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Pharmacological and Non-Pharmacological Management of Obstructive Sleep Apnea

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Abstract: Obstructive sleep apnea (O.S.A.), also referred to as obstructive sleep hypopnea – is a sleep disorder that involves cessation or significant decrease in airflow in the presence of breathing effort. It is the most common type of sleep-disordered breathing. It is characterized by episodes of total or partial airway collapse and decreased oxygen saturation or sleep arousal. As a result of this disturbance, sleep is interrupted and non-restorative. It significantly raises morbidity and mortality in both developed and developing countries. This review aims to review relevant studies on obstructive sleep apnea. The method used is a computerized search method, the pathophysiology, clinical presentation, complications, diagnostic procedures, and therapeutic choices from the literature. The effects of O.S.A. on cardiovascular health, mental disease, quality of life, and driving safety are severe. This course of action highlights the interprofessional team's involvement in treating obstructive sleep apnea, its pathophysiology, and its causes.

Keywords: obstructive sleep apnea (OSA), mandible advancements, oral appliances, pharmacotherapy.

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1. INTRODUCTION

A common obstructive sleep apnea (OSA) syndrome involves loud snoring or choking, frequent awakenings, interrupted sleep, and excessive daytime drowsiness due to total or partial airway blockage brought on by pharyngeal collapse during sleep. When the airway gets blocked, the inspiratory airflow may be reduced (hypopnea) or absent (apnea). Obstructive sleep apnea/hypopnea syndrome is defined as five or more episodes of apnoea or hypopnea per hour of sleep with accompanying symptoms (such as excessive daytime sleepiness, tiredness, or reduced cognition) or 15 or more such episodes per hour of sleep without accompanying symptoms [1,2]. It is now widely recognized that OSA usually co-occurs with serious issues such as severe cardiovascular diseases, cognitive aftereffects, and mental disorders. There is mounting evidence connecting the syndrome to stroke, arrhythmias, heart failure, hypertension, and coronary artery disease. Cognitive impairment, issues with focus and concentration, executive function, and fine motor coordination are common complaints among OSA patients. Finally, during the illness, depression might be a major problem. Population-based research shows that symptomatic OSA affects 4% of males and 2% of women over 50 in terms of epidemiology. The frequency of OSA patients without clinical symptoms may reach 20–30% among middle-aged persons, even though OSA is typically asymptomatic. Male, obese, and 65 or older individuals with OSA are more prevalent. Obesity is undoubtedly the most important risk factor for OSA because it increases the likelihood of the condition by six times for every 10% increase in weight. The androgenic pattern of body fat distribution, notably the accumulation in the trunk and neck area, may make men more susceptible to OSA. Additionally, the neurologic control of the muscles that widen the upper airways and regulate breathing may be impacted by sex hormones. Hormone replacement treatment may prevent or lessen OSA, resulting in postmenopausal women being more likely to experience it than premenopausal women. As people age, their chances of acquiring OSA rise. Compared to persons aged 30-64, the prevalence of OSA is 2-3 times higher in elderly adults (>65 years). Despite this, OSA in kids with adenotonsillar hypertrophy has been documented. Finally, it appears that race influences the likelihood of developing the illness. Compared to white people, African Americans are more prone to OSA and experience its onset at a younger age. Clinical manifestations (Table 1) include sleep-disordered breathing, which results in frequent snoring episodes and extended breathing pauses of more than 10 seconds, disturbs sleep [2]. It is related to both hypercapnia and hypoxia as well. Even though clinical indicators of OSA appear inconsequential, the risk of cardiovascular diseases (CVD), such as myocardial infarction, stroke, hypertension, atrial fibrillation, pulmonary hypertension, and stroke rises. This risk is attributed to several factors, including systemic inflammation, metabolic dysfunction, endothelial dysfunction, and excessive sympathetic activity [3–7]. 425 million persons worldwide suffer from moderate to severe OSA, while 936 million have mild to severe OSA, according to a recent review[1]. Constant positive airway pressure is one of the available treatments.

Table 1: Most common symptoms associated with OSA

Nocturnal	Diurnal
Snoring	Excessive sleepiness
Witnesses apnoeas	Morning headaches
Choking at night	Depression/ irritability
Nocturia	Memory loss
Insomnia	Decreased libido

(CPAP), behavioral modification, mandibular advancement devices, and surgical surgery. Over the short term, patient compliance may range from 42% to 75%; greater compliance may be brought on by variables such as improved patient education and follow-up visits[9,10]. Despite CPAP being the gold standard because it can reduce blood pressure and sleep fragmentation caused by OSA while simultaneously boosting blood oxygenation[11–13], short-term patient compliance may range from 42% to 75%. Medications such as corticosteroids and nasal saline rinses have shown modest improvement in CPAP compliance when combined with other forms of conventional treatment, such as mask customization and warm humidification. Even though the strategies above have been shown to increase CPAP compliance, earlier studies suggest that up to 24% of patients may not start or even finish their CPAP prescription because of things like being unable to take time off work, insurance issues, switching doctors, and CPAP intolerance. Because of the need for a more realistic strategy for management, pharmacological therapy has been thoroughly investigated as a possible alternative to OSA treatment. More research and resources are still needed to demonstrate the effectiveness of pharmacological treatment, increase treatment adherence rates, and extend accessibility. Its estimated prevalence ranges from 3% to 7% in men, 2% to 5% in women, and up to 78% in highly obese people. OSA is caused by decreased motor tone in the tongue or airway dilator muscles, resulting in a complete or partial upper airway obstruction during sleeping[2,14]. Patients with OSA usually have a lower quality of life, drowsiness during the day, and mental, metabolic, and cardiac difficulties. OSA affects people of all ages but is most common in middle-aged, obese males and becomes more common with age. Obesity is the primary risk factor for these populations' other frequently diagnosed disorders[15].

2. PATHOGENESIS

In OSA, the development of upper airway blockage is influenced by anatomical and neuromuscular variables. The human pharynx can be viewed as a collapsible tube used for talking, swallowing, and breathing; it lacks hard skeletal support and is subjected to multiple stresses during typical inhalation, which encourages collapse. The pharynx is susceptible to collapsing due to negative pressure within the airway, the presence of soft tissues, and bony structures, which increase extraluminal tissue pressures[16]. On the other hand, the pharyngeal dilator muscles' tonic and phasic contractile activity helps to maintain pharyngeal patency. Upper airway obstructions are induced by an imbalance between these opposing forces in patients with sleep-disordered breathing. A smaller upper airway is more prone to collapse anatomically than a bigger one. Furthermore,

according to the Venturi effect, as airflow velocity increases at the site of an airway structure, pressure on the pharyngeal lateral wall decreases, and the likelihood of pharyngeal collapse increases considerably. Numerous imaging studies have demonstrated that the upper airway cross-sectional area of OSA patients is lower when awake compared to control people [17,18]. As a result, OSA is frequently associated with various alterations in the upper airways' anatomy, which shorten the pharynx. Excessive fat deposits, notably bigger parapharyngeal fat pads, have been documented in OSA patients. The thickness of the lateral parapharyngeal muscle walls leads to airway constriction in people with obstructive sleep apnea[17]. The disease has been associated with tonsil and tongue growth, retrognathia, and inferior hyoid bone displacement[19–21]. Obesity can cause an increase in neck circumference, fat accumulation in peripharyngeal tissues, and increase the chance of pharyngeal collapsibility by diminishing lung volume. Another anatomically based risk factor for pharyngeal collapse in OSA is pharynx length [22]. It has been noted that OSA patients' pharynxes are longer than those without the condition[23]. To emphasize the importance of the sleep state in the etiology of this condition, it is important to underline that abnormal breathing events only occur during sleep. As a result, in addition to the physically imposed mechanical pressures on the upper airways, the decreased activity of the pharyngeal dilator muscle[24,25]

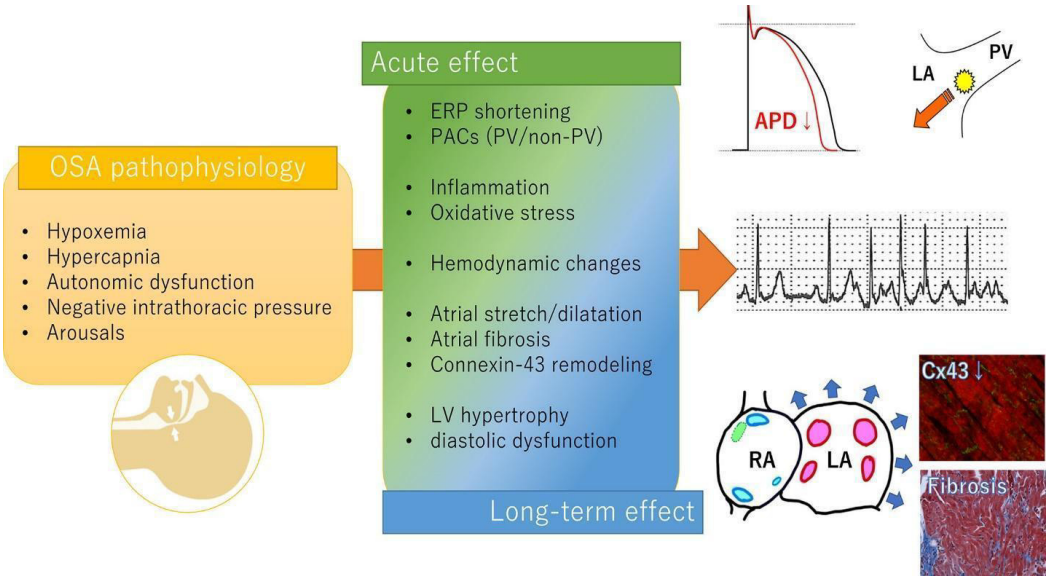


Fig 1: pathophysiology of obstructive sleep apnea[26]

Sleep plays a critical role in determining airway collapse. In healthy people, the pharyngeal cross-sectional area was lower during sleep than during alertness, and the phasic activity of numerous dilator muscles was lower during rapid eye movement sleep[27,28]. It is true that during sleep, the reflex mechanisms from chemoreceptors and mechanoreceptors that regulate the activity of the pharyngeal dilator muscles are reduced[24,25]. It has been observed that in OSA patients, pharyngeal dilator muscle activity increases while awake to compensate for altered pharyngeal anatomy[29]. When you sleep, you lose this balancing mechanism, which causes pharyngeal collapse. For instance, it has been discovered that in OSA patients, the onset of sleep is associated with significantly greater decreases in the activity of the pharyngeal dilator muscles than in controls[30]. Long-term structural remodeling caused by OSA's long-term effects is critical for promoting AF. A substantial intracardiac pressure deficit also helps with structural remodeling. Transmural pressure is one hypothesized mechanism of heart remodeling in OSA patients. Even in patients with normal systolic blood pressure (120 mm Hg), OSA with significant negative intrathoracic pressure of 60 mm Hg raised transmural pressure to 180 mm Hg throughout the night, a comparable etiology to hypertensive patients[26]. (Fig-2).

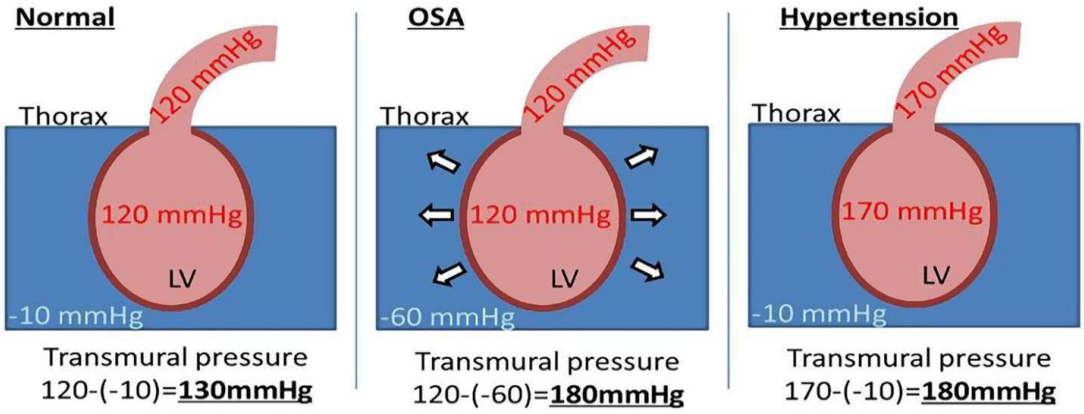


Fig 2: Raised transmural pressure to 180 mm Hg throughout the night to hypertensive patients

3. DIAGNOSIS

Clinical diagnosis is found on a physical examination and medical history (Table 2). Questioning patients about their nocturnal and daytime symptoms is crucial, and speaking with the patient's bed partner might provide important details about their sleep patterns. OSA should be suspected in those with systemic or pulmonary hypertension, metabolic syndrome, heart failure, or arrhythmias because of the tight link between OSA and cardiovascular illness. The evaluation of obesity, neck circumference, retrognathia, micrognathia, macroglossia, and inferior hyoid bone displacement are all included in the physical examination. Thyroid function tests are frequently recommended, and it is important to consider hypothyroidism, acromegaly, and Marfan's syndrome as potential underlying causes of OSA. Questionnaires and standardized tests can be used to measure the severity of daytime hypersomnolence. The Epworth drowsiness Scale, a self-report questionnaire that assesses a person's propensity to nod off in everyday scenarios, is one of the most used tools for detecting drowsiness.[31]. To measure alertness and drowsiness with objectivity, the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test was utilized. The first count is how long a patient nod off while lying in pitch-black room [32]. The second evaluates a patient's capacity to stay awake under particular circumstances, such as sitting in a dark room[33]. Objective sleep investigations are required to validate the clinical suspicion of OSA, determine its severity, and inform treatment decisions. The continuous monitoring of oxygen saturation while you sleep is one technique used to detect obstructive sleep apnea. This approach is practical and affordable but frequently lacks the rigor or specificity needed to be useful in clinical settings[34]. The gold standard for the diagnosis is still polysomnography. Progressive hypoxia is brought on by obstructions (apneas or hypopneas), which makes breathing more difficult against the blocked airway until the individual is usually awakened[35] (Figure 3).

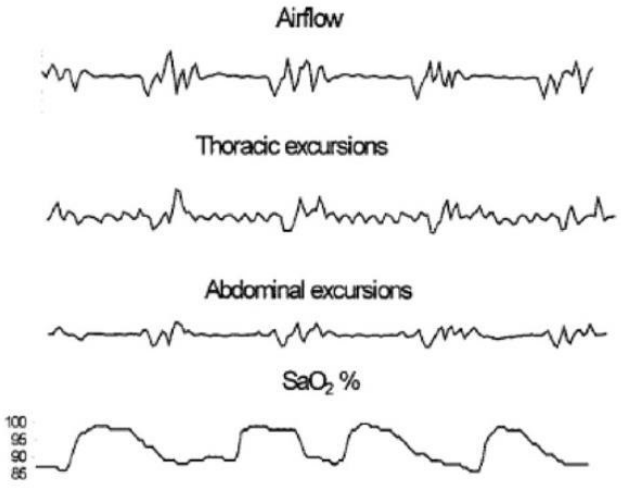


Fig 3: Polygraphic recording of an obstructive

During polysomnographic studies, several physiological variables are measured and recorded. At the same time, the patient sleeps, including pulse oximetry, an electroencephalogram, an electrooculogram, nasal and oral airflow measurements, chest wall movements, electromyogram, and electrocardiogram. Obstructive apnea is defined as a cessation of airflow for at least 10 seconds despite ongoing inspiratory effort; hypopnea is defined by one of the following three features: more than 50% airflow reduction, moderate airflow reduction (b50%) associated with oxyhemoglobin desaturation and moderate airflow reduction with electroencephalographic evidence of awakening[2]. The diagnostic criteria of OSA syndrome are summarized in Table 2[2]. The apnea-hypopnea index (AHI), calculated by dividing the number of events by the number of hours of sleep, is the most useful and objective way of classifying the severity of the disease (Table 3). Using the AHI, OSA can be classified as 'mild' (AHI 5–14), 'moderate' (AHI 15–29\) or 'severe' (AHI≥30) [107].

Classification of severity of OSA apnea-hypopnea index (AHI).

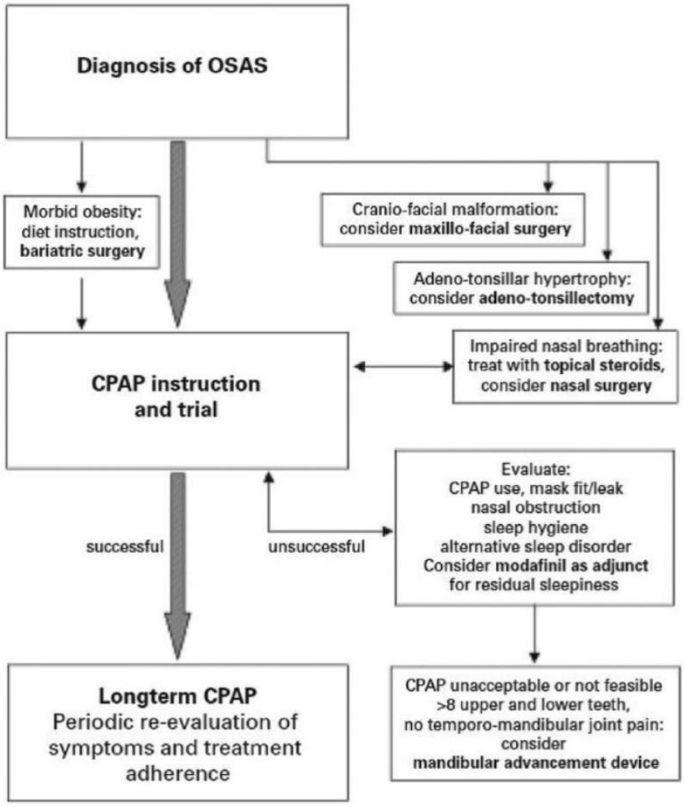
Diagnostic criteria and classification of severity of OSA syndrome.

Excessive daytime sleepiness that is not better explained by other factors	
Two or more of the following that are not better explained by other factors:	Choking or gasping during sleep
	Recurrent awakenings from sleep
	Unrefreshing sleep
	Daytime fatigue
	Impaired concentration
Overnight monitoring demonstrates ≥5 obstructed breathing events per hour during sleep.	

Mild	Moderate	Severe
AHI 5-14	AHI 15-29	AHI >30

The diagnostic criteria of OSA syndrome are summarized in Table 2.

4. MANAGEMENT AND TREATMENT OPTION[36]



Patient Education we informed the patient when the diagnosis of OSA is verified and its severity is established. We let the patient know about the risks that make OSA worse and the effects of leaving OSA untreated. We stress the need to inform patients about the increased risk of auto accidents brought on by untreated OSA as well as the dangers of operating hazardous machinery when sleep-deprived[37]. Additionally, we warn patients about the cardiovascular risks linked to OSA and advise them to refrain from engaging in activities that call for attention and alertness. Additionally, we let patients know that positive airway pressure (PAP) therapy is a continuous treatment that does not effectively treat OSA. It is uncommon for risk factor management to reverse OSA completely. Behavior modification - Behavior adjustment is suggested for individuals with OSA with a modifiable risk factor. These include giving up alcohol and sedatives, losing weight (if overweight), changing sleeping positions (if a patient has positional OSA), and sleeping differently.

5. WEIGHT LOSS AND EXERCISE

It is advised to have weight loss and exercise for individuals with OSA who are overweight or obese [38–41]. Behavioral change, nutritional treatment, exercise, medication therapy, and surgery are methods for losing weight. Early referral to a bariatric surgeon, in particular for persons with OSA and

obesity (class II/III, BMI 35 kg/m^2) and who are unable to tolerate or refuse PAP treatment, is also recommended.

6. ENDOTYPES AND PHENOTYPES OF SLEEP APNEA

OSA is a difficult illness caused by several unknown factors. As a result, numerous scientists and medical experts have begun to define OSA as a heterogeneous disease based on endotypes (underlying causes) or phenotypes (clinical manifestations). Other respiratory illnesses, such as asthma, chronic obstructive pulmonary disease (COPD), and acute respiratory distress syndrome (ARDS), have been defined as different disorders, even though OSA has not yet been fully recognized. Reduced anatomical compromise, reduced pharyngeal dilator muscle function, high loop gain, and low arousal threshold are endotypes found in OSA and are risk factors for waking due to respiratory disturbances. At the same time, OSA phenotypes can be classified into five categories: interrupted sleep, little symptoms, upper airway symptoms with tiredness, upper airway symptoms dominating, and sleepiness dominating. Because endotypes are linked to varied underlying causes of OSA, adopting the view that OSA is a complex chronic disease may be useful because it would allow for a more patient-specific treatment plan. This review will focus on the pharmacological and non-pharmacological therapeutic options for OSA.

7. UPPER AIRWAY ANATOMIC OCCLUSION OR IMPAIRED ANATOMY

Weight Loss Medication: In adults, obesity is still the most frequent risk factor that causes or worsens OSA. Obesity is expected to affect around 45% of patients with OSA[42–44]. Obesity increases the risk of pharyngeal collapse by accumulating fat around the neck and upper. This study found a link between obesity and sleep apnea[45]. AHI is the number of apneas or hypopneas documented during the study per hour of sleep. It is used to categorize the severity of OSA. AHI orlistat, liraglutide, naltrexone/bupropion, and phentermine/topiramate extended-release (ER) are considered to have minimal or no OSA. However, only phentermine/topiramate ER, liraglutide, and orlistat have been studied for weight loss in people with OSA. A randomized clinical trial looked at the efficacy of phentermine 15 mg + topiramate 92 mg extended-release for moderate to severe OSA. The experiment included 45 participants with moderate to severe OSA who were not receiving the gold standard treatment of continuous positive airway pressure. Wang et al. investigated the impact of weight loss on upper airway morphology in 67 OSA patients (apnea-hypopnea index 310 events/h). Weight loss in the subjects was achieved through lifestyle adjustments, bariatric surgery, bypass, or banding. Magnetic resonance imaging (MRI) was used to assess the upper airway's structural and fat percentage alterations. The researchers discovered that reducing weight reduced the volume of upper airway soft tissue, which was strongly associated with a lower apnea-hypopnea index (AHI)[45]. The primary objective was AHI, which demonstrated a significant benefit in the phentermine 15 mg in combination with topiramate 92 mg extended release with lifestyle modifications treatment group compared to the placebo group, which received lifestyle modifications. The primary outcomes of interest were changes in AHI between baseline, week 8, week 28, and withdrawal. Secondary outcomes were the respiratory disturbance index, apnea index, hypopnea index, desaturation index, mean nightly oxygen saturation, overnight minimum oxygen saturation, and arousal index. The treatment group's average number of apnea-hypopnea occurrences decreased from 44 to 14 per hour, while the placebo group increased from 45 to 27 per hour. Aside from the reduction in AHI, the treatment group lost 10.2% of their body weight, and there was a positive, significant connection between the percent change in weight and change in AHI ($p = 0.0003$)[46]. AHI was researched alongside the arousal index, the sleep quality defined as the number of arousals from REM and NREM sleep per hour. The phentermine 15 mg/topiramate 92 mg extended-release group had a least-squared mean decrease in arousals of 19.5, while the placebo group decreased 21.2. The difference between the groups, however, was not statistically significant. There were several drawbacks to the randomized control trial, including a small sample size that might not be representative of the general population, a brief study period, and no discernible differences between groups in the arousal index, diastolic blood pressure, desaturation index, minimum overnight oxygen saturation, and glycemic and lipid values. The weight loss experienced by the placebo group due to lifestyle changes may be responsible for the inability to detect significant differences between groups[46]. Two randomized controlled studies examined Liraglutide's effects on weight loss and their connection to less severe OSA. Blackman et al. assessed AHI after 32 weeks of treatment in the SCALE- Sleep Apnea trial to see whether liraglutide 3.0 mg improved OSA severity compared to placebo. Both the treatment and placebo groups of patients received food and exercise coaching; however, the treatment group's dose was first titrated at 0.6 mg/day and increased weekly by 0.6 mg increments until a daily dose of 3.0 mg was reached. Liraglutide (12.2 events/h) caused a greater mean reduction in AHI than the placebo (6.1 events/h). The OSA severity group, baseline BMI, or gender of the patients had no bearing on the therapeutic benefits of AHI. The p-values for each subcategory are all higher than 0.05. Additionally, liraglutide caused a greater average weight loss (5.7%) compared to placebo (1.6%) and showed a statistically significant link between weight loss and a decline in OSA outcomes. This study has several advantages over earlier investigations into the effects of weight loss and OSA treatment, including a larger sample size. Polysomnographic (PSG) tests were conducted to increase reliability, and the results were evaluated at dedicated sleep sites. The 32-week duration and the 23% withdrawal rate in both groups of patients were disadvantages, albeit[47]. Overall, these investigations showed that the medications used in the trials were successful at causing weight loss, which decreased AHI. Another critical factor is weight loss, not the medication used, influencing the decrease in AHI seen in these trials. Sprung et al. are currently doing a two-by-two factorial design study. One hundred thirty-two patients were randomly allocated to one of four treatment groups: liraglutide 1.8 mg once daily with CPAP, CPAP alone, or no treatment. The project is in its early stages, and no preliminary findings have been published[48]. However, the study did uncover numerous strengths and limitations. In this study, diabetes was utilized as an inclusion criterion to reflect a typical OSA patient[49,50]. The current trial study limits liraglutide to 1.8 mg once daily; however, this could be increased to 3.0 mg daily, resulting in higher weight loss and improved OSA. This is because liraglutide 3.0 mg was not yet approved at the trial. There are currently two randomized controlled trials examining the use of orlistat in obese people. The study design is similar in that a hypocaloric diet was begun, followed by a maintenance diet. During the first year, Rössner et al. administered a placebo and a

nutritionally appropriate meal designed to produce a 600-kcal deficit to both groups. Patients who completed the run-in phase were randomly assigned to receive 60 or 120 mg thrice daily for the next year[51]. Similarly, Sjöström et al. did a trial like the previous one, except orlistat 120 mg thrice a day was used[51,52]. The studies did not measure OSA results. However, orlistat weight loss may be advantageous. The studies did not measure OSA results. On the other hand, weight loss by orlistat may be advantageous, but more research is needed to determine the association.

8. NASAL DECONGESTANTS

Nasal breathing impairment or obstruction is another mechanism hypothesized for obstructive sleep apnea[53–55]. It has led to the idea that nasal decongestion may help with OSA symptoms. A randomized, placebo-controlled, double-blind crossover study was conducted in OSA patients with chronic nasal obstruction. Patients were enrolled after completing overnight tests and given either a placebo or oxymetazoline 0.05% 0.4 mL injected in each nostril. Oxymetazoline, a sympathomimetic vasoconstrictor, was observed to lower mean AHI in both NREM and REM, 31.65 16.98 vs. 22.64 16.05. It not only indicated a reduction in OSA severity, but it also dramatically increased oxygen saturation during sleep. Wijesuriya et al. conducted a prospective, double-blind, randomized control experiment on people with OSA who had suffered a spinal cord injury. OSA is a common long-term result of a spinal cord injury or tetraplegia[56,57]. Sleep trials were conducted on participants randomly given a nasal spray containing 0.5 mL of 5% phenylephrine or a placebo. The severity of sleep apnea reported nasal congestion, sleep quality, and oxygenation during sleep were all assessed. While nasal resistance was reduced overall, it did not affect any sleep severity indicators[56]. More research on people with primary OSA is needed to determine the efficacy of phenylephrine nasal spray. Another study looked at the effects of combining pseudoephedrine with domperidone. Patients were given one to two capsules at bedtime containing 60 mg of pseudoephedrine and 10 mg of domperidone. If the BMI was less than 28, one capsule was administered; if the BMI was between 28 and 30, one or two capsules were administered, depending on whether snoring was present; and if the BMI was greater than 30, two capsules were administered. The results showed a 9.4 (95% CI, 6.8-12.1, p 0.0001) mean drop in mean oxygen saturation and an overall improvement in mean oxygen saturation, percent time with oxygen saturation 90%, and 4% oxygen saturation desaturation index. However, the conclusions of this study were based primarily on the Epworth Sleepiness Scale score and oximetry data. The inability to collect and evaluate the influence on AHI and improvement in OSA severity was a major limitation of this investigation.

9. IMPROVING PHARYNGEAL DILATOR FUNCTION

Serotonin has predominantly excitatory central effects on 5-HT receptor activation, notably 5-HT2a/c and 5-HT1a in upper airway motor neurons and respiratory neurons. This activity is hypothesized to cause upper airway collapse in OSA patients because it is diminished centrally during REM sleep. Serotonin inhibits the 5-HT2a/c and 5-HT3 receptor subtypes [44] in the peripheral nervous system. Because of their involvement in multiple areas in the central (CNS) and peripheral nervous systems (PNS) that govern respiration, serotonin reuptake inhibitors (SSRIs) have been studied as viable alternative therapies.

Table 2. Drugs commonly used in the treatment of obstructive sleep apnea.

Medication	Dosage in Clinical Trials	Adverse effects
Paroxetine	20 mg daily	Nausea, drowsiness, insomnia, dryness of mouth, headache
Fluoxetine	20 mg daily	
Protriptyline	10mg daily	
modafinil	200-400 mg daily	Headache, nervousness, insomnia, decreased appetite, nausea, rhinitis
Armodafinil	150-250 mg daily	

10. TYPES OF ORAL APPLIANCES

Oral appliances can be divided into three main categories based on their mode of action.

1. First, soft palate lifters aim to reduce vibrations from the soft palate by elevating both the soft palate and uvula. However, there needs to be more evidence regarding their effectiveness [58,59].
2. Second, tongue retaining devices (TRD) use suction pressure to hold the tongue forward during sleep, preventing the tongue from falling back into the pharyngeal airway[60,61].
3. The third category is the oral appliances advancing the mandible and the attached tongue during the night, known as mandibular advancement devices (MADs),
mandibular advancement appliances (MAAs),
mandibular repositioning appliances (MRAs),
or mandibular advancement splints (MASs)[60].
4. "Customized maxillary oral appliance (CMOA)" to provide a new therapeutic option for managing moderate OSA

10.1. Advantages of Oral Appliances

- Relatively simple.
- Reversible and
- Cost effectiveness[62–64].

10.2. Disadvantages of Oral Appliances

MAD complications may include loosened teeth, joint pain, muscular aches, tissue ulcers, an inability to touch the back teeth together, permanent tooth movement, and excessive salivation when the device is initially removed in the morning [64]. According to studies, up to 20% of those who use jaw-forwarding devices for a long time develop irreversible tooth movement.

10.3. Mechanism of Action of Oral Appliances

Oral appliances expand and stabilize the oro and hypopharyngeal airway space by pushing the mandible forward and stretching the linked soft tissue, particularly the tongue

(American Sleep Disorders Association, 1995). A tooth-borne device must be securely attached to the teeth, but a tooth-and-tissue-borne appliance, such as a modified activator, is passive and fits loosely. Both of these gadgets have been demonstrated to reduce snoring and enhance the occurrence of OSA[64–66]. When comparing differentially designed oral appliances in different patient groups, the findings may not correctly reflect differences between the appliances but rather differences between the patient groups, such as intra-oral and pharyngeal anatomical differences. The MAD is the most often used oral appliance therapy to treat OSA[58].

10.4. Mechanism of action

It is widely assumed to be anterior displacement of the mandible and connected tongue, resulting in enhanced upper airway patency[67–69]. Size, material, degree of customization to a patient's dentition, coupling mechanism (i.e., the method by which two pieces connect to produce mandibular advancement), occlusal coverage (i.e., coverage of the surfaces of the teeth that contact each other when the mouth is closed), ability to titrate mandibular advancement (only two-piece devices can be titrated), amount of mandibular mobility permitted, and amount of oral mobility. In addition, the concept of customized MADs has evolved from the initial "monobloc" kind of device, in which the upper and bottom sections are securely joined, to the more modern "duobloc" versions. Temporomandibular pain can occasionally be caused by the inflexible monobloc MADs' limits on mandibular movements. Because the top and bottom halves are different but dynamically connected, titratable MADs allow for fine-tuning mandibular advancement. Although higher protrusion may not always result in better outcomes, the literature argues that it is important in increasing MAD efficacy. As a result, it is crucial to define the patient's optimal mandibular protrusion for MAD therapy and alter it based on how well the treatment is tolerated vs successful. However, until now, no proven standard is available for determining this optimal MAD protrusion. Several factors need to be considered when selecting a device:

- Two-piece MAS allows more mandibular movement and has a greater range of settings than one. As a result, they tend to be more comfortable and more effective.
- MAS that maintain mandibular advancement while permitting lateral jaw movement, jaw opening, or jaw closing may reduce the risk of complications and achieve better patient acceptance. However, limited data suggest that vertical opening should be minimized[70].
- Custom-fitted MAS are preferable to self-administered over-the-counter prefabricated varieties because they appear to be more effective and comfortable and are more likely to be retained by both the upper and lower teeth, ensuring that the lower jaw does not fall out of the appliance during sleep[71–73].
- Full occlusal coverage may be desirable to distribute the dental forces associated with mandibular advancement, thereby reducing the risk of tooth movements.

11. OTHER APPLIANCES DESIGN

11.1. Silencer system

This appliance has titanium precision attachments at the incisor level that allow for sequential advancement of up to 8 mm by 2 mm, 6 mm of lateral mobility, 3 mm on either side and vertical pin height replacement[74]. Only this appliance allows you to adjust it in both an "open and close" and a front-to-back position. This appliance is one of the most expensive due to its titanium metal hinge component.

11.2. Klearway oral appliance

The Klearway oral appliance uses a maxillary orthodontic expander to advance the mandible gradually. Klearway, a fully adjustable oral appliance, treats mild to moderate OSA and snoring[75]. Klearway, comprised of thermoactivated acrylic, fits comfortably and easily into the dentition. The patient begins modest steps of mandibular advancement, which inhibits the patient's quick jaw movements, which are highly unpleasant. Because the appliance allows lateral and vertical jaw mobility, the patient can yawn, swallow, and drink water while wearing it.

11.3. PM positioner

The PM positioner attaches the upper and lower splints to the bilateral orthodontic expanders. This gadget is made of a thermoplastic material that must be heated in hot tap water every night before being introduced into the mouth[76]. The mandible cannot move when the appliance is worn because the adjustment hardware is tightly bound on the buccal side of the molar teeth.

11.4. Oral pressure appliance

It combines continuous positive airway pressure (nasal CPAP) with a non-adjustable mandibular repositioning device. In contrast to nasal CPAP, which uses a mask over the nose or the nose and mouth to supply air pressure, the air pressure is delivered through a thin tube that fits across the roof of the patient's mouth. To use the more efficient nCPAP, patients no longer need to wear a nasal mask, headgear with elastic straps, or sleep on their backs. Pressures necessary to address snoring and obstructive sleep apnea are much lower when administered by OPAP rather than nasal delivery.

12. SUMMARY

Clinical trials in OSA on the potential effects of more than two dozen medicines on OSA were investigated in human randomized controlled trials. No treatment, however, has been demonstrated to consistently and significantly improve OSA[55]. Because both have been shown to raise pharyngeal dilator muscle tone, most current pharmaceutical approaches to treat OSA have mostly focused on modulating serotoninergic and cholinergic activity. Among the drugs known to enhance upper airway tone, paroxetine[77], fluoxetine, and ondansetron[78], as well as mirtazapine[79], physostigmine[80], and donezepil[80,81], all improved sleep-disordered breathing to some extent. Trials looking at the effects of cholinergic inhibitors such as physostigmine[80] and donezepil[81] have yielded promising findings. However, because only a limited number of patients participated in these studies and because their features significantly differed from those of the typical OSA group (those with Alzheimer's disease), it is possible that the findings from these trials do not generalize to more common OSA patients seen in clinics. The outcomes of these trials might not apply to more common OSA patients, including Local drug injection into the upper airway, which is another fascinating treatment strategy for OSA. The purpose of this technique is to lessen nasal obstruction, mucosal edema, and

adhesion forces. It may also enhance reflexes that promote pharyngeal dilator tone. The effects of fluticasone[82], xylometazoline[83], phosphocholinamin[84], and surfactant[85] on the OSA severity indices were minimal. Daytime sleepiness was only assessed in the study using xylometazoline, and active medication had no appreciable influence on the findings.

13. CONCLUSION

Although very common, obstructive sleep apnea (OSA) frequently goes undiagnosed. Loud snoring, nocturnal awakenings, and daytime tiredness are symptoms. Patients experiencing symptoms should be the focus of evaluation and treatment to reduce symptoms and, perhaps, cardiovascular risk. The hurdles to diagnosis and treatment have significantly decreased in recent years thanks to a method that involves home sleep apnea testing followed by the start of auto-titrating continuous positive airway pressure therapy in the home. This technique has also made it easier for primary care doctors to manage OSA regularly.

14. AUTHORS CONTRIBUTION STATEMENT

Dr Jahnavi Purna Gorripati conceptualized and gathered the data regarding this article. Dr. Surekha Dubey Godbole analyzed these data, and necessary inputs were given to the design of the manuscript. All authors discussed the methodology and results and contributed to the final manuscript.

15. CONFLICT OF INTEREST

Conflict of interest declared none.

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