Obstructive sleep apnoea (OSA) - a silent killer in anaesthesia?

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ABSTRACT
Sleep-disordered breathing (SDB) encompasses a wide range of disorders that afflict both adults and children. These disorders are often unrecognised preoperatively and the pathophysiological consequences may impact severely on the patient in the peri-operative period.

Introduction

The first physician to describe the clinical features of obstructive sleep apnoea was Broadbent in 1877. In 1898, Wells reported on curing several patients of sleepiness after treating an upper airway obstruction. The term Pickwickian syndrome was coined in 1956, when Burwell studied obese patients with somnolence and attributed their sleepiness to daytime hypercapnia. In 1965, Gastaut *et al*. first described polysomnographic findings in patients with sleep apnoea.

These disorders only became recognised as an important entity in the early 1970s, after the first international symposium on "hypersomnia with periodic breathing", which highlighted the co-morbidities of OSA, particularly cardiovascular consequences. In 1973, Guilleminault characterised insomnia with sleep apnoea as a new syndrome, and the terms "sleep apnoea syndrome" and "obstructive sleep apnoea syndrome" were coined to emphasise the occurrence of this syndrome in non-obese subjects.

In the early 1980s, the treatment of several cases of OSA with tracheotomies resulted in the reversal of their symptoms, highlighting the importance of treating the airway obstruction. Physicians have in general become more aware of sleep-disordered breathing and the necessity to make a diagnosis. A recent survey showed that pulmonologists and ENT surgeons were more likely to refer patients for polysomnography than other physicians.

As anaesthesiologists we need to be more aware of obstructive sleep apnoea syndromes, as patients often are undiagnosed, and their condition may have serious implications for the impending surgery. We may, in fact, be the first doctors to actually diagnose the condition. It is reported that, in the USA, OSA affects 4% of men and 2% of women between the ages of 30 and 60. It is estimated that, among middle-aged adults, 93% of women and 82% of men with OSA are **undiagnosed**.

"The anaesthesiologist is often the first caregiver to make a presumptive diagnosis of OSA."

Definitions

SDB encompasses a spectrum of disorders, ranging from snoring with minor airway collapse without sleep arousal to severe sleep apnoea with complete airway obstruction and frequent arousals from sleep.

Primary snoring

Approximately 10% of all children snore without associated apnoea or gas exchange abnormalities or excessive arousals. Primary snoring is generally regarded as being benign and most children outgrow the condition.

Snoring or upper airway resistance syndrome (UARS)

This is characterised by snoring without complete airway collapse and frequent arousals.

Obstructive sleep apnoea

This is characterised by complete airway obstruction of more than 10 seconds despite ongoing respiratory effort, five or more times per hour and associated with a decrease in oxygen saturation of more than 4%.

Obstructive sleep hypopnoea

OSH is defined as a decrease of more than 50% in airflow during sleep, for more than 10 seconds, 15 or more times per hour, is associated with snoring and may be associated with a decrease in saturation of more than 4%.

In 1999, the American Academy of Sleep Medicine Task Force included UARS in the OSA-hypopnoea syndrome, and defined it as the demonstration of five or more obstructive apnoeas-hypopnoeas or respiratory event-related arousals per hour of sleep.

OSA can be classified on the basis of the number of apnoeas-hypopnoeas per hour of sleep index, also known as the apnoea-hypopnoea index (AHI), or as the number of apnoeas and hypopnoeas plus respiratory event-related arousals per hour, known as the respiratory disturbance index (RDI).

Mild OSA is when the AHI is <5 per hour or the RDI is <15 per hour. Moderate OSA is when the AHI is 5 to 15 per hour and the RDI is <30 per hour, and severe OSA is when both the AHI and RDI are >30 per hour. UARS has also been separately defined as an RDI of fewer than four per hour with arterial oxygen saturation greater than 93%. In our role as anaesthesiologists, the debate surrounding exact definitions is of less importance than the recognition of the co-morbidity accompanying a patient with significant sleep-disordered breathing.

Pathophysiology

Sleep apnoea is either central or obstructive. In central apnoea, obstruction occurs without respiratory effort, as opposed to the continued respiratory effort in OSA. Central apnoea may coexist with OSA.

OSA in children occurs predominately in children with bony, nasal and tonsillar pathology and warrants a separate discussion. In adults, obesity is by far the most common physical characteristic associated with OSA, occurring with a frequency of 60 to 90%. The aetiology of OSA in non-obese patients appears to be different, and consists of predominately craniofacial and orofacial abnormalities. Excess neck fat may, however, be present in non-obese snorers, and this, together with pre-existing bony abnormalities, may increase the severity of the OSA.

The patency of the upper airway during sleep is dependent on the balance between collapsing intrapharyngeal negative suction pressure, and the dilating forces provided by the pharyngeal muscles. The contraction of the diaphragm against the high resistance offered by the narrowed upper airway creates a sub-atmospheric intra-airway pressure, which may narrow the collapsible segments in the pharynx. The upper airway collapses in three major areas, namely the retropalatal, retroglossal and retroepiglottic. The dilator muscles, which relax during sleep, are the tensor palatine, genioglossis and hyoid muscles respectively. The balance is finely controlled in the individual who is awake, probably by intrapharyngeal pressure-sensitive receptors, as this balance is disturbed by local anaesthesia to the pharyngeal walls. During non-REM sleep, the activity of the pharyngeal muscles decreases and upper airway resistance increases. MRI-imaging shows that the lateral compliant pharyngeal walls are the most important site of collapse. In REM sleep, the muscle activity is completely abolished and upper airway resistance increases dramatically until the point of complete airway collapse. A normal night's sleep consists of four to six cycles of non-REM sleep, followed by REM sleep.

There are three reasons why obese patients suffer from OSA.

1) Obesity correlates well with pharyngeal area. Fat is deposited in the pharyngeal tissues, particularly in the lateral pharyngeal walls, but also results in an increase in size of the uvula, tonsils, tonsillar pillars, tongue and aryepiglottic folds. This pattern of fat deposition is thought to change the long axis of the pharynx from transverse to antero-posterior. The dilator muscles work in an antero-posterior direction and thus, in effect, they will have little action in opening the airway.
2) The excess fat deposition will lead to a decrease in transluminal pressure by increasing extraluminal pressure, making airway collapse more likely.
3) Pharyngeal area is dependent on the lung volume, and the FRC is decreased in obesity.

Studies have shown conclusively that weight reduction leads to an improvement in symptoms of OSA, probably by decreasing the effect of the above three factors.

The incidence and severity of OSA correlates better with neck circumference than obesity. Obese OSA sufferers have significantly fatter necks compared with equally obese non-OSA patients.

The following respiratory events occur over the course of an apnoeic spell:

- Oxygen saturation declines as a function of the initial PaO_2 and FRC, and the duration of the apnoea.
- $PaCO_2$ rises as a function of the apnoea.
- Ventilatory effort progressively increases as the apnoea proceeds as a function of the lowered PaO_2 and rising $PaCO_2$, leading to a progressively more negative intra-airway pressure.
- Arousal usually results from increased neural traffic through the reticular activating system from the above-mentioned events. Arousal can also be caused by carotid body activation by the low PaO_2, chemoreceptor activation by the high $PaCO_2$, or by activation of pressure-sensitive receptors in the upper airway. Arousal is essential for survival; however, if repeated often enough, the physiologic events that surround the arousal response will result in serious systemic pathophysiological consequences.

Systemic pathophysiology of OSA

The clinical consequences of a patient with significant OSA are that patients frequently complain of the following symptoms: daytime sleepiness and fatigue, morning headaches, impaired memory and concentration, irritability, depression and anxiety, decreased libido and impotence. As anaesthesiologists, our concerns relate more to the clinical consequences that could increase the morbidity and mortality of these patients perioperatively.

Hypertension

OSA is an independent risk factor for hypertension. The Wisconsin sleep cohort study demonstrated a higher incidence of hypertension in patients with an AHI of five or more per hour. Approximately 40% of OSA patients have hypertension. The treatment of OSA often leads to a decrease in daytime systemic blood pressure.

Nieto *et al.* suggest that vascular dysfunction may partially explain the relationship between OSA, hypertension and cardiovascular disease, with the development of endothelial dysfunction where an imbalance exists between vasodilator (nitric oxide) substances and vasoconstrictor substances (endothelin). This endothelial dysfunction may arise because of the repetitive hypoxaemia and pressor responses that are present in these patients. Since endothelin has sustained hypertensive effects, the nocturnal increases in blood pressure may result in sustained daytime increases in blood pressure. Hypertension associated with OSA may be generated by sympathetic over-activity triggered by intermittent hypoxemia, large negative fluctuations in intrathoracic pressure and arousal from sleep. Hypertensive patients who do not exhibit the normal decrease in blood pressure during the night have been shown to be at increased risk of cardiovascular events. Unrecognised OSA patients who have nocturnal elevations in blood pressure may then also be at an increased risk of developing adverse cardiovascular events.

Cardiovascular disease

The Sleep Heart Health Study reported that OSA is associated with relative odds of 2.38 for heart failure. A relationship was

shown between low oxygen saturation (<75%) and the presence of arrhythmias. The high incidence of arrhythmias may explain the higher incidence of nocturnal angina and myocardial infarction in these patients. Myocardial ischaemia is postulated to result from a combination of increased left ventricular afterload, sympatho-adrenal stimulation and post-apnoeic tachycardia. Reduced capacity for fibrinolysis has also been reported in patients with OSA, possibly increasing their risk for coronary occlusion.

Patients with established OSA also exhibit a decrease in heart rate variability and an increase in blood pressure variability. This has been shown to be a predictor for the development of significant cardiovascular dysfunction in a number of other clinical states, e.g. myocardial infarction. The decrease in heart rate variability and the increase in blood pressure variability in otherwise healthy patients with OSA may predispose them to the future development of cardiovascular dysfunction.

OSA has also been implicated in the development of mild pulmonary hypertension. It usually does not lead to outright heart failure in the absence of daytime hypoxemia or coexistent pulmonary disease. OSA patients demonstrate transient fluctuations in pulmonary artery pressures and pulmonary wedge pressure coincident with apnoeas, which may lead to a progressive increase in pulmonary artery pressure.

Cerebrovascular disease

An odds ratio of 3.2 for the occurrence of stroke has been reported in snorers and an odds ratio of 8 has been reported for stroke in patients with witnessed apnoeas, sleepiness and obesity with snoring. Proposed mechanisms underlying the increased risk of stroke in OSA patients are multifactorial and include hypertension, reductions in cerebral blood flow, altered cerebral autoregulation, impaired endothelial function, accelerated atherogenesis, thrombosis and paradoxic embolism.

Pulmonary disorders

Two studies have demonstrated increased asthma severity, with frequent nocturnal exacerbations, in patients with OSA. It is hypothesised that this may be neurogenically mediated from upper airway vibration, apnoea-associated hypoxemia or inspiratory efforts against an occluded pharynx.

Inflammatory changes

Evidence shows that OSA can be associated with upper airway inflammation and changes in systemic indicators of inflammatory function. The cycle of hypoxia-reoxygenation that is typical in OSA may be responsible for the increase in neutrophil superoxide generation and the increased reactive oxygen species, produced from monocytes and granulocytes. It has also been reported that OSA is associated with increased circulating levels of intracellular adhesion molecule 1, monocyte chemoattractant protein 1 and interleukin 8. It is possible that this pro-inflammatory effect of OSA could account for the association of this disorder with cardiovascular disease and asthma severity.

Obesity metabolic syndrome

Obesity is the most common metabolic abnormality seen in OSA and is predominantly central in pattern. BMI, body weight and the sum of fat skin folds are good predictors for the degree of OSA. Leptin concentrations correlate with AHI and with biochemical markers of the metabolic syndrome.

Implications for airway management

In a large series where patients were undergoing surgery for OSA, the incidence of failed intubation was 5%. Routine oropharyngeal examination may not always detect the excess pharyngeal tissue found in patients with OSA, and anaesthesiologists should always have a high index of suspicion regarding difficult intubation.

The risk of airway obstruction after extubation is also increased in OSA. In a recent review of 135 patients undergoing surgery for OSA, the incidence of post-extubation obstruction was 5%. Patients who still have residual anaesthesia, neuromuscular block or opioid or sedative drugs on board are at much higher risk for post-extubation obstruction. Regional anaesthesia, with or without general anaesthesia, often provides a much safer option in that the opioid- and sedative-induced airway obstruction may be avoided. This, in fact, is the recommended method.

It is recommended that the ease of mask ventilation and intubation at the start of the case, together with the length and type of surgery and the severity of the OSA, should determine whether to leave the patient intubated for a period of postoperative ventilation until the residual effects of anaesthesia are worn off. Extubation in the reverse trendelenburg or semi-upright position minimises compression of the diaphragm by the abdominal contents.

It must be remembered that, in the postoperative setting, sleep architecture is disturbed.

During the first three days after surgery, pain is usually at its most severe, requiring opioids, and deep stage 3 and 4 non-REM and REM sleep is suppressed. During the following three days, deep REM sleep rebounds and, during this stage, natural deep sleep-induced apnoea is increased. In patients with moderate to severe OSA, a high care environment should always be utilised during the postoperative period.

"It is not unreasonable for the attending anaesthesiologist to postpone surgery until a definitive diagnosis is made if there is a high index of suspicion for severe OSA."

Diagnosis

The anaesthesiologist is often the first caregiver to make a presumptive diagnosis of OSA. The essential items on history that need to be present for a presumptive diagnosis of OSA in a patient presenting for anaesthesia are a history of snoring, snorting and apnoea during sleep, and daytime sleepiness. Other risk factors that enhance the probability of OSA are:

1. Obesity (BMI >30 kg/m^2)
2. Neck circumference >40 cm
3. Male
4. Family history
5. Age >40 years
6. Respiratory allergies and nasal congestion
7. Underlying hypertension

The gold standard for the diagnosis of OSA is the overnight polysomnogram. This involves admission to a sleep facility and includes electroencephalography, electrooculography, electromyography, oxygen saturation, oral and nasal airflow, respiratory effort, electrocardiography and leg movement recordings. At least two hours of sleep are required for proper diagnosis. Home sleep studies have been used as a screening test, but have a number of limitations in that they do not use an EEG and thus cannot distinguish sleep from wakefulness. Split-night polysomnography is also used, where the first half of the night is used for diagnostic recording and the second half for CPAP titration. This can underestimate the severity of the OSA, as the longest REM sleep occurs during the second half of the night.

Treatment

1. Lifestyle modification

Mild forms of OSA can be managed by modifying risk factors for OSA through weight reduction, positional therapy, avoiding alcohol and sedatives, and avoiding sleep deprivation. A critical amount of weight loss must occur before a significant reduction in AHI is seen. In the majority of cases, weight loss alone does not cure OSA.

2. CPAP

Nasal CPAP therapy for OSA was first reported in 1981 and is now regarded as the standard of care for patients with OSA. Air is provided under pressure by way of a nasal or face mask, which acts as a pneumatic splint in the pharynx, preventing collapse of the pharyngeal airway. CPAP therapy can be used for all categories of OSA and represents the first line of treatment for moderate to severe OSA.

Positive airway pressure can be provided as continuous, bi-level or auto-titrating. In patients who are unable to tolerate exhaling against high pressure, bi-level positive airway pressure, which allows for independent adjustment of inspiratory and expiratory pressures, may be used. In the last decade, auto-titrating CPAP has also been introduced that continuously adjusts pressures to meet the patient's variable needs, thereby reducing the overall mean airway pressure. Loube *et al.* recommend CPAP therapy for all patients with an RDI of more than five per hour associated with daytime sleepiness, impaired cognition, mood disorders and insomnia, documented cardiovascular disease or stroke. Compliance rates vary between 65% and 90%. Compliance rates are higher in the more severe OSA patients, in whom the relief of symptoms is perceived to be greater.

Common side effects of CPAP are rhinorea, nasal congestion and dryness, mask discomfort, conjunctivitis from air leaks, skin abrasions, claustrophobia, irritation from device noise, difficulty exhaling, aerophagy, chest discomfort and bed-partner intolerance. Nasal congestion and mask intolerance are the most common complaints. Humidified air and nasal steroids are used to alleviate these problems.

Effective CPAP therapy reduces the number of nocturnal respiratory disturbances and improves nocturnal oxygenation, sleep architecture, daytime sleepiness, neurocognitive performance, driving performance and perceived health status. Cardiovascular co-morbidities such as hypertension, arrhythmias, nocturnal ischaemia and left ventricular function may also improve with CPAP therapy.

3. Oral devices

Oral devices work by mechanically displacing the tongue and jaw forward, creating more space in the posterior pharynx. These devices are not suitable for patients with severe OSA or those where the primary obstruction is in the nose.

4. Surgical treatment

Surgical therapy for OSA is often directed towards site-specific obstruction. Surgical techniques involve the excision of soft tissues deemed to be causing the obstruction, such as an uvulopalato-pharyngoplasty (UPPP), with or without nasal procedures, tonsillectomy and glossoplasties. UPPP has a surgical response rate, defined as a reduction of more than 50% in AHI or RDI and a RDI below 20, of 40 to 65%. Surgical treatments involving primary skeletal mobilisation, such as maxillomandibular advancement, and mandibular osteotomy with genioglossis advancement are also done for patients with failed medical therapy, severe OSA or in patients with discrete craniofacial abnormalities.

In extreme cases, where all else has failed, tracheostomy can be considered as a final option, especially in the morbidly obese patient with severe OSA who has significant nocturnal oxygen desaturation and/or associated cardiovascular disease.

The Stanford surgical approach consists of a two-phased approach to the direct surgical treatment of suspected regions of obstruction. Patients are first evaluated with lateral cephalometry and fibre optic endoscopy. Phase one encompasses nasal reconstruction, UPPP or uvulopalatal flap, and a limited mandibular osteotomy with genioglossis advancement. Phase two involves maxillo-

mandibular advancement, to treat refractory hypo-pharyngeal obstruction, by advancing the mandible at least 10 cm. The overall success rate with phase one surgery may be as high as 81%. In a study of 175 patients who underwent maxillomandibular advancement, published by Li in 2003, the mean age of the patients was 43.5 and the cure rate was 97%. The mean hospital stay was 2.4 days and the mean postoperative RDI was 7.2, compared with the mean preoperative RDI of 72.3. A maxillary expansion device in conjunction with limited ostoetomies has been used with success in young patients who are already undergoing orthodontic treatment and in whom life-long nasal CPAP seems a limited option.

Patients receiving surgery for OSA should be closely monitored postoperatively in an ICU to detect complications early.

Anaesthetic implications

All central depressant drugs decrease the activity of the upper airway muscular dilators, which, in obese patients, leads to early collapse around a pharynx that is abnormal from excessive fat deposition. Commonly used anaesthetic drugs that are shown to cause pharyngeal collapse are propofol, thiopental, narcotics, benzodiazepines, small doses of neuromuscular blockers and even nitrous oxide. Opioids are particularly dangerous, as they may also cause a poor ventilatory response to the ensuing hypoxaemia and hypercarbia.

It is also important to understand that normal sleep architecture is disturbed in the postoperative setting. During the first three days after surgery, pain scores are at their peak, and deep stage 3 and REM sleep are often suppressed. Opioid requirements are increased at this stage and life-threatening apnoea may occur during drug-induced sleep. During the following three days, deep REM sleep rebounds and, during this time, life-threatening natural deep sleep apnoea may occur. The risk of prolonged apnoea during sleep is increased for approximately **one week** in the postoperative OSA patient.

The dangers pertaining to difficult airway management have already been alluded to. It is important to stress that the extubation of these patients can be more dangerous to the patient than intubation. Anaesthesiologists may not be as vigilant as they should be, and patients are often out of their sight in the recovery room setting. Recovery room staff are often poorly trained and recognise obstruction only when the patient has desaturated to dangerous levels.

A large retrospective review of 135 patients undergoing surgery for OSA showed an incidence of life-threatening post-extubation obstruction of 5%. Patients who are extubated in theatre should remain under the constant vigilance of an anaesthesiologist until handed over to an appropriate high-care facility. It is often prudent to leave the patient intubated for a few hours in intensive care until a full recovery from surgery has taken place. The use of alternative forms of analgesia other than opioids should be entertained to avoid the risk of opioid-induced sleep apnoea.

If a patient is using a CPAP system prior to surgery, this should be applied in high care. Benumoff suggests that CPAP should not be applied too early in the immediate post-extubation period, as it may hamper the initial observations and recovery of the patient. He suggests that it may interfere with suctioning and the management of PONV, impair the monitoring of facial and mucous membrane colour and the level of consciousness, and may impair communication by the patient. The requirements (settings) may also not be the same in the immediate postoperative setting, where the patient has mainly drug-induced sleep apnoea.

As the majority of patients with OSA are obese, the anaesthetic implications of anaesthetising obese patients also need to be taken into consideration. These will not be dealt with in this review.

Conclusion

Anaesthesiologists need to have a high index of suspicion in identifying the undiagnosed patient with OSA who presents for surgery that may be totally unrelated to OSA. Operating on these patients often needs to be postponed until a diagnosis is made and appropriate investigations have been carried out. In addition, arrangements need to be made for adequate intra-operative and postoperative care. The diagnosed OSA patient presents numerous challenges to the anaesthesiologist and intensivist, as the co-morbidities associated with severe OSA may impact not only on the conduct of the anaesthetic and postoperative management, but also influence the perioperative morbidity and mortality of these patients significantly. SAJAA

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