

Obstructive Sleep Apnea

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Obstructive sleep apnea (OSA)/hypopnea syndrome (OSAHS) is increasingly becoming of great concern to a variety of medical disciplines as the scope of associated disease is becoming increasingly apparent and alarming. No longer is OSAHS treated to only improve daytime sleepiness. The concerns go far beyond the anesthesiologist's wariness of a potentially difficult airway. We will review new evidence regarding the diseases associated with OSAHS, the identified problems for the perioperative period, the current recommendations for dealing with these problems and speculate a little about how this might be dealt with in the future as evidence and clinical trial results accumulate.

During sleep, either by a narrowing or a slackening in the upper airway, patients with OSAHS experience repeated episodes of apnea/hypoventilation, oxygen desaturation, sympathetic arousal and awakening, leading to fragmented sleep. Obstructive apnea in OSAHS is defined by a minimum of a 10s cessation of breathing and the severity index is determined by the number of apneas per hour of sleep (mild 5-15, moderate 15-30, severe > 30). Hypopneas are defined by a greater than 50% decrease in airflow or oxygen desaturations of more than 3% for 10s or more.

During an obstructive apnea the diaphragm and the auxiliary respiratory muscles become completely desynchronized. This augments already negative intrathoracic pressure further to a point that causes arousal, either due to the muscle work or the extreme pressure gradient and/or hypoxemia. The arousal restores muscle tension to normal and free air exchange resumes. This cycle may arise 300-400 times a night for a patient with severe OSAHS, leading to fragmented sleep and explains the serious daytime somnolence and cognitive deficits that mark this syndrome.

OSAHS may occur from infancy through adulthood. Currently the prevalence of OSAHS in middle age is 2% for women and 4% for men although OSAHS is known to be under reported (80% of cases are believed to be undiagnosed). It is estimated that over the next 10 years there will be an 8 fold increase in the number of patients carrying this diagnosis.

OSAHS is usually (and definitively) diagnosed by a sleep study (polysomnography) which monitors the EEG, electrooculogram (for REM sleep), ECG, thoracoabdominal excursions (by respiratory inductive plethysmography), oronasal airflow (by thermistor or airflow pressure transducer) and pulse oximetry. Also determined in a sleep study is the nasal CPAP (nCPAP) needed to relieve the obstruction. CPAP treatment improves airflow and prevents apnea. As a result, oxygen desaturation is reversed as is hypercapnia.

Because there are an insufficient number of sleep labs and polysomnography is expensive, OSAHS can also be diagnosed by a validated questionnaire such as the Epworth sleepiness scale or the Berlin questionnaire that includes questions about

snoring daytime somnolence, hypertension, age, weight, gender, neck circumference, etc. Additionally, workers are looking for a reliable biomarker that could diagnose OSAHS with a blood test. Leptin, neuropeptide Y, and orexin-A (a neuropeptide implicated in appetite and sleep regulation) have shown promise, but neither are sensitive nor selective when used alone.^{1,2}

OSA and Hypertension (HTN)

Approximately 40% of patients with OSAHS also have HTN and about 40% of patients with HTN have detectable OSAHS.³ A debate is ongoing as to whether this relationship is causative or a confounding association due to comorbidities such as obesity and body fat distribution common to both. For instance, ‘upper body obesity’ exemplifies male fat distribution, affects the neck and narrows the upper airway while at the same time is a known risk factor for hypertension, insulin resistance, hyperglycemia and overall vascular risk.⁴

The Wisconsin Sleep Cohort Study⁵ showed a dose-response relationship between the severity of sleep OSAHS and the *de novo* appearance of HTN 4 years later, independent of confounding factors. OSAHS disrupts the linkage between sleep stage and sympathetic tone. Because hypoxemia/hypercapnea and intrathoracic pressure changes cause sympathetic activation leading to surges in BP, loss of the nocturnal BP dipping pattern may be a factor in the development of HTN.⁶ Even during wakefulness, normotensive patients with OSAHS exhibit increased sympathetic tone, increased BP variability and decreased HR variability. All three of these findings are associated with an increased risk of future HTN.⁷

Obese patients have increased aldosterone, indicating elevated renin-angiotensin-aldosterone system (RAAS) activation. Perhaps the elevated sympathetic activity, hyperinsulinemia, and hyperleptinemia associated with OSAHS, coupled with the RAAS activation of obesity contributes to the increased prevalence of HTN in those with both OSAHS and obesity.⁸

Cycles of hypoxia-normoxia can lead to the generation of oxygen free radicals – or reactive oxygen species (ROS). ROS and angiotensin II both increase vasoconstrictor activity, which could be the etiologic mechanism for some types of HTN.⁹

Treatment of OSAHS with nCPAP attenuates the hemodynamic responses induced by apnea, including BP surges and increased sympathetic nerve activity. Whether this results in decreased daytime BP has not shown consistent results. However, several recent studies indicated that patients with more severe levels of OSAHS do have a positive response to HTN. Additionally, nCPAP seems to improve the response to HTN pharmacotherapy.³

OSAHS and Inflammation and Cardiovascular Risk

Patients with OSAHS have increased levels of the proinflammatory cytokines IL-6, TNF α , C-reactive protein as well as activated coagulation factors XIIa, VIIa, thrombin-antithrombin complex, and soluble P-selectin.^{10,11, 12} Additionally, cholesterol is elevated in OSAHS and decreases with one month of effective nCPAP therapy. Circulating levels of cholesterol, proinflammatory factors and activated coagulation factors are all associated with an increased incidence of coronary artery disease (CAD), CHF and stroke. The Sleep Heart Health Study showed an increase in CAD, CHF and stroke with increasing severity of OSAHS.¹³

OSAHS and Stroke

Greater than 70% of patients with stroke have OSAHS.¹⁴ Whether OSA was caused by the stroke or contributed to it has been a subject of some debate. While no prospective studies have shown a convincing relationship other than the Sleep Heart Health Study (see above), a study in which polysomnography was performed in matched stroke, fully recovered TIA patients and normals did demonstrate a similar incidence and severity of OSAHS in stroke and TIA that was significantly greater than those of the matched normals, suggesting OSAHS was present before the stroke and may have been a contributing factor.¹⁵

OSAHS and Arrhythmia

Two million Americans adults have atrial fibrillation (AF), a prevalence that has tripled since the 1960s. Fifty percent of patients with AF also have OSAHS. The presence of OSAHS predicted AF after CABG and doubles the risk of recurrent AF after cardioversion. Nocturnal elevations in sympathetic activity along with dramatic shifts in cardiac transmural pressures and chamber dimensions caused by forceful ventilatory efforts against an obstructed airway may combine to contribute to AF in these patients. Accordingly, studies are needed to determine whether aggressive treatment of AF patients with OSAHS will help prevent the recurrence of AF.¹⁶

OSAHS and Cardiac Disease

There is growing research evidence for an independent association between OSA and cardiovascular disease (CVD), mainly hypertension and coronary artery disease (CAD). However, a causal link has not yet been convincingly documented. Peker et al. performed an epidemiologic study in 182 patients without evidence of CVD.¹⁷ Their results showed a strong causal relationship, showing that the patients with OSAHS who were effectively treated developed CVD at the same incidence as the non-OSA patients, while the ineffectively treated OSAHS patients had markedly higher rates of HTN, CAD, and CV events such as a MI and cardiac death.

OSAHS and Pregnancy

There is emerging evidence that OSAHS in parturients may be associated with small birth weight, maternal HTN and, perhaps, pre-eclampsia. The pregnancy-induced

changes in the upper airway may predispose parturients to OSAHS. Coupled with the pregnancy-induced decrease in FRC may additionally predispose them to hypoxemia episodes, sympathetic activity surges, and proinflammatory cytokines.¹⁸

OSAHS and Gastric Reflux

There seems to be a relationship between OSAHS and nocturnal GERD. However, it is not yet been determined to be a causal relationship as has been the case with HTN. One consideration is that the diaphragm is intimately associated with the lower esophageal sphincter. During apneas, the work of the diaphragm increases greatly, leading to loss of cardia muscle tone. This loss of tone may tip the balance towards GERD when one considers that the greatly increased negative intrathoracic pressure created during an obstruction may actually be sucking gastric contents into the esophagus. This may lead to microaspiration and help explain the increased incidence of asthma in patients with nocturnal GERD. Indeed, investigations have shown that nocturnal GERD decreases with nCPAP treatment.¹⁹

OSAHS and Brain Function

Several characteristics of OSAHS suggest a component of central neural participation in the genesis and the maintenance of the syndrome which acts together with the peripheral anatomic elements (e.g., obesity, narrowed airway). In normal subjects, recovery from an obstruction occurs quickly by activation of airway muscles to restore tone. Conversely in OSAHS patients, restoration of airway muscle tone is delayed until arousal, thus suggesting that central control or afferent innervation that responds to airway closure is dysfunctional. Macey et al. have reported that OSAHS patients have unilateral gray matter loss in regions such as the left ventrolateral frontal cortex, an area known to modulate upper airway moter function, as well as the anterior cingulated cortex and the cerebellum, which are regions known to modulate cardiovascular and respiratory control. This gray matter loss occurred in well perfused regions and did not appear to be to the result of hypoxic damage. The loss preferentially targeted areas associated with upper airway function, including expressive areas for speech. The latter is of interest a 38% of OSAHS patients had speech impediments such as stuttering from childhood.

OSAHS and Perioperative Considerations^{20, 21 , 22}

Given that a third of adult males and about half that prevalence in females may have OSAHS, but only 20% may be aware that they have this condition, anesthesia providers should be on the alert for this syndrome in surgical patients. Anesthesiologists should question patients about snoring (over half of all people who know they snore, actually have OSAHS), frequent awakenings, daytime somnolence and other symptoms of OSAHS, particularly in patients with known comorbidities such as HTN, AF or GERD.

Airway Considerations

OSAHS patients are known to be more difficult to intubate and emergency equipment should be available. Siyam and Benhamou found that approximately one quarter of

OSAHS patients were difficult to intubate but found no other predictor of difficulty in this group. As many of these patients are also obese, predictors of difficult intubation in this population, such as neck circumference (> 19 inches associated with difficult intubation), should be considered.

On emergence, care should also be exercised as these patients should be considered at risk for obstruction and hypoxia if they drift back into unconsciousness. Therefore, it is recommended that before extubation that OSAHS patients be awake, communicative, breathing spontaneously with adequate tidal volumes and oxygen saturation. Half sitting or reverse Trendelenburg position may also be helpful.

OSAHS and Complications

PACU complications are more common and may include HTN, dysrhythmia, O₂ desaturation, airway obstruction and reintubation. Sedatives and opioids may exacerbate these complications as well as sleep-related apneic episodes and so care is advised in using these medications. Gupta et al studied OSAHS versus matched controls in a retrospective study in knee and hip replacement surgery and found 24% of OSAHS patients had serious complications in the postoperative period (vs 9% of controls) and their length of stay averaged nearly 2 days longer. There are case reports of patients with OSAHS dying suddenly on the ward following anesthesia. In most of these cases the diagnosis of OSAHS was unknown at the time of surgery. The ASA Closed Claims Project revealed 19 cases involving patients with OSAHS. All but one sustained death or brain damage related to adverse respiratory system events.

Outpatient surgery for patients with OSAHS is controversial. Studies exist that seemingly support both sides of the argument. The type of surgery and the use of post-operative opioids are probably the most important consideration although some experts consider that local and regional anesthesia is a safer option for individuals in this group who are being discharged home after surgery.

Future Considerations

Nasally applied CPAP may become the norm for the pre-operative preparation of surgical patients with OSAHS. Pulmonary hypertension, right heart failure and HTN have all been shown to improve within a month of nCPAP treatment. There is a suggestion from some studies indicating a reduction in postoperative complications when perioperative nCPAP is employed. Normally, a full sleep study is needed to determine the proper pressures to use for nCPAP, one that will keep the upper airway patent without being so uncomfortable as to prevent sleep. Unfortunately, sleep studies are expensive and difficult to schedule due to a shortage of sleep labs. Recent studies suggest that questionnaire-based diagnosis and an 'arbitrary' algorithm for determining the optimum CPAP may be equally effective to the more traditional techniques. Which ever protocol is adopted in the future, it is clear that anesthesia providers will find themselves in the position, because of the negative effects of OSAHS in the surgical patient, to diagnose and treat OSAHS.

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