REVIEW ARTICLE

Obstructive Sleep Apnea: A review of current treatment options

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Introduction

Obstructive sleep apnea (OSA) is a disorder that is characterized by obstructive apneas and hypopneas due to repetitive collapse of the upper airway during sleep. It has many potential consequences, including excessive daytime sleepiness, impaired daytime function, metabolic dysfunction, and an increased risk of cardiovascular disease and mortality.

The management of obstructive sleep apnea is reviewed here. The prevalence, risk factors, natural history, clinical manifestations, and diagnosis of OSA are discussed separately.

The management of a patient with OSA begins by firmly establishing the diagnosis and its severity. Disease severity guides management by identifying patients who are at greatest risk for adverse outcomes and by providing a baseline from which to measure the effectiveness of treatment [1].

Once the diagnosis of OSA is confirmed and its severity determined, the results of all testing should be reviewed with the patient. The patient should be educated about the risk factors, natural history, and consequences of OSA [1]. In addition, the patient should be warned about the potential consequences of driving or operating other dangerous equipment while sleepy and counseled to avoid activities that require vigilance and alertness.

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Finally, it should be determined whether treatment is indicated and, if so, which therapy is most appropriate. The benefits of successfully treating OSA include clinical improvement (eg, less daytime sleepiness, better quality of life, improved hypertension)[2-6], reduced health care utilization and costs[7,8], and, possibly, decreased mortality[9].

Indications

Behavior modification is indicated for all patients who have OSA and is a modifiable risk factor. Whether OSA-specific therapy (positive airway pressure, an oral appliance, upper airway surgery) is also indicated depends upon the frequency and severity of both respiratory events (eg, apneas, hypopneas) and oxyhemoglobin desaturation episodes during sleep, as well as the severity of any clinical sequelae. When indicated, OSA-specific therapy should be initiated concomitantly with behavior modification, rather than being delayed until the success or failure of behavior modification has been determined[1].

The American Academy of Sleep Medicine (AASM) recommends offering positive airway pressure therapy to all patients who have OSA on the basis of expert consensus[1]. They define OSA as either an obstructive respiratory disturbance index (RDI) greater than 15 events per hour, or an obstructive RDI between 5 and 14 events per hour that is accompanied by daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings due to gasping or choking. The obstructive RDI is the number of obstructive apneas, obstructive hypopneas, and respiratory effort related arousals per hour of sleep (it is recommended that oxyhemoglobin desaturation be $\geq$4 percent to score an obstructive hypopnea, but $\geq$3 percent is considered an acceptable alternative).

Alternative therapies (eg, an oral appliance or upper airway surgery) may be offered to patients who decline positive airway pressure therapy and who have mild to moderate OSA, amenable upper airway anatomy, and a preference for such treatment.

It is important to note that cardiovascular diseases (eg, systemic hypertension, ischemic heart disease, arrhythmias) are not among the clinical and physiological sequelae attributable to OSA that are listed above.

The benefit of using an AHI greater than five events per hour (instead of a higher value) as the threshold for therapy in symptomatic patients was illustrated by a trial that randomly assigned 16 patients with an AHI of 5 to 15 events per hour to receive continuous positive airway pressure (CPAP) or a sham therapy [12]. CPAP improved symptoms and daytime function.

The benefit of therapy for patients with an increased frequency of RERAs and daytime sleepiness, but an AHI of five events per hour or less, was illustrated by a trial that used a respiratory disturbance index (RDI, the number of apneas, hypopneas, and RERAs per hour of sleep) greater than five events per hour as the threshold for initiating positive airway pressure therapy [13].

Types of therapies

Overweight or obese patients should be encouraged to lose weight. Patients with positional OSA should change their sleep position. All patients should abstain from alcohol and avoid medications that may worsen their OSA. In general there are three broad types of therapies: positive airway pressure, an oral appliance and/or upper airway surgery. The choice of therapy depends upon the severity of the OSA, patient preference, and upper airway anatomy.

For patients with severe OSA (AHI >30 events per hour and/or severe clinical sequelae), severe hypoxemia (ie, the SpO2 repeatedly goes below 80 percent), or sustained hypoxemia (ie, ≥5 minutes with an SpO2 below 88 percent), we use positive airway pressure as first-line therapy. This is based upon the variable efficacy of oral appliances in this patient population.

For patients with mild or moderate OSA (AHI ≤30 events per hour without severe clinical sequelae) who do not express a preference, we prefer positive airway pressure rather than an oral appliance because the former is superior at reducing the frequency of obstructive events. However, we would initiate an oral appliance rather than positive airway pressure if the patient prefers an oral appliance. This is based upon the recognition that several patients prefer an oral appliance, however, adherence is an essential aspect of successful treatment. Both modalities are effective compared to no treatment or a sham treatment, and both modalities have a similar effect on symptoms.

While the above approach encompasses most patients with OSA, there are a few uncommon scenarios in which we deviate from this strategy. For patients with severe, life-threatening apnea that cannot be controlled by other means, tracheotomy may be the only treatment option. We consider apnea to be life-threatening if there are apnea-related bradyarrhythmias such as asystole, apnea-related tachyarrhythmias such as atrial flutter or ventricular tachycardia, or the SpO2 repeatedly falling below 75 percent. For patients whose OSA is due to a surgically correctable obstructing lesion, surgical resection of the obstructing lesion is first-line therapy. Examples of surgically correctable lesions that may obstruct the upper airway include tonsillar hypertrophy, adenoid hypertrophy, or craniofacial abnormalities.

Whenever positive airway pressure is the therapy chosen, available modes include continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), and autotitrating positive airway pressure (APAP). We generally favor CPAP because it is the most familiar and best studied. A trial of BPAP or APAP is appropriate for patients who do not tolerate CPAP. BPAP is appropriate initial therapy for patients with coexisting central sleep apnea or significant hypoventilation.

Behavior modification

Weight loss

Weight loss should be recommended to all patients who are overweight or obese [1,14]. This is based on evidence that weight loss improves overall health, decreases the apnea hypopnea index (AHI, the number of apneas and hypopneas per hour of sleep), improves quality of life, and probably decreases daytime sleepiness[15-17].

The effects of weight loss on OSA were illustrated by a trial that enrolled 72 consecutive overweight patients (mean BMI 32 kg/m2) with mild OSA (mean AHI 10 events per hour of sleep) [17]. The patients were randomly

assigned to receive a single session of general nutrition and exercise advice, or a more intensive program that included a low calorie diet for three months plus nutrition and exercise counseling for one year. Patients in the latter group had significantly greater weight loss, reduction in the AHI, and improvement in quality of life compared to the control group. There was no difference in the degree of improvement in daytime sleepiness, but the relevance of this is uncertain since the degree of daytime sleepiness was barely abnormal at baseline. Studies that included patients with more severe OSA and more daytime sleepiness at baseline suggest that weight loss also improves daytime sleepiness[15,16].

The effect of weight loss achieved via bariatric surgery (ie, gastric banding, gastric bypass, gastroplasty, biliopancreatic switch, or duodenal switch) on OSA is uncertain. Several observational studies have found that the frequency of respiratory events (eg, apneas, hypopneas) during sleep decreases following bariatric surgery[18-20]. Most notably, a meta-analysis of 136 studies (22,094 patients) found that OSA resolved in 86 percent of patients who underwent bariatric surgery[19]. However, the meta-analysis was criticized because most of the studies were case series, the resolution of OSA following bariatric surgery was not defined by polysomnography, and patients with OSA, sleep-disordered breathing, or obesity hypoventilation syndrome were combined under the label OSA.

A subsequent meta-analysis of 12 studies (342 patients) was performed to address these limitations [21]. Bariatric surgery was associated with a significant decrease in the BMI (from 55 to 38 kg/m2) and reduction in the mean AHI (from 55 to 16 events per hour of sleep). Although the improvement in the AHI was substantial, the final value was still abnormal.

Patients whose OSA improves or resolves after weight loss should strive to maintain their weight loss, since weight gain is associated with worsening of OSA [22,23]. Such patients should also be followed closely because OSA may recur even in patients who maintain their weight loss [24-26]. Counseling regarding ongoing diet modification and exercise, as well as referral to a nutritionist may be beneficial.

Sleep position

During the diagnostic sleep study, some patients will be observed to have OSA that develops or worsens during sleep in the supine position. These patients tend to have less severe OSA, to be less obese, and to be younger[27]. Sleeping in a non-supine position (eg, lateral recumbent) may correct or improve OSA in such patients and should be encouraged. However, sleeping in a non-supine position should not be used as the primary therapy unless normalization of the AHI when sleeping in a non-supine position has been confirmed by polysomnography[1,27].

The benefit of sleeping in a non-supine position was demonstrated by a crossover trial in which 13 patients with positional OSA (mean AHI 17 events per hour) were randomly assigned to sleep in a non-supine position or to receive continuous positive airway pressure (CPAP) for two weeks[28]. Both interventions significantly improved the AHI and oxyhemoglobin saturation compared to baseline, although CPAP was more effective in improving each of these parameters. There were no differences in the degree of improvement of clinical outcomes, such as daytime sleepiness.

Approximately one-half of patients who are encouraged to sleep in the lateral position will learn to do so and will maintain the behavior[29]. A number of devices have been developed to reduce the likelihood of sleeping in the supine position, including posture alarms, special pillows, and modified nightshirts. A simple device that can be made at home is a snug-fitting T-shirt with a pocket sewn over the spine and tennis balls placed in the pocket. Obese patients may benefit from a harder type of ball, such as a baseball. The discomfort associated with rolling into the supine position is generally enough to prompt the patient to roll back into the lateral position without awakening. This technique appears to be limited by poor adherence[30].

In some patients, sleeping in a semi-recumbent position (ie, elevated head-of-the-bed or a reclining chair) may also be helpful. However, this position has not been as well studied.

Alcohol avoidance

All patients with OSA should avoid alcohol, even during the daytime, because it can depress the central nervous system, exacerbate OSA, worsen sleepiness, and promote weight gain. The effect of alcohol consumption was illustrated by a series with seven patients who had varying degrees of upper airway obstruction during sleep, ranging from snoring alone to OSA[31]. Following alcohol ingestion, the duration and frequency of obstructive respiratory

events and the degree of oxyhemoglobin desaturation increased in five patients (71 percent). Two patients who had snoring alone at baseline developed frank OSA after alcohol ingestion.

Positive airway pressure (PAP) therapies

Positive airway pressure (PAP) splints the upper airway open. As a result, respiratory events due to upper airway collapse (eg, apneas, hypopneas) are prevented.

Positive airway pressure therapy is generally considered first-line therapy for OSA. It can be delivered as continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), autotitrating positive airway pressure (APAP), or adaptive servo-ventilation[1]:

- CPAP delivers positive airway pressure at a level that remains constant throughout the respiratory cycle. It is used most often because it is the simplest, the most extensively studied, and associated with the most clinical experience. A pressure relief setting (ie, lowers the positive airway pressure at the onset of exhalation) is sometimes used to improve comfort and tolerance of the device.
- BPAP delivers a preset inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP). The tidal volume is related to the difference between the IPAP and EPAP. As an example, the tidal volume is greater using an IPAP of 15 cm H2O and an EPAP of 5 cm H2O (difference of 10 cm H2O), than an IPAP of 10 cm H2O and an EPAP of 5 cm H2O (difference of 5 cm H2O). There is no proven advantage to using BPAP instead of CPAP for the routine management of OSA [33]. APAP increases or decreases the level of positive airway pressure in response to a change in airflow, a change in circuit pressure, or a vibratory snore (signs that generally indicate that upper airway resistance has changed). The degree of improvement of major outcomes conferred by APAP and CPAP is similar[34,35]. However, APAP is preferred by more patients[34], although it has not been shown to improve adherence.
- Adaptive servo-ventilation provides a varying amount of inspiratory pressure superimposed on a low level of CPAP. It can be helpful in patients who develop central apneas when treated with CPAP (ie, complex sleep apnea), as well as in patients who require medications that can suppress respiration (eg, opiates), because it compensates for episodes of central apnea.

Outcomes

There is high quality evidence from meta-analyses of randomized trials that positive airway pressure therapy reduces the frequency of respiratory events during sleep, decreases daytime sleepiness, and improves quality of life[2-5]. This was best illustrated by a meta-analysis of 22 randomized trials (1160 patients) that compared nocturnal CPAP to a control [4]. Controls included sham CPAP, placebo tablets, or conservative management, such as weight loss and sleep hygiene. Nocturnal CPAP significantly improved both subjective and objective sleepiness, quality of life, cognitive function, and depression. Mortality was not evaluated in this meta-analysis.

No randomized trial has found that positive airway pressure therapy improves mortality in patients with OSA. This may be because early randomized trials that compared positive airway pressure to either no therapy or a sham therapy usually measured outcomes other than mortality, such as the frequency of respiratory events during sleep and daytime sleepiness. Now that the beneficial effect of positive airway pressure on these outcomes is widely accepted, it is unlikely that similar trials will ever be performed to evaluate mortality because of concerns about whether it is appropriate to randomize a patient to no treatment. However, an observational study of 385 patients who were being evaluated for OSA found an 8-year survival of 100 percent among patients who were treated with CPAP, compared to 63 percent among all patients, suggesting that treatment may improve mortality[9]. Other observational studies similarly suggest that CPAP improves mortality [36,37].

Favorable outcomes likely depend on adherence to positive airway pressure therapy. However, it is estimated that 20 to 40 percent of patients do not use their positive airway pressure device and many others do not use it all night, every night [38-44]. Adherence with positive airway pressure therapy is reviewed separately.

Oral appliances

A multidisciplinary approach is required to manage a patient who has OSA with an oral appliance. This begins

with a medical assessment and sleep study to confirm the diagnosis of OSA, determine whether treatment is indicated, and, if so, whether an oral appliance is appropriate therapy [1]. Dental evaluation follows, which includes assessment of suitability for oral appliance therapy, device selection, and fitting. Once oral appliance therapy is initiated, the effectiveness should be evaluated by objective testing, since subjective assessment alone is often unreliable. Long-term follow-up should be performed by both a medical and a dental clinician.

Patient selection

Once it has been confirmed that a patient has OSA and the severity of the OSA measured, it must be determined whether treatment is indicated and, if so, whether an oral appliance is an appropriate modality. Oral appliances are appropriate for patients with any of the following characteristics:

- Mild to moderate OSA, defined as an apnea hypopnea index (AHI, the number of apneas and hypopneas per hour of sleep) of 5 to 30 events per hour.
- Treatment beyond behavior modification is indicated. Behavior modification refers to weight loss, abstinence from alcohol.
- Preference for an oral appliance, rather than positive airway pressure therapy.
- Non-adherence with positive airway pressure therapy, non-responsiveness to such therapy, or refusal of such therapy.

Oral appliances are most appropriate for patients with mild or moderate OSA because they may be less effective in patients with severe OSA (ie, AHI >30 events/hour). Patients with severe OSA usually receive positive airway pressure as first-line therapy, although severe OSA is not an absolute contraindication to oral appliances (successful treatment has been reported).Upper airway surgery may be preferable to oral appliances in patients who have an upper airway obstruction that is causing the OSA (eg, tonsillectomy, adenoidectomy) and can be ameliorated surgically [1,2].

Advantages

Patients may prefer oral appliances over positive airway pressure because they are easier to use, more easily portable, quiet, and do not require a power source[3]. Oral appliances may also be a useful substitute for positive airway pressure during travel.

Contraindications

- Patients in whom rapid initiation of treatment is desirable (eg, patients with severe symptomatic OSA, sleepiness while driving, severe hypoxemia, or active cardiovascular comorbidities) should be treated with positive airway pressure instead of an oral appliance. The former may be more effective and can be initiated quickly, while the latter requires incremental advancement of the mandible over weeks to months.
- Severe oxyhemoglobin desaturation (large magnitude or prolonged) should prompt initiation of an alternative therapy (usually positive airway pressure) because oral appliance therapy may induce suboptimal improvement[3].
- Dental conditions such as temporomandibular joint disease, periodontal disease, insufficient dentition to support appliance retention in the mouth, and inadequate range of motion of the jaw are relative contraindications and require expert dental assessment prior to consideration of treatment with an oral appliance[1, 45]. Limited capacity for mandibular protrusion (<6 mm) may also be a contraindication, but the evidence for this is not strong. One study found that 34 percent of patients with OSA may not be suitable candidates for treatment with an oral appliance [6.]

The two major types of oral appliances are mandibular advancement splints and tongue retaining devices:

Mandibular advancement devices (MAD) are anchored to the dental arches and induce mandibular advancement resulting in several beneficial anatomical changes. These changes can include anteroposterior and lateral retrolingual and velopharyngeal enlargement, resulting in increased cross-sectional areas and upper airway volume.

Tongue retaining devices (TRD) use a suction cavity to pull the tongue out of the mouth, thus improving retrolingual dimensions. These devices have not been well studied. One clear advantage is that they can be used in edentulous patients.

Device titration

The MAD need to be titrated. The amount of advancement required for a clinical response generally ranges from 50 to 90 percent of the maximum protrusion[13]. However, this can vary substantially among individuals, with some patients failing treatment regardless of the degree of advancement. There is as yet no reliable clinical method of determining the amount of advancement needed.

Follow-up

Once the dentist has completed the titration of MAD therapy, patients should generally be reevaluated by someone with expertise in the treatment of sleep disorders soon after, in order to assess the clinical and polysomnographic efficacy of treatment. This consists of asking whether the symptoms of OSA have resolved and by performing full polysomnography or level 3 portable monitoring with the oral appliance in place 1,2.

Adverse effects

Most patients experience early side effects, particularly dental discomfort (usually of the upper and lower incisors). Other early side effects include temporomandibular joint pain, dry mouth or excessive salivation, gum irritation, and bruxism[7].

Occlusal changes are the major long-term adverse effect of oral appliances. They are characterized by backward movement of the upper front teeth and forward movement of the lower front teeth and mandible, ranging from 0.4 to 3 mm [31,32]. Most of the changes occur within the first two years, after which they appear to stabilize. In one observational study of 70 patients with an average follow-up of 7.4 years, occlusal change was identified in 86 percent[33].

Surgery

A brief review of available surgical options has been dicussed here. There is no consensus regarding the role of surgery in the absence of a strictly defined anatomic lesion [45]. Uvulopalatopharyngoplasty (UPPP) is one of the most common surgical procedures that is performed in this context. It involves resection of the uvula, redundant retrolingual soft tissue, and palatine tonsillar tissue. UPPP appears to achieve a surgical cure (defined as a postoperative AHI of <5 events per hour of sleep) in only a minority of patients [46], and may compromise subsequent CPAP therapy by promoting mouth leaking and reducing the maximal level of pressure tolerated by many patients treated with CPAP[47]. Moreover, improving or correcting the sleep-related breathing disorder is not guaranteed to improve the patient's symptoms, since symptoms can never be attributed to the OSA with absolute certainty.

Laser-assisted and radiofrequency ablation (RFA) are less invasive variants of UPPP. Other common surgical procedures for OSA include septoplasty, rhinoplasty, nasal turbinate reduction, nasal polypectomy, palatal advancement pharyngoplasty, tonsillectomy, adenoidectomy, palatal implants (ie, Pillar procedure), tongue reduction (partial glossectomy, lingual tonsillectomy), genioglossus advancement, and maxillomandibular advancement [33]. A systematic review reported that most of the evidence related to such surgical treatments is from case series [48]. Meta-analyses of data extracted from these series suggest that UPPP, laser-assisted uvulopalatoplasty, radiofrequency ablation, and maxillomandibular advancement (MMA) decrease the AHI. MMA is most consistently associated with a decreased AHI, although the morbidity of MMA has not been determined. These meta-analyses were limited by a serious risk for bias and inconsistency among the series.

Only a small number of trials have directly compared surgery to either conservative management or a nonsurgical therapy [49]. Overall, the trials have failed to consistently demonstrate a benefit from surgical therapy.

Novel devices

A randomized control trial published by Berry et al among a total of 127 patients who were treated with a expiratory positive airway pressure (EPAP) device (Provent) was suggestive of an overall decrease in AHI up to 42.7% (EPAP) versus10.1% (sham) (P<0.0001) at 3 months. A randomized control study involving larger number of patients is likely to be helpful [50].

Hypoglossal nerve stimulation (HGNS) is known to recruit lingual muscles, reduce pharyngeal collapsibility and treat OSA. The study by Schwartz and colleagues [51] showed that HGNS produced marked dose-related increases in airflow without arousing patients from sleep. The study was performed in small group of patients (30)

with OSA and definitely opens up doors for a new therapeutic approach to treat OSA especily for patient who are intolerant to PAP therapy. Larger multicenter trials will surely provide more highlight on this therapy in near future.

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