From Journal of the American Board of Family Medicine > Clinical Review

Sleep Apnea: From the Nose to the Heart

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Authors and Disclosures

Posted: 06/13/2002; J Am Board Fam Med. 2002;15(2) © 2002 American Board of Family Medicine

Abstract and Introduction

Abstract

Background: Obstructive sleep apnea (OSA) is a disorder consisting of repetitive obstruction of the upper airway during sleep accompanied by ineffective respiratory effort.

Methods: We developed this clinical review using an extensive MEDLINE review of the literature and data from our laboratories. This review examines (1) the prevalence of OSA; (2) the pathophysiology involved including the causes of obstruction, the physiologic stimuli, and resulting autonomic changes; (3) the cardiovascular manifestations; and (4) the therapeutic approaches to patients with OSA with emphasis on arrhythmia management.

Results and Conclusions: OSA is highly prevalent and largely underdiagnosed. As part of a much broader spectrum of respiratory disturbances during sleep, OSA can result in a multitude of systemic manifestations. Structural changes occur in the airway to obstruct airflow during OSA, and the resulting apnea activates hypoxic and hypercapnic reflexes, which in turn lead to profound elevation in sympathetic nerve activity and cyclical changes in parasympathetic nerve activity. These autonomic effects are thought to contribute to the associated cardiovascular diseases (eg, hypertension) and frequently observed brady- and tachyarrhythmias. The ultimate goal in the treatment of OSA is to restore airway patency and sleep continuity and to improve daytime functioning and quality of life. Treatment usually results in improvement of clinical symptoms.

Introduction

Sleep-disordered breathing is a term used broadly to describe regular respiratory disturbances during sleep, a condition for which primary care physicians have very limited formal training.[1] Included in this broad description is the sleep apnea-hypopnea syndrome, which can be further divided into three types: central, obstructive, and mixed. Central sleep apnea-hypopnea is a period of at least 10 seconds during which airflow is absent (apnea) combined with a complete or partial absence of respiratory effort.[2] Obstructive sleep apnea-hypopnea (OSA) consists of repetitive obstruction of the upper airway during sleep in which ineffective respiratory efforts occur. Mixed sleep apnea-hypopnea is a period of either complete or diminished airflow resulting from a combination of central (lack of respiratory drive and, thus, breathing effort) and obstructive mechanisms. Pure central sleep apnea-hypopnea has been found to make up less than 10% of the patients at most sleep laboratories.[2] We will, therefore, focus this review on the more prevalent type of sleep-disordered breathing, OSA.

Methods

We undertook an extensive MEDLINE review of the literature using the key words "sleep apnea," "arrhythmias," and "autonomic nervous system," as well as data from our laboratories. This review examines (1) the prevalence of OSA; (2) the pathophysiologic mechanisms involved, including the causes of obstruction, the physiologic stimuli, and resulting autonomic changes; (3) the cardiovascular manifestations; and (4) the therapeutic approaches to patients who suffer from OSA, with emphasis on arrhythmia management

Prevalence

Even though OSA was defined more than 30 years ago, only in the past decade has awareness of the syndrome among both medical professionals and the public become more common.[3] Despite this increased awareness, many patients have treatable OSA undiagnosed by both the primary care physician and the specialist.[3-5] The incidence of OSA among middle-aged men and women varies from 1% to 5% and 1.2% to 2.5%, respectively,[6-10] and has been shown to increase with age.[11,12] In one study done on 358 elderly volunteers (mean age of 72.4 years), the incidence

of OSA was found to be 7%. Furthermore, there was a correlation between age and the apnea index.[13] The variability in the incidence of OSA is thought to be due to differences in population studied (age, body mass index, genetic factors), methods of monitoring sleep and respiration, criteria for defining an abnormal respiratory event, and the number of apneas or hypopneas per hour of sleep considered abnormal.[3,4]

The incidence of OSA is higher in African Americans than it is in white Americans,[14] and it is likely that the prevalence in general is much greater than that reflected by sleep clinic referrals, particularly among elderly persons and women.[14-16] In addition, it is believed that as much as 40% of patients with essential hypertension have undiagnosed and therefore untreated OSA.[5,17-19] Thus, although the estimates of incidence vary, it is clear that OSA is a syndrome that pervades the general population and is currently underdiagnosed.

Pathophysiology

Causes of Obstruction

Sounds of snoring originate in the collapsible part of the airway, where there is no rigid support, which implicates a primary role of the nasopharyngeal inlet, pharynx, and tongue in sleep and breathing disturbances. The key force that promotes the closure of the upper airway is the negative pressure applied to the airway during inspiration, which is determined by the inspiratory effort and the physical dimensions of the upper airway. Any narrowing from the level of the anterior nares, nasal cavity proper, and nasopharynx will lead to greater negative pressure required to produce any given level of airflow into the lungs.[20] The primary force holding the airway open is the activity of the dilator muscles that give tone and tension to the pharyngeal muscles. One suggested mechanism that might be important in producing upper airway obstruction is a difference in timing between the hypoxic-hypercapnic drive to inspiration and activation of the dilator muscles.[21] If inspiration is initiated before there is any activation of the dilator muscles, the upper airway is at risk of closure by this suction effect.[22]

Another cause of OSA is nasal obstruction. The nose, best viewed as a variable resistor, contributes to nearly 40% of total airway resistance.[23] This resistance is greatly influenced by the vasomotor reaction of the nose to several factors, such as hormonal effects, metabolic changes, and numerous pharmacologic agents.[23] Olsen et al[24] measured the respiratory effort in a patient during sleep and suggested that the oral airway resistance was greater than the nasal airway resistance. With the nasal pathway being the preferred route for nocturnal breathing, an increase in nasal resistance will invariably increase the possibility of collapse of the nonrigid portion of the upper airway, namely, the pharynx. Causes of nasal airway obstruction are many, including enlarged adenoids commonly seen in patients with allergic rhinitis and bony structural defects.

Physiologic Stimuli

To understand OSA fully, it is vital to understand the physiologic stimuli that initiate the arousal and the increased inspiratory effort associated with the end of an apneic episode. In a patient with OSA the typical progression of each apnea and the cardiovascular consequences can be summarized as follows (Figure 1): First, there is an initial decrease in the drive to breathe caused by decreased sensitivity of the peripheral and central chemoreceptors. As a result, the airway collapses, leading to the apneic event that limits gas exchange at the lungs. The subsequent hypoxic-hypercapnic state increases the drive to breathe. The breathing effort, however, is impeded by the obstructed airway, which causes further impairment of gas exchange. Eventually, the severe hypoxia and hypercapnia produce a breathing effort adequate to terminate the apneic event. This effort often elicits arousal, which disrupts the progression of sleep, and results in disturbed sleep architecture. The cycle, as illustrated in Figure 1, repeats many times during the night.

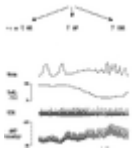

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Figure 1.

(Top panel) Schematic of obstructive sleep apnea (OSA) cycle, with accompanying sympathetic neural and cardiovascular responses. Bottom panel - sample tracings of cardiovascular and sympathetic neural activity responses to an episode of OSA. Of note are a progressive rise in arterial pressure and sympathetic neural activity during apnea and bradycardia toward the end of the apneic episode. HR = heart rate, BP = blood pressure, SVR = systemic vascular resistance, Resp = respiration, SaO_2 = arterial oxygen saturation, ECG = electrocardiogram, ABP = arterial blood pressure, SNA = sympathetic neural activity.

The primary stimuli for the cardiovascular and respiratory responses that occur during apnea are the resulting hypoxemia and hypercapnia. As Pao_2 levels decrease and Pao_2 levels increase during apnea, chemoreceptors in the carotid bodies, aortic arch, and brainstem (medulla) are activated, leading to an increased inspiratory drive. Although hypoxemia plays a major role, the chemoreceptor sensitivity to carbon dioxide is the primary drive for increased ventilation. In addition, changes in intrathoracic pressure (associated with ineffective inspiratory efforts) during apnea have been shown to play a role in the acute cardiovascular responses.[25,26] These changes in intrathoracic pressure can influence venous return, ventricular filling, arterial and cardiopulmonary baroreflexes, and the release of atrial natriuretic peptide.[4,27] Thus, it is the interplay of all these physiologic stimuli that result in the autonomic and cardiovascular changes associated with OSA.

Acute Autonomic Manifestations

The changes in heart rate and blood pressure associated with acute OSA are thought to be primarily a result of alterations in the autonomic nervous system during each apneic episode.[28,29] During each apneic event there is a progressive increase in sympathetic nerve activity throughout the episode, reaching a peak at termination of the apnea, after which there is a marked decrease during recovery.[21,30,31]

The increase in sympathetic nerve activity during apnea is mainly the result of acute hypoxia and hypercapnia.[30-33] Leuenberger et al[30] showed that with mild apneic events (duration < 20 seconds), pretreatment with 100% oxygen effectively eliminated most of the increase in sympathetic nerve activity. In a similar study, Smith and colleagues[31] found that longer apneic events while breathing oxygen produced a modest increase in sympathetic nerve activity, the magnitude of which was greatly attenuated relative to apneic events while breathing room air. Together these studies show that hypoxemia plays the predominant role in mediating the sympathoexcitation, although other factors also contribute. Hypercapnia alone, when sufficiently severe, can increase sympathetic nerve activity, but it appears that the synergistic interaction between hypercapnia and hypoxia is the more important effect at the Pco_2 levels achieved during apnea.[33,34] Ventilation can impose an inhibitory effect on sympathetic nerve activity,[35] but this effect is removed during apneas. An apneic episode therefore causes disinhibition of respiratory modulation of sympathetic nerve activity, thereby allowing the chemoreceptor activation to predominate in mediating the sympathoexcitation.

Cardiovascular Responses

The increase in sympathetic nerve activity is accompanied by several changes in the cardiovascular system.[29,36,37] An increase in activity at the end of each apneic event leads to vasoconstriction, increasing peripheral vascular resistance in the systemic and oftentimes pulmonary vasculature, and resulting in a progressive rise in arterial pressure, as shown by the tracing in Figure 1. Other studies have shown that arousal from non-REM sleep elicits an increase in peripheral vascular resistance and arterial pressure.[38,39] In addition, patients with OSA have been found to have higher levels of sympathetic activity (nerve activity and catecholamine levels) while awake compared with nonapneic persons.[21,31,32,40] Effective treatment of OSA has been found to decrease daytime sympathetic nerve activity,[32,41] thus supporting the link between increased daytime sympathetic nerve activity and OSA.

This chronic increase in daytime sympathetic nerve activity has been implicated in the development of daytime hypertension and cardiac arrhythmias.[5,21,29,36] In addition, OSA has been shown to be associated with increased risk for stroke,[42] coronary artery disease,[43] and congestive heart failure.[44] Compared with the general US population,

OSA patients are twice as likely to have hypertension and three times as likely to have ischemic heart disease, and have four times as much cerebrovascular disease.[45] Although there is a generalized increase in cardiovascular morbidity, in the following section we focus on two major cardiovascular disease processes associated with OSA, namely, hypertension and cardiac arrhythmias.

Hypertension

For years researchers have investigated a causal relation between OSA and daytime hypertension. One primary impetus for these investigations could be the recognition that as much as 40% of patients with resistant essential hypertension have undiagnosed OSA.[5,17-19] Moreover, the relation between OSA and daytime hypertension seems to be strongest in those who are younger than 50 years.[5,46-48] Although some studies suggesting a link between OSA and hypertension have been criticized for not controlling for possible confounding variables (obesity, male sex, coexisting disease, preexisting drug therapy, and age), most of the literature strongly suggests that OSA can cause persistent hypertension.[5] Recent data from a study of 1,741 patients (741 men; 1,000 women) found OSA to be independently associated with hypertension in both men and women, while controlling for possible confounders (age, body mass index, sex, menopause or hormone replacement therapy, alcohol use, smoking, and race).[49]

In dogs, occlusion of the upper airway (simulating OSA) has been shown to induce chronic hypertension.[50] In humans, several researchers have shown a significant association between OSA and hypertension after controlling for body mass index.[25] In addition, Young et al[51] found that the apnea-hypopnea index was predictive of both sleep and daytime blood pressure. These data suggest that as OSA worsens, there is a concomitant increase in both sleep and daytime blood pressure. Several other studies have also shown a similar dose-response relation between OSA and blood pressure.[25,46,48,49] Recent data from the Sleep Heart Health Study indicate an association between OSA and hypertension in 6,132 middle-aged to older men and women of different ethnic backgrounds.[52]

The cause of a dose-response relation between the severity of OSA and blood pressure is most likely multifaceted. As noted above, during OSA there are both acute and chronic increases in sympathetic nerve activity, which have been implicated in the increased sleep and daytime blood pressure. In addition, given that many OSA patients are obese, the association between obesity and hypertension must not be neglected. This multifaceted nature of OSA and hypertension is further supported by the variability in blood pressure response to treatment of OSA. In addition to improving the symptoms associated with OSA, several studies have shown that treatment with nasal continuous positive airway pressure (nCPAP) or tracheostomy might lower both daytime and nighttime blood pressure in OSA patients.[35,53-56] The magnitude of this response varies and might be related to nocturnal desaturation frequency.[55]

Dimsdale et al[54] recently reported the results of a double-blind placebo-control trial comparing treatment of OSA in patients using nCPAP and placebo on nocturnal and daytime blood pressure. The placebo in this study was nCPAP at 2-cm H_2O compared with nCPAP at 10-cm H_2O in the treatment group. Results from this study suggest that, compared with placebo, treatment with nCPAP is associated with a greater decrease in nocturnal mean arterial blood pressure. Furthermore, the effectiveness of nCPAP compared with placebo in decreasing daytime mean arterial blood pressure is unclear. Dimsdale et al[54] did show a decrease in daytime mean arterial blood pressure with treatment using both nCPAP and placebo for 7 days. There was no significant difference between the nCPAP and placebo trials, however. Whether this finding is the result of a true placebo effect or the result of an underpowered study is unclear. In a similar study Faccenda et al[55] reported a difference between nCPAP and placebo on both nocturnal and daytime blood pressure in OSA patients. Unlike the Dimsdale et al study, Faccenda et al used an oral placebo instead of nCPAP at 2-c m H_2O.[54,55]

Although further research is needed to define more clearly the effects of treatment of OSA on blood pressure, it appears that treatment with nCPAP results in a modest decrease in nocturnal and daytime blood pressure. In addition, it is unclear from the data whether the effect of treatment of OSA on blood pressure is different in hypertensive patients compared with OSA patients with high normal blood pressures.[56] Most of the studies to date have primarily studied patients with high normal blood pressure. Furthermore, when left untreated, OSA leads to greater changes in daytime blood pressure, and eventually structural changes can occur within the vasculature to the point that treatment

for the OSA will not effectively lower blood pressure. Thus, a possible reason that treatment of OSA in some cases is ineffective in lowering blood pressure might be that the hypertension has become an organic disease.

Cardiac Arrhythmias

The relation between cardiac arrhythmias and sleep apnea was assessed by several authors. While some found an increase in both bradyarrhythmias and tachyarrhythmias, others found a low incidence in patients without serious cardiac or pulmonary disease. This discrepancy is confounded by the unknown incidence of sleep apnea in the healthy persons, and the high incidence of hypertension and cardiovascular disease in patients with sleep apnea. Nevertheless, most experts agree that cardiac arrhythmias occur more frequently in patients who have sleep apnea and that the incidence increases with the number of apneic episodes and the degree of arterial oxygen desaturation.

Bradyarrhythmias. Atrioventricular block and asystoles have been reported in up to 10% of patients with sleep apnea. In a series of 400 patients with sleep apnea syndrome, sinus arrest (>2.5 seconds), second-degree atrioventricular block, and sinus bradycardia were found in 11%, 8%, and 7% of patients, respectively.[57] There were no important differences in age, body weight, apnea-hypopnea index, or minimum oxygen saturation between those with and without arrhythmias. These arrhythmias, however, were observed only when oxygen saturation was less than 72%. Several studies have suggested that sinus bradycardia (<30 bpm) and sinus arrest (>2.5 seconds) do not occur in healthy asymptomatic persons, although second-degree atrioventricular block, namely, Mobitz type I, have been reported in up to 7% of cases.[57] Koehler et al[58] looked at the factors involved in the pathogenesis of heart block in patients with sleep apnea and have concluded that almost 90% of these episodes occur during rapid eye movement sleep and during an oxygen desaturation of at least 4%. In contrast to the previous reports by Guilleminault et al,[57] no oxygen saturation threshold value was found.

Recent studies have evaluated the electrophysiologic characteristics of the sinus node and conduction system of patients with sleep apnea.[59-62] These studies found that sinus node and atrioventricular conduction were normal or only slightly abnormal in all patients while awake, suggesting that the changes in heart rhythm are not due to fixed or anatomic disease of the sinus node and atrioventricular conduction system, but rather are due to autonomic changes, namely, an increase in vagal tone. That intravenous atropine administration eliminates the marked sinus arrhythmia and bradyarrhythmias observed in patients with sleep apnea syndrome[61] supports this hypothesis. Hypoxemia and cessation of breathing are essential for the development of bradycardia in patients with apnea, and the degree of bradycardia seems to correlate with the severity of hypoxemia.[62] The bradycardic response to hypoxia is usually counteracted by the hyperventilation at the termination of each apneic episode. As such, marked bradycardia is apparent only with the cessation of breathing during each apneic event.

Tachyarrhythmias and ventricular ectopy. Ventricular ectopy has been reported in up to 66% of patients with sleep apnea syndrome.[63] This incidence is significantly higher than what is reported in asymptomatic healthy persons (0% - 12%).[57] Unlike patients who do not have sleep apnea, patients with this syndrome experience ectopy mostly during sleep, suggesting a direct relation between arrhythmias and sleep apnea. Similarly, ventricular tachycardia, although less common, is also more common in patients with sleep apnea (0% - 15%) compared with the general population (0% - 4%). In most studies, the occurrence of ventricular tachycardia is almost exclusive to apneic events.[58,64] The mechanism by which sleep apnea causes ventricular arrhythmias is not known, but the decrease in arterial oxygen saturation among other factors has been shown to play an important role. Shepard et al[65] studied the relation between ventricular ectopy and oxyhemoglobin desaturation in patients with OSA and found an increase in premature ventricular contraction frequency with oxygen saturation decreasing below 60%. The authors concluded that patients with OSA whose arterial oxygen saturation is less than 60% are at increased risk and should be managed accordingly

Diagnosis

The approach to patients with suspected sleep-related disorders should start with a thorough clinical evaluation, including a detailed history and physical examination, then a sleep study to confirm the diagnosis. A major challenge to diagnosis is the distinction between benign snoring and snoring related to apnea. A thorough investigation into the

various signs and symptoms through a detailed history and a simple questionnaire to assess daytime sleepiness (The Stanford Sleepiness Scale[66] or the Epworth Sleepiness Scale[67]) can help measure the severity of the condition. Such an evaluation is particularly important for the elderly patient, who might have other disorders, such as nocturnal myoclonus and possibly dementia, that could render history taking harder.

The most common symptoms include chronic loud snoring, excessive daytime sleepiness, personality changes, fatigue, depression, headache, and impairment of thinking.[68] The physical examination should focus on ruling out any discrete anatomic lesion, located anywhere from the nasal vestibule to the larynx, that could increase the likelihood of an obstructive event. Common physical findings include septal deviation, adenotonsillar hypertrophy, retrognathia, and crowding of the upper airway structure. Assessment of nasal obstruction and oropharyngeal or hypopharyngeal narrowing is made using fiberoptic endoscopy. Fiberoptic pharyngoscopy with the Mueller maneuver (forced expiration against closed upper airway) can replicate the obstructive events that occur during sleep in patients with OSA.[69,70] Obesity, increased nuchal circumference, and a high body mass index are also common. Other signs to look for are cor pulmonale, hypertension, bradycardia or asystole during sleep, and pedal edema.[68,71]

Based on the history, sleepiness scale scores, and physical examination, if OSA is highly suspected, then overnight polysomnography is strongly indicated. It should be emphasized that particular attention must be paid to the manifestations of OSA in the elderly because of the associated increase in morbidity and mortality. Indeed, several investigators have found that sleep apnea can increase vascular morbidity and possibly mortality in untreated cases.[72] In one study, the respiratory disturbance index was found to be an independent predictor of cardiovascular mortality in patients with coronary artery disease. A careful sleep history and polysomnography are therefore essential and should be obtained often in the workup of an elderly patient with cardiac disease or hypertension who has a history of loud snoring. A suggested approach to patients with a history of loud snoring is provided in Figure 2.

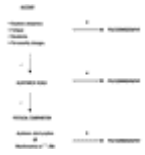

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Figure 2.

Suggested approach to patients with a history of loud snoring. Please note that although symptoms of obstructive sleep apnea (OSA) are sufficient to proceed with polysomnography, a sleepiness scale and a complete physical examination should always be obtained in patients suspected of having OSA.

Because the cost of overnight polysomnography is expensive ($1,000 - $1,400), several different portable devices have been developed to record nocturnal breathing and oxygenation at home for the diagnosis of OSA.[73] Although the cost of these home studies is much less ($400 - $500) than overnight polysomnography, the home studies have been found to have a lower efficacy for OSA diagnosis compared with overnight polysomnography.[74] Recently, Chervin et al[74] performed a cost-utility analysis comparing polysomnography, home testing, and no sleep testing for the diagnosis of OSA. Polysomnography resulted in the greatest gain in 5-year quality-adjusted life-years (QALYs) compared with home testing and no sleep testing. Furthermore, Chervin et al showed that the incremental charges for polysomnography, compared with home testing or no testing, were $13,400 and $9,200, respectively, per QALY gained.[74] Compared with other medical procedures (ie, renal dialysis costs $47,200 in 1996 dollars and screening asymptomatic patients for carotid stenosis costs about $120,000 in 1997 dollars), the benefits gained from using overnight polysomnography for the diagnosis of OSA seem justified.[74]

Clinical Management

An effective therapeutic approach must be started as soon as the diagnosis of sleep apnea has been established so that the associated morbidity and mortality are limited. Proper patient counseling pertinent to each treatment modality must be discussed. The ultimate goals are to restore airway patency and sleep continuity and to improve daytime functioning and quality of life. The resolution of the clinical signs and symptoms of OSA are reflected by a decrease in the apnea-hypopnea index and an increase in the oxyhemoglobin saturation level.[71] The treatment of sleep apnea

entails modification of behavioral factors, medical treatment, use of nCPAP, application of oral or dental devices, and surgical procedures. Relief of the syndrome usually results in improved clinical symptoms.

Nonsurgical Treatment

Behavior Change and Pharmacologic Treatment

Behavioral changes, such as weight loss, avoidance of alcohol, sedatives, antihistamines, and smoking, and body position training, are key in the management of patients with OSA. This therapy requires active patient participation, however, and rarely achieves the desired outcome.[71,75] Similarly, pharmacologic treatment with progesterone, mazindol, and other drugs has been scarcely effective and disappointing.[76]

Nasal Continuous Positive Airway Pressure and Intraoral Appliances

Currently, nCPAP is the most common and most successful treatment for OSA. Nasal CPAP functions as a pneumatic stent to keep the upper airway open during inspiration by preventing the pharyngeal collapse associated with the negative inspiratory pressure. In addition, genioglossus dysfunction observed in patients with OSA has been normalized after treatment with nCPAP.[77] Tousignant et al,[78] using the standard gamble method, showed an average gain of 5.4 QALYs in 19 patients whose OSA was treated with nCPAP. Furthermore, the cost-utility ratio in the Tousignant et al study was between Can$3,397 and Can$9,792 for each QALY.[78]

Compared with many other clinical interventions, nCPAP is clearly a cost-effective treatment choice for OSA. Moreover, nCPAP has consistently been shown to be effective in lowering the apnea-hypopnea index in OSA patients. For example, Clark et al[79] showed a 60% decrease in the apnea-hypopnea index in OSA patients managed with nCPAP. Tousignant et al,[78] using nCPAP, found improvement in 9 of 12 symptoms commonly associated with OSA. Furthermore, all patients in this study showed a decreased severity of polysomnographic indicators of OSA after treatment with nCPAP. Ferguson et al[80] also showed dramatic improvements in the apnea-hypopnea index with treatment. Before treatment, patients had an average apnea-hypopnea index of 17.6 +/- 13.2; after treatment with nCPAP, the average apnea-hypopnea index was 3.6 +/- 1.7. Using the Medical Outcomes Study Short Form-36 questionnaire to assess quality of life in OSA patients, D'Ambrosio et al[81] found marked impairment of all aspects of quality of life (physical functioning 75%, vitality 41%, role functioning [physical 54%, emotional 61%, social 66%], general health 88%, and mental health 76%). After 8 weeks of treatment with nCPAP, the following improvements were seen: vitality 75%, social functioning 90%, and mental health 96%. Thus, nCPAP is consistently associated with a significant clinical outcome.

Although nCPAP has been shown to improve quality of life and survival,[82] its use is sometimes limited by poor long-term compliance.[83] Nasopharyngeal symptoms that are common in patients with OSA, such as dryness, sneezing, mucous in the throat, blocked nose, and rhinorrhea, tend to increase with use of nCPAP.[84] Intraoral appliances have been described as an alternative to nCPAP for the treatment of mild OSA. They modify the upper airway by either advancing the mandible or retaining the tongue.[85] In one study, snoring improved in most patients, and OSA was diminished in approximately one half of patients.[85] Long-term compliance ranges from 50% to 100%, with excessive salivation and temporomandibular joint discomfort being the major complaints.[85]

Clark et al[79] compared the clinical efficacy of nCPAP and anterior mandibular positioning devices using a crossover clinical trial and found nCPAP to be clinically more effective than anterior mandibular positioning devices in treating OSA. The apnea-hypopnea index decreased on average 59.5% (33.86 +/- 14.30 to 11.15 +/- 3.93) with nCPAP treatment compared with 38.9% (33.86 +/- 14.30 to 19.94 +/- 12.75) using anterior mandibular positioning devices. Participants in the study did prefer the anterior mandibular positioning devices to the nCPAP, however. In a similar study, Ferguson et al[80] used a randomized crossover clinical trial to compare nCPAP with anterior mandibular positioning devices. The apnea-hypopnea index decreased from 17.6 +/- 13.2 to 3.6 +/- 1.7 using nCPAP compared with a decrease from 19.7 +/- 13.8 to 9.7 +/- 7.3 with anterior mandibular positioning devices. Similar to the Clark et al study findings, patients in the Ferguson et al study overwhelmingly preferred the anterior mandibular positioning devices to nCPAP. Treatment with anterior mandibular positioning devices appears, therefore, to be a realistic alternative to nCPAP in patients who are noncompliant with nCPAP.

Surgical Treatment

Surgical treatments of OSA include invasive procedures that carry certain risks and might not be uniformly effective.[71] The goal of surgery is to augment the upper airway and relieve any obstruction. When nasal symptoms are the primary complaint, nasal surgery includes septoplasty, turbinectomy, or repair of alar collapse, when necessary. When the obstruction is at the velopharyngeal level, the surgery of choice is uvulopalatopharyngoplasty. This single-staged procedure involves removal of part of the soft palate, uvula, and tonsils, as well as part of the posterior pharyngeal wall. The success rate of this surgery is nearly 50% to 60% at 4 years.[86] This low figure has been attributed to poor patient selection. Potential complications include difficult intubation, hemorrhage, nasal regurgitation or stenosis, velopharyngeal insufficiency, and voice and resonance change.

Laser-assisted uvulopalatoplasty has been introduced as an office setting procedure to treat patients with loud snoring.[87] A carbon dioxide laser is used to create full-thickness vertical trenches on either side of the uvula, thereby shortening and thinning this structure. Nevertheless, despite a reduction in snoring frequency and loudness, there is little evidence to support its use in the treatment of OSA. Other surgical procedures, such as midline glossectomy to reduce the bulk of the tongue and maxillomandibular osteotomy and advancement to increase the retrolingual space, have also been used to treat persistent snoring and OSA.[88,89] The rationale is to augment the posterior airway space at the base of the tongue. In patients with severe OSA and morbid obesity, tracheotomy is still a highly effective alternative.[71] A suggested algorithm for the management of patients with OSA is provided in Figure 3.

Figure 3.

Suggested approach to management of patients with obstructive sleep apnea. A more aggressive approach might be justified for patients with serious coexisting cardiovascular conditions.

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Treatment of Cardiac Arrhythmias

Patients with OSA have been shown to suffer from high morbidity and mortality. In a study conducted by Partinen et al,[90] the mortality rate in patients managed with weight loss only was 11 of 100 patients in 5 years, and almost one half was due to vascular events. He et al[91] calculated the cumulative survival in 385 OSA patients and found the probability of cumulative 8-year survival to be 0.96 +/- 0.02 (SE) in patients with an apnea index of less than 20, and 0.63 +/- 0.17 for an apnea index of more than 20. Despite a higher mortality rate, a cause-and-effect relation between cardiac arrhythmias and death in patients with sleep apnea has not been established. What has been shown is a decrease in the incidence of death after certain therapies in patients who have OSA. In his study of 385 men with OSA, He et al[91] found that none of the patients treated with tracheostomy or nCPAP died. Similarly, Partinen et al[90] found a 0% mortality rate per 100 patients per 5 years in the surgically treated population.

Bradyarrhythmias

Clinical decisions regarding the implantation of permanent pacemakers in patients with OSA-associated bradyarrhythmias can be difficult, largely because clear and accepted indications are lacking for pacemaker therapy. Published guidelines regarding pacemaker implantation are notably sparse regarding the specific scenario of bradyarrhythmias occurring during sleep apnea,[92] and extrapolation from the existing recommendations is limited: most class I and class IIA indications specifically require either symptoms or a threshold degree of bradycardia in the awake state; these circumstances are by definition hard to define in the OSA patient.

Certainly, therapy for OSA is mandatory, but the additional role of pacemaker therapy is less clear. Bradycardia and heart block occurring during apneic episodes can be eliminated by treatment with nCPAP or tracheostomy,[82,91] and no fixed or structural conduction system abnormalities are apparent in most of these patients when evaluated by electrophysiology studies.[60] Nevertheless, no prospective outcome studies or randomized trials comparing pacemaker implantation with OSA treatment alone exist to validate or refute this approach.

Stegman et al[93] described OSA as a suspected cause of asymptomatic bradyarrhythmias in 7 patients. Treatment with nCPAP or tracheostomy was effective without adverse outcome for a mean of 22 months follow-up. In a retrospective review, Koehler et al[61] investigated the outcome of patients with sleep apnea-related bradyarrhythmias. Seventy-one men with OSA-associated bradyarrhythmias were compared with a group of 61 age- and weight-matched patients with OSA but no bradyarrhythmias. No causal relation between OSA-related bradyarrhythmias and mortality could be established.

In view of these limited observations and the pathophysiologic findings of OSA-related bradycardia discussed previously, it appears reasonable to reserve pacemaker implantation for those patients in whom symptomatic bradyarrhythmias persist despite effective treatment of OSA[94] or in whom therapy for OSA is unsatisfactory.[95]

Tachyarrhythmias

Similarly, no information is available regarding the specific role of implantable cardiac defribrillators or antiarrhythmic drug therapy in the management of ventricular arrhythmias in the setting of OSA. The frequency of ventricular tachycardia in patients with OSA might not be notably higher than in patients without OSA, and all reports of ventricular tachycardia in this population are of nonsustained ventricular tachycardia. There does appear to be a relation with OSA specifically in that these patients will characteristically have ventricular tachycardia during sleep. Thus, it would appear reasonable to perform electrophysiologic studies for risk stratification only in those patients with indications for a study based on symptoms during wakefulness. In our laboratories, we include patients with unexplained syncope or near syncope and patients with nonsustained ventricular tachycardia, concomitant coronary artery disease, and depressed ejection fraction. If the existence of substrate for ventricular tachycardia has been determined, it is likely that OSA might exacerbate the severity of ventricular tachycardia. As such, with treatment of OSA it is likely this exacerbation of ventricular tachycardia will be eliminated. Even so, further evaluation and treatment of persistent ventricular tachycardia should not be precluded after treatment of OSA.

Conclusion

Sleep apnea is a common but underdiagnosed disorder with a multitude of related systemic manifestations beyond the well-recognized obstructive phenomena. Pathophysiologic understanding of this disorder is best approached from the perspective of integrated structural, neural, and cardiopulmonary relations. Indeed, the obstruction to airflow during sleep can occur at multiple anatomic levels and is dynamically responsive to hypoxic and hypercapnic reflexes. It is these responses, particularly the cyclical alterations in sympathetic nerve activity in response to apnea and recovery and the parasympathetic responses related to hypoxemia, that likely contribute to associated cardiovascular disease, namely, hypertension. In addition, frequently observed bradyarrhythmias and tachyarrhythmias appear to be the result of these autonomic fluctuations.

The reasons for the increased mortality in patients with sleep apnea are not established, but it is clear that therapy directed at alleviating the obstruction to airflow does improve patient outcomes. nCPAP is the mainstay of treatment and, in fact, improves arrhythmic and cardiovascular disturbances as well. In selected patients, surgical therapy is still warranted, with tracheostomy the most common approach. Finally, the approach to cardiac arrhythmias should be done with an understanding of the autonomic changes that accompany an apneic episode. Daytime high-degree atrioventricular block might not be occurring during waking hours and thus might not require pacemaker implantation. Similarly, the approach to tachyarrhythmias in the setting of OSA should be similar to our management of ventricular arrhythmias in the absence of this disorder, as no specific recommendations are available for this population

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