Obstructive Sleep Apnoea: A Clinical Review

RK Gupta*, A Chandra**, AK Verma***, S Kumar*

Abstract

Obstructive sleep apnoea (OSA) is a common medical disorder associated with considerable morbidity and is being recognised and diagnosed with increasing frequency. Patients with OSA are frequently overweight and usually present with longstanding history of snoring and excessive daytime sleepiness along with accompanying obesity. The diagnosis is established with Polysomnography (PSG), although the decision as to who should be sent to a sleep laboratory must be individualised, especially for those patients whose main complaint is snoring. The most important factor in the pathogenesis of OSA is a narrow and floppy pharyngeal airway. Of the several treatment modalities which are available presently, the most successful is the application of continuous positive airway pressure (CPAP) during sleep.

Introduction

Charles Dickens was the person who provided the first comprehensive description of what, about 130 years later, came to be known as obstructive sleep apnoea (OSA) in Charles Dickens’ series, Posthumous Papers of the Pickwick Club, first published in 1865 which gave strength to a poorly understood relationship between obesity and Pickwickian syndrome. In 1918, Sir William Osler described the constellation of the clinical features of the obstructive sleep apnoea (OSA) syndrome. In 1918, Sir William Osler described relationship between obesity and Pickwickian syndrome. It was recognised in the early 1970s, that these symptoms may reflect disturbed breathing during sleep. Gastaut and associates in 1965 showed that cessation of respiration was due to the obstruction of upper airway and Obstructive Sleep Apnoea was recognised. This observation opened an entirely new area of respiratory medicine, namely sleep-related breathing disorders (SRBD). Following discussion will define the Obstructive Sleep Apnoea (OSA) syndrome, along with the diagnostic investigations, present a set of guidelines to be followed in deciding who should be referred to a sleep laboratory, review some of the current concepts of the pathogenesis of airway occlusion during sleep, and briefly describe the current treatment modalities available in the management of OSA.

Anatomic Factors Affecting the Patency of Upper Airway During Sleep

In normal sleep there is an orderly progression of stages of sleep, starting with light sleep (stages I and II), progressing to deeper sleep (stages III and IV), and ending up with rapid eye movement (REM) sleep. During non-REM sleep (stages I-IV) breathing is slow and regular, while during REM sleep the breathing pattern is erratic, with rapid, shallow respirations. Normally, with each inspiration the pressure in the upper airway increases, and the pressure exerted by the tissues surrounding the site of collapse. In patients with OSA, pharynx is narrower and more floppy than normal subjects due to fat deposition in the parapharyngeal fat pads, in the tongue and under the mandible. Imaging studies have also demonstrated that the total volume of fat surrounding the airway is greater in apnoeic than in BMI-matched normal individuals, suggesting that fat deposition in neck has an important role to play in the pathogenesis of OSA. This relative hypotonia is particularly pronounced in REM sleep, where most of the disordered breathing events occurs. Other factors that have important bearing on upper airway narrowing include genetics, gender, pharyngeal dilators muscle dysfunction, soft tissue oedema (secondary to snoring/ apnoea related trauma), airway tissue properties (surface tension), vascular perfusion and posture of individual (supine versus lateral).

Definitions

Apnoeas are defined as complete cessation of oronasal flow lasting more than 10 seconds. During these episodes the patient exhibits a paradoxical movement of the chest wall: that is, in drawing of the chest wall on inspiration, as well as reduction in oxygen saturation. In addition to apnoeas, there may be episodes characterized by a marked reduction (up to 50%) in tidal volume, without complete cessation of respiratory flow. Such events are termed ‘hypopnoea’. The total number of apnoeas and hypopnoeas per hour of sleep is called the ‘apnoea / hypopnoea index’ (AHI). A respiratory effort related arousal event (RERA) is a sequence of breaths characterised by increasing effort leading to an arousal from sleep but at the same time does not fulfil criteria for apnoea or hypopnoea. Respiratory Distress Index (RDI) is a parameter that includes apnoea, hypopnoea along with RERAs. Normal individuals generally have AHI of less than 5.

Mild Sleep Apnoea, AHI : 5-15 events per hour
Moderate Sleep Apnoea, AHI : 15-30 event per hour
Severe Sleep Apnoea, AHI : greater than 30 events per hour
Upper Airway Resistance Syndrome (UARS) was first described by Guilleminault in 1993. UARS is characterised by abnormal respiratory effort, nasal airflow limitation, minimal or no oxygen desaturation (maintained at >90%) and frequent sleep arousals in the absence of obstructive apnoeas. UARS is a part of spectrum of SRBD beginning with snoring and ending with apnoea. In contrast to sleep apnoeas, clinical features of UARS include headache, insomnia, irritable bowel syndrome, attention deficit disorders, depression and light headedness.

The definitions of a normal number of disordered breathing events during sleep are still relatively arbitrary, however, because of the lack of large-scale studies of respiration in normal asymptomatic subjects. Moreover any definition must take into account the age of the individual, since apnoeas are more common in the elderly than in the younger population.

Three different types of apnoea can be distinguished. Firstly, central sleep apnoea in which cessation of breathing is caused by a disturbance in ventilatory control at the level of the central nervous system; and there is no effort to breathe when asleep. Secondly, obstructive sleep apnoea in which the respiratory control is normal, but there is an obstruction, usually at the level of the pharynx, which physically interrupts the flow of air although vigorous effort to breathe on the part of patient is present. Lastly, mixed sleep apnoea which is a combination of both components. Obstructive sleep apnoea is by far the most common disorder. A typical patient with obstructive sleep apnoea syndrome will have 30 or more apnoeas per hour of sleep, each lasting for not less than 10 seconds; along with apnoea there will be a concurrent drop in oxygen saturation, sometimes to dramatically low levels.

Epidemiological studies demonstrate the presence of OSA to be two to three times more in men than women. Post-menopausal women are at higher risk for OSA than pre-menopausal women. Gender differences in the prevalence of OSA may be related to the body fat distribution. Men have a more central body fat distribution, including the neck, thereby increasing the risk for narrowing and closure of upper airway.

**Diagnostic Criterion**

Individuals must fulfil criterion A or B, plus criterion C to be diagnosed with OSAS:

A. Excessive Daytime sleepiness that is not explained by other factors;
B. Two or more of the following that are not explained by other factors:
   - Choking or gasping during sleep;
   - Recurrent awakenings from sleep;
   - Un-refreshing sleep;
   - Daytime fatigue;
   - Impaired concentration;
C. Overnight monitoring demonstrate 5 to 10 or more obstructive breathing events per hour during sleep or greater than 30 events per 6 hours of sleep. These events may include any combination of obstructive apnoea, hypopnoea or respiratory effort related arousals (RERAs).

**Clinical Features**

**Symptoms**

Snoring: Snoring is the cardinal complaint of the patients with sleep apnoea. There is a close association between snoring and sleep apnoea. Nearly all patients with OSA are heavy snorers and have been so for many years. This close relationship between snoring and sleep apnoea points to the importance of enquiring about snoring during the medical interview. One difficulty in trying to elicit a history of snoring is that the patient may be unaware that he or she is a heavy snorer. Bed partners are the crucial informants of nocturnal events. Usually, however, the patient is well aware of the fact that he or she is a heavy snorer because of severe social problems caused by snoring. Bed partners or family members of patients with OSA typically describe a sequence of events beginning with the onset of quiet sleep, then transition to progressively louder snoring, followed by a period of cessation of snoring when the patient becomes restless, makes gasping movements, and looks as if he/she is struggling to breathe. The silent period is finally terminated by a characteristic loud snort, and the same sequence of events starts again. Patients with OSA go through hundreds of such sequences over the course of one night.

Excessive daytime sleepiness: Excessive daytime sleepiness is a chief clinical consequence among patient with OSA. When eliciting the history of this symptom the physician should remember that some daytime sleepiness, particularly post-prandial sleepiness in the afternoon, is common. However, overt sleep seldom occurs. Patients with OSA fall asleep easily under the most inappropriate circumstances: for example, while talking, eating, driving short distances, or engaging in sexual foreplay and intercourse. In general, daytime sleepiness directly relates to the severity of sleep apnoea. A standard instrument, Epworth Sleepiness Scale, is a useful tool to assess the degree of self-rated sleepiness. A value above 10 is considered abnormal.

Morning symptoms: Morning tiredness, fatigue, and lack of refreshing sleep are other associated symptoms. Patients with OSA may complain that when they wakeup in the morning, they feel the same way that they did when they went to bed the night before. Rarely, they may complain of morning headache or nausea.

Restless sleep: Agitation, restlessness, and abnormal body movements are common during episodes of obstructive apnoea. Patients themselves may note crumpled and disturbed bed-sheets, pillows, or comforters in the morning or their bed partners may complain about being accidentally hit during the night.

Other symptoms: Other, progressively less common, symptoms include intellectual deterioration, depression, impotence, sleep walking, sexual dysfunction and enuresis.

**Signs**

The most common physical sign of OSA, present in at least 70% of patients with this condition, is excess weight, defined as weighing more than 120% of the predicted normal, or having a body-mass index greater than 25 kg/m². Examination of the nose and throat is usually normal. Neck circumference greater than 40 cm predicts OSA with a sensitivity of 61% and specificity of 93%, regardless of gender. Overt anatomical abnormalities which cause narrowing of the nasal or pharyngeal airway, such as enlarged adenoids, deviated nasal septum, nasal valve obstruction, tonsilar hypertrophy, macrognathia, and retro- or micrognathia are rare, but should be looked for during physical examination. More commonly, examination of the throat results in a subjective impression that the patient has a “small mouth”; occasionally, the uvula is bulky, resting on the base of the tongue even during phonation. Systemic hypertension may
sometimes be present and, in fact, when seen in a relatively young person who snores and is obese, should initiate a search for sleep apnoea. OSA has been described in association with other systemic diseases such as hypothyroidism, acromegaly, diaphragmatic and vocal cord paralysis, and Shy-Drager syndrome, as well as in some patients with congestive cardiac failure or those undergoing haemodialysis.

**Diagnosis**

The main diagnostic test for OSA is an overnight sleep study carried out in a sleep laboratory. The usual parameters recorded continuously throughout the duration of sleep are:

1. Electroencephalogram (EEG) to monitor sleep states,
2. Electroocculogram (EOG) for monitoring eye movements,
3. Electromyogram (EMG) for muscle tone,
4. Respiratory airflow by nasal probes,
5. Respiratory effort by bands placed around chest and abdomen,
6. Arterial oxygen saturation, and
7. EMG of Anterior tibialis muscle to monitor for the presence of periodic leg movements.

In lab Polysomnography represents the gold standard for diagnosing sleep apnoea.2 However, emphasis should not be laid on elevated AHI in diagnosing OSA, as patients with similar AHI may have dramatically different sleep and outcomes. Furthermore, it is not the AHI itself but also its outcomes (hypertension, myocardial infarction, stroke, cardiac arrhythmias, excessive daytime sleepiness) that are of utmost importance.

Realizing that upper airway abnormalities are common in patients with OSA, measurements of upper airway structure and function may be useful. These include various imaging techniques (e.g., CT scanning of the pharynx and larynx, and radiographic views of the laryngeal and pharyngeal airway), acoustic reflection measurements of the pharyngeal area and distensibility, nasal airflow resistance as a reflection of nasal patency, and maximum expiratory/inspiratory flow-volume loops to detect upper airway obstruction. All of these measurements suffer from the fact that they can only be performed on patients in the awake state. Furthermore, most of them (except for the acoustic reflection technique) provide a static, rather than dynamic picture of the upper airway. Cinefluoroscopy during sleep has been done in several centres, but it entails a significant radiation hazard to the patient. Other useful investigations dictated by clinical considerations include thyroid-function tests, growth-hormone determination, renal function tests, haemoglobin, awake arterial blood gases and carbon dioxide and hypoxic responses to assess the control of breathing.

**Treatment**

The treatment of OSA may be divided into five modalities:

- Avoidance of factors which aggravate or precipitate apnoea;
- Weight loss;
- Medications;
- Nocturnal continuous positive airway pressure (CPAP); and
- Surgery.

Sedatives, tranquilizers, antihistamines, and alcohol have been shown to increase the number of disordered breathing episodes during sleep. Alcohol may not only aggravate the severity of OSA, but may also convert a non-snorers into a snorer and a non-apnoeic snorer into an apnoeic snorer. Consequently, patients with OSA should be advised to discontinue the use of alcohol and of any tranquilizers or sleeping pills.

It has been reported that 60%-70% of patients with OSA are obese. Obesity predisposes to the development of OSA by causing a narrowing of the pharynx and aggravates the hypoxemia of OSA by reducing functional residual capacity, thus creating areas of ventilation/perfusion mismatch. Weight loss of even 5 kg-10 kg is beneficial. Although the mechanism of improvement is not fully understood, it is probably multifactorial, consisting of improvement in pharyngeal structure and function, neuromuscular control, and an increase in functional residual capacity. The extent of weight loss and the degree of improvement are not always directly related, although it has been shown that a 1% change in weight is associated with a 3% change in AHI. Bariatric surgery should be considered in all patients with BMI 35 mg/kg2 or more.4

A number of medications, such as nasal decongestants, respiratory stimulants, and tricyclic antidepressants have been used in treating patients with OSA. However, the efficacy of this therapy has not yet been established. One agent which has been tested in a small, double-blind, controlled trial is protryptyline. It works by suppressing the REM sleep, where most episodes of severe hypoxemia occur. Recent animal work suggests that this drug may also increase the tone of the upper airway muscles, thus stabilizing the airflow and making it less susceptible to collapse. The anticholinergic side effects of protryptyline, such as dry eyes, dry mouth, difficulty in initiating urination, and difficulty with ejaculation are common with the dosages used (10-30 mg) and limit the usefulness of this medication. Stimulants like Amphetamines, Methylphenidate, and Modafinil increases alertness. They are most often used in the treatment of Excessive Daytime Sleepiness (EDS) seen in patients with OSA. Modafinil, like other CNS stimulants, increases the release of monoamines, specifically the catecholamines, norepinephrine and dopamine from the synaptic terminals. However, Modafinil also elevates the hypothalamic histamine levels which make it a “wakefulness promoting agent” rather than a classic amphetamine-like stimulant. Several other drugs like acetazolamide, medroxyprogesterone, theophylline, doxapram and almitrine are under investigation.

The most important advance in the medical treatment of OSA occurred with the introduction of continuous positive airway pressure (CPAP)9 which was first described by Sullivan. CPAP can be applied through nasal mask, nasal inserts, or a full face mask (in patients who breathe through their mouth during sleep).3 CPAP has the advantage of being non-invasive and has been shown to decrease the number of apnoeic and hypoxic episodes during sleep. The equipment is now commercially available and consists of a blower and a flexible mask which fits tightly over the nose, but not the mouth, producing only minimal discomfort to the patient. The blower is able to deliver room air at a positive pressure to the patient’s nose and oropharynx. Positive pressure provides a “pneumatic splint” which keeps the pharynx open, thus reversing OSA.23 In addition, it may increase functional residual capacity (FRC), leading to improvement in hypoxemia. CPAP is 100% effective not only in abolishing obstructive apnoeas, but also, somewhat unexpectedly, the central ones as well.5,12 The usual pressure required to reverse the apnoeas ranges between 5 cm and 15 cm H2O. CPAP treatment has no major side-effects other than occasional irritation of the
conjunctiva, resulting from air leaks around the mask, and some irritation of the nasal mucosa, resulting from the flow of dry air.24 When the system is properly adjusted and custom-fitted, the patients do not find it uncomfortable, and the constantly improving blower design keeps the noise to a minimum.

Surgical treatment of obstructive sleep apnoea is directed primarily toward the correction of definite anatomical deformities which clearly obstruct the upper airway, such as deviated nasal septum, obstruction of the nasal valve, or enlarged adenoids or tonsils.13 Thus, the surgeries that can be offered to patients with OSA include nasal surgeries (septoplasty, sinus surgery and others), Tonsillectomy with/without adenoidectomy, uvulopalatopharyngoplasty (UPPP), laser assisted uvuloplasty (LAUP), radiofrequency volumetric tissue reduction, sliding genioplasty and maxillo-mandibular advancement osteotomy. In patients with idiopathic OSA (i.e., without obvious anatomical deformities) uvulopalatopharyngoplasty (UPPP) has recently become popular. UPPP was introduced by Fujita and colleagues in 1981 in US for the first time. This operation involves tonsillectomy, uvulectomy, partial resection of the soft palate, and removal of redundant pharyngeal mucosa. The overall aim is to widen the oropharyngeal aperture. Successful treatment is reported only in 40 to 50% of patients. Clearly, only those patients, in whom the site of airway obstruction is relatively high, behind the palate, would have the highest chance of benefiting from UPPP. Unless rigorous pre-operative measurements identifying the site of airway obstruction are carried out, the success of the UPPP seems to be a chance occurrence.13

Conclusion

The field of sleep medicine is a relatively new arena that has undergone numerous changes in few recent years. There have been a number of significant advances as far as the diagnosis, consequences and management of sleep apnoea is concerned. Increasing awareness and medical attention to the sleep related breathing disorders have resulted in enormous increase in the number of referrals to sleep labs over a decade or so. Despite of increasingly better ways and infrastructure to diagnose OSA currently, as it comes to the management part, we are still not having a treatment modality that can assure compliance along with cure. It is our hope that continuous high quality research and practice will engender further understanding and treatment of patients with OSA.

References