgeons should build a strong groundwork which resolves these concerns through ensuring that OSA patients receive the best possible care. Team members must maintain constant contact and follow-up. Coordination and follow-up amongst teammates are essential for effective OSA treatment.

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