

OBSTRUCTIVE SLEEP APNEA: UNJUSTIFIED DIAGNOSTIC CHALLENGES

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Obstructive sleep apnea (OSA) is a common disease which is associated with high morbidity and mortality. In developed countries, understanding of the nature and the consequences of OSA and its effects on the physiologic process has evolved considerably over the past two decades. In Saudi Arabia, OSA is still underdiagnosed and undertreated due to lack of awareness on the part of physicians and the public at large. One of the greatest challenges for physicians dealing with this major medical problem is the lack of appropriate facilities even in tertiary centers. This review discusses the pathophysiology, clinical features, and approach to patients with OSA using limited resources.

Obstructive sleep apnea syndrome is increasingly recognized as a common condition and major health problem. Epidemiologic studies estimate that it affects 2%-4% of middle-aged adults,¹ and is associated with significant morbidity, largely due to impaired daytime function, with excessive daytime sleepiness and consequent increased risk of accidents, and to cardiovascular complications. The prevalence of obesity among the Saudi population is about 20%-30%, according to one estimate.² There are no epidemiological studies of the prevalence of OSA in the Saudi population, but due to the close association between obesity and OSA, the prevalence in this population may be high. Even in developed countries, the small number of cases of adults who have been diagnosed reflects insufficient awareness of sleep apnea among physicians and the public at large.³ The magnitude of this problem in Saudis may be even larger. Therefore, awareness of this problem by medical practitioners and the public of this country is needed.

Apnea is defined as an absence of airflow at the nose and mouth for 10 seconds or longer. Central apnea is characterized by absence of both airflow and respiratory efforts. Obstructive sleep apnea is defined as the absence of airflow despite persistent respiratory efforts. Mixed apneas begin centrally and are followed by an obstructive portion.

They closely resemble obstructive apneas in their pathophysiology and management.

It has recently been recognized that hypopnea can produce the same effect.⁴ Definitions of hypopnea are less universal than those of apnea, and vary from one laboratory to another. The most commonly used definition is decrement in airflow by 35%-50% for 10 seconds or more that is associated with a 4% fall in oxygen saturation and/or terminated by an arousal.^{4,5}

The frequency of apnea during sleep increases with age. Up to five apneas per hour in young adults and up to 10 apneas per hour in asymptomatic elderly men are considered physiologic.⁶ Universally accepted criteria for the significant apneas are lacking. It has been proposed that 15 apneas per hour plus hypopnea with symptoms are significant.^{4,5} This is the definition now commonly used, and is referred to as the apnea hypopnea index (AHI) or respiratory disturbance index (RDI).

Pathophysiology

The pathophysiology of apnea has been extensively investigated. The suspicion of investigators that upper airway obstruction is fundamental in the pathogenesis of sleep apnea was confirmed by the observation that tracheostomy can reverse the clinical manifestations.⁷ A few patients have obvious anatomic narrowing of the upper airway due to micrognathia, retrognathia, adenotonsillar hypertrophy or macroglossia. However, the majority of patients are free of such disorders. Obesity often contributes to this obstruction in the form of increased size and fat content of the pharyngeal tissues, soft palate and uvula, a large tongue and vascular congestion, and pulse edema of the pharyngeal mucosa.^{8,9} Pharyngeal compliance may also be increased in patients with OSA, predisposing them to upper airway narrowing when exposed to negative inspiratory pressure. Many patients compensate for this narrowing during wakefulness by compensatory increase in the activity of upper airway dilator muscles. With sleep onset, this compensatory response is reduced or lost, creating imbalance between forces that promote collapse of the pharynx and opposing forces that support upper airway patency. This imbalance leads to closure or critical narrowing of the airway. The subsequent reduction or absence of ventilation causes hypoxia and hypercapnia, leading to a progressive increase in ventilatory efforts that

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eventually triggers arousal or awakening. Awakening restores activity to the upper airway dilator muscle, resulting in airway patency and ventilation, followed by a subsequent return to sleep. This cycle can repeat itself hundreds of times each night, resulting in repetitive episodes of hypoxia and hypercapnia with marked disruption of sleep.

Clinical Features

The typical patient with OSA is middle aged, moderately obese and hypertensive. However, not all patients exhibit this pattern.¹ The cardinal symptoms of obstructive sleep apnea are snoring and excessive daytime sleepiness. However, both symptoms may be denied or minimized by the patient. The patient may not be aware of snoring unless informed by his or her family. Sleepiness develops slowly over years and patients may forget what normal alertness is like. In our society, middle-aged women staying at home may not be aware of sleepiness unless it is very severe.

The symptoms of OSA can be classified into problems during sleep, such as insomnia, due to interruption of normal sleep patterns, frequent arousal, witnessed apnea, nocturnal choking, symptoms of gastroesophageal reflux, dry mouth, sore throat or polyurea. Problems when awake include excessive daytime sleepiness and the desire to sleep even after long hours of sleep. Patients may nap frequently without feeling refreshed and complain of morning headache, confusion, fatigue, loss of concentration, poor work performance, changes in mood, and loss of libido. Patients may present with complications of the disease (listed below). Physical examination may rule out secondary causes of upper airway obstruction such as increased neck circumference, small oropharyngeal space, large tongue, nasal obstruction, retrognathia or micrognathia. It is also essential to rule out other diseases that can cause OSA, such as hypothyroidism, acromegaly, neuromuscular disease and dislocated temporomandibular joint.

Complications of OSA

Patients with OSA may demonstrate a number of physiologic changes during sleep, depending on the severity of the obstruction. These include gas exchange abnormalities such as intermittent hypoxemia and hypercapnia, and central nervous system arousal leading to increases in sympathetic nervous system activity. In addition, large fluctuations in the intrathoracic pressure during airway obstruction may influence venous return, right ventricular filling and vagal tone, and increase peptide secretions such as renin, aldosterone and atrial natriuretic hormones.¹⁰ Recent studies document that OSA is associated with increased mortality^{9,11,12} systemic

hypertension,¹³ pulmonary hypertension,¹⁴ cardiac arrhythmia, ischemic heart disease¹⁵ and cerebrovascular accidents.¹⁶ OSA can also lead to excessive daytime sleepiness and neurocognitive disturbance, causing occupational hazards and increased motor vehicle accidents.¹⁷

Diagnosis

The following ancillary investigations may be done as part of the patient evaluation. A complete blood cell count may reveal polycythemia. Electrocardiography may reveal evidence of myocardial ischemia, arrhythmia and cor pulmonale. Arterial blood gases (ABG) may detect abnormal gas exchanges, hypoxia or hypercapnia or both due to co-existing pulmonary disease, pulmonary hypertension secondary to OSA, or other ventilatory disorders such as obesity hypoventilation syndrome. TSH serum levels may diagnose hypothyroidism.

When the diagnosis of sleep apnea is suspected, patients should ideally have polysomnography in a sleep laboratory. Unfortunately, this gold standard diagnostic utility is not readily available in many facilities in Saudi Arabia. Therefore, when faced with a patient who demonstrates a high probability of obstructive sleep apnea, clinicians may have to utilize alternative diagnostic methods.

Pulse oximetry study is a component of polysomnography and records the events and frequency of oxygen desaturation. Guidelines published by the American Sleep Disorders Association in 1994 recommended that pulse oximetry not be used to evaluate OSA.¹⁸ Nevertheless, when polysomnography is not available, a commonly encountered problem in our practice, pulse oximetry may be the only tool available to investigate and monitor the effect of therapy, and despite its limitations should be used as an alternative, particularly when urgent evaluation is needed.

Oximetry Interpretations

There is no consensus on the optimal way to interpret oximetry results in diagnosing sleep disorder breathing. The sensitivity and specificity of oximetry depends on criteria used to define a positive test and depends on the readout format used either as a quantitative or qualitative method.

Quantitative Method

This is a printout of the duration and number of desaturation events. Several studies define positive oximetry as a sustained drop in arterial oxygen desaturation of more than 4%, to a value less than 90%. This has a sensitivity of 41% to 65% and specificity of 97% to 100%, depending on desaturation values defined as abnormal.¹⁹⁻²¹ The sensitivity and specificity of identifying significant

obstructive sleep apnea was 65% and 74%, respectively,²¹ when a criterion of a 2% desaturation from baseline was used.

Qualitative Method

The qualitative method was proposed by Series and colleagues²² and relies on visual estimation of fluctuations of desaturation from the baseline. No fixed level of desaturation is required for a positive study. This method was investigated by the same authors in 240 patients with suspected OSA, using 10 fluctuations per hour of oximetry as the diagnostic cut-off value. The sensitivity and specificity were 98% and 48%, respectively. The advantage of this method is its simplicity, as it relies only upon straightforward visual analysis and counting the events rather than complex quantitative criteria. The disadvantage is the subjectivity of interpretation, and the fact that the interpretation is highly reader-dependent, and influenced by reader experience.

Limitations of Pulse Oximetry

In addition to missing other sleep disorders that cause excessive daytime sleepiness, pulse oximetry has major limitations in the diagnosis of obstructive sleep apnea. Regardless of which method is used to interpret the result of oximetry studies, this will result in either underdiagnosis of the obstructive sleep apnea (false-negative) or overdiagnosis of obstructive sleep apnea (false-positive).^{23,24} Studies examining the cost effectiveness of pulse oximetry in comparison to either split night polysomnography for diagnosis and treatment or one-night diagnostic polysomnography concluded that polysomnography is more cost effective and results in better patient compliance with therapy.^{25,26}

The proposal of using pulse oximetry in diagnosis of obstructive sleep apnea is only for patients with severe symptoms that are indicative of a diagnosis of OSA and when initiation of treatment is urgent and standard polysomnography is not readily available.^{27,28}

In practice it is essential to estimate the pre-test probability of OSA and to appreciate the limitations of oximetry. The two approaches outlined above give the clinician several options for evaluating the patient with suspected obstructive sleep apnea in the absence of facilities to do polysomnography studies. If the pre-test probability of OSA is high, then a fall in SaO₂ >4% may be sufficient to diagnose OSA or to exclude severe OSA, which is associated with significant morbidity and mortality. If the pre-test suspicion is low, then the qualitative approach (Series criteria) may be sufficient to exclude significant obstructive sleep apnea. If suspicion is still high, despite indeterminate oximetry study, using 4% as a diagnostic criteria, then using fall in oxygen saturation of more than 2% will increase the test sensitivity.

A more complicated issue in the use of oximetry studies is to assess the efficacy of therapy. There are no formal

studies to specifically answer this indication. But if repeated oximeter study on therapy revealed improvement in the symptoms, and the oximetry study showed normal oxygen saturation, then the treating physician and the patient may be reassured that therapy is adequate.

Treatment

The rationale in diagnosing and treating obstructive sleep apnea is based on the following: 1) susceptibility of patients with OSA to major cardiovascular and hypoxic complications, and 2) the consequence of excessive daytime sleepiness. I will discuss a practical approach in dealing with this disease based on what is available.

Secondary Causes

It is important to exclude or treat secondary causes before further evaluation. Secondary causes that may predispose a patient to OSA include nasal obstruction, tonsillar/adenoid hypertrophy, large uvula, hypothyroidism,

such as lipoma or goiter.

Behavior Changes

Changes in behavior should include avoiding narcotics, sedative agents and alcohol. Weight reduction is effective in decreasing apneic events, oxygen desaturation and the amount of sleep disruption.^{29,30} The relationship between weight loss and improvement in the number of apneas and hypopnea is not linear; a large improvement in OSA can occur with minimal weight loss. The number of apneas will decrease by approximately 50% with 10% weight loss.^{30,31} If weight reduction is sustained no other therapy may be required. However, this is difficult to maintain and often fails despite behavior modification. Surgical techniques such as gastroplasty and gastric bypass have produced favorable results in OSA. The risk of operation must be weighed against potential benefits. Sleep posture modification is a reasonable therapeutic alternative for patients with posture-dependent OSA. Unfortunately, body positions may change frequently during the night and sleep training may be difficult to sustain in the long term.

Oral Appliances

Several studies demonstrate that oral appliances can be a useful alternative to positive airway pressure with mild to moderate sleep apnea.^{32,33} A wide variety of appliances are available, differing both in construction and in the manner in which they alter the oral cavity. The most common oral devices used are tongue-retraction devices that enlarge the airway by keeping the tongue in an anterior position and preventing it from falling back during sleep, and the Herbst appliance, which forces the mandible forward, thereby enlarging the oral cavity. The advantage of such appliances is that they are generally well tolerated and easy to manufacture locally by dentists in collaboration with sleep

specialists. The disadvantage is that they are not effective first-line therapy in severe obstructive sleep apnea and can lead to temporomandibular-joint discomfort.

Continuous Positive Airway Pressure (CPAP)

The pressure generated by a CPAP machine that delivers through nasal mask works as a pneumatic split, therefore preventing narrowing and closure of the upper airway regardless of the site of the obstruction. The CPAP machine is easy to operate, runs on household current, weighs approximately 2 kg, is portable and available in Saudi Arabia for 4000-12,000 SR. The most important choice in favoring one machine over another is the amount of pressure generated by the machine, which should be between 0 to 20 cm H₂O. Other accessories may not be necessary to avoid extra costs.

The American Thoracic Society (ATS) official statement regarding the indications and the standards for the use of nasal continuous positive airway pressure (NCPAP) in sleep apnea syndrome³⁴ should serve as a guideline for physicians recommending NCPAP. The level of positive pressure required to sustain patency of the upper airway during sleep should ideally be determined in a sleep laboratory. Short of this it is reasonable to start the patient at low pressure (average of 6-8 cm H₂O), increased gradually. Overnight oximetry should be repeated with any changes aiming for resolution of the symptoms and normal oxygenation.

Autotitration-CPAP

Several recent studies suggest that auto-CPAP devices compared favorably with fixed CPAP devices with respect to reducing the mean AHI/RDI and arousal frequency and improving nocturnal hypoxia.^{35,36} Therefore, although this has not been studied yet, it is reasonable to start the patient on AUTO-CPAP if it is available and to take the average pressure and to repeat the oximetry study on subsequent nights to assess the effectiveness of the selected pressures.

Pharmacologic Agents

Several pharmacologic agents have had variable effectiveness in patients with OSA. In several small series of patients, protriptyline has been shown to reduce the frequency of obstructive apneas and to improve the level of oxygen desaturation.^{37,38} The modest decrease in the frequency of apnea is due in part to a reduction in the percentage of rapid eye movement and reduction in apnea duration. Use of this medication is limited by its anticholinergic side effects, such as dry mouth, sweating, constipation, urinary retention and erectile dysfunction. Progesterone has been used in OSA but experience is limited and the results have been mixed.^{39,40} Progesterone may be beneficial in cases of hypoxemia and carbon dioxide retention due to its effect on the central respiratory drive.³⁹

Oxygen Therapy

Oxygen therapy has produced variable success in patients with obstructive sleep apnea.^{41,42} It may reduce oxygen desaturation but not improve daytime sleepiness.⁴² Therefore, its routine use is not recommended but is reserved for patients who remain hypoxic despite optimal N-CPAP therapy.

Surgical Treatment

Over the past few years different surgical procedures have been developed. The goal of such surgical approaches is to augment the upper airway and to correct its disproportionate anatomy. Surgical approach should be reserved for those with correctable anatomic problems and be considered only for those who failed other less invasive modalities of therapy.

Conclusion

OSA is a major health problem with high morbidity and mortality. One of the greatest challenges besides lack of awareness of this disease among physicians and the public is absence of the sophisticated sleep laboratories that are essential in diagnosing and treating these disorders. The diagnosis and treatment of OSA using polysomnography is a simple task and more cost effective. The current challenges we encounter in managing patients with OSA are not justified. Therefore, health care planners should consider the urgent need for specialized sleep laboratories, particularly in tertiary centers.

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