Chapter

129

Diagnosis and Treatment of Obstructive Sleep Apnea

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INTRODUCTION

Even though obstructive sleep apnea (OSA) was recognized as a clinical entity nearly 35 years ago[1,2], awareness regarding this condition outside the domain of sleep medicine was slow to evolve. Increasing awareness regarding sleep disordered breathing and wider availability of sleep laboratories have resulted in a spurt in the research in sleep disordered breathing from several parts of the world including India. Still, OSA remains largely unrecognised and undiagnosed[2]. The reasons for failure to recognise the syndrome include lack of training in sleep medicine, a general lack of awareness, and the non-availability and cost involved in the diagnostic work-up of a patient with suspected OSA. Since OSA is common, it has considerable effects upon patients and their families, it increases the risk of other diseases, and can be effectively treated. It is important to improve the way these patients are diagnosed. In this review, we have attempted to summarize the current understanding regarding the pathogenesis, clinical presentation, diagnosis, and therapeutic options for patients with OSA.

DEFINITION

The *obstructive sleep apnea syndrome* (OSAS) is defined as sleep disordered breathing associated with daytime symptoms, most often excessive sleepiness[3]. According to the consensus statement of the American Academy of Sleep Medicine Task Force[3,4], an *apnea* involves upper-airway collapse, and is defined as nearly complete cessation of airflow associated with oxygen desaturation or an arousal from sleep. *Hypopnea*, which is associated with partial collapse of the upper airway is considered to be existing on a pathologic continuum with apnea. The condition is usually associated with loud snoring and hypoxemia, and apneas are typically terminated by brief arousals, which result in marked sleep fragmentation and diminished slow wave sleep (SWS) and rapid eye movement (REM) sleep. Patients with OSA are usually unaware of this sleep disruption, but the changes in sleep architecture contribute significantly to the prominent symptom of chronic daytime sleepiness found in these patients[4].

Conventionally, the apnea–hypopnea index (AHI) which measures the frequency of reductions in airflow associated with upper-airway collapse or narrowing that occurs with the state change from wakefulness to sleep has been used to characterize OSA. However, though AHI measures the frequency of disordered breathing events, it does not quantify other processes that may be operative in the pathophysiology of OSA[4,5].

However, upper airway narrowing with sleep onset is a normal phenomenon and several factors such as obesity, craniofacial abnormalities among others may accentuate it. These accentuating phenomena are not ''all or none'' in nature, and thus upper airway narrowing during sleep is a continuously variable phenomenon within a population and, indeed, to some extent across nights within an individual[4,5].

EPIDEMIOLOGY

In most of the studies, AHI of 5 or more determined by overnight PSG in a patient with daytime sleepiness, disturbed or unrefreshed sleep has been considered as the diagnostic criteria for OSAS[6,7]. Prevalence of OSA in various studies published from abroad and India[8,9] are listed in Table 1.

Table 1: Prevalence of OSA

Western data
0.3% to 5% of the population is affected
2% to 4% of middle-aged men and 1% to 2% of middle-aged women are affected
1 of 5 white adults with an average body mass index (BMI) of 25 to 28 kg/m^2 has mild OSA (AHI ≥5); 1 of 15 has moderately severe disease (AHI ≥15).
Data from India
Mumbai (hospital-based prevalence study)
In age group 35-65 years, OSA: 19.5%; OSAS: 7.5%
New Delhi (Community-based prevalence study)
OSA: 13.7%; OSAS 3.6%

OSA = obstructive sleep apnea
OSAS = obstructive sleep apnea syndrome
AHI = Apnea-hypopnea index

Table 2: Risk factors for obstructive sleep apnea

Demographic characteristics
Older age
Male sex
Familial aggregation
Risk factors that are linked by strong published evidence to OSA
Body habitus
Obesity
Central body fat distribution
Neck circumference
Anatomical abnormalities of the craniofacial region and upper airway
Other suspected (potential) risk factors
Genetic predisposition
Smoking status
Menopause
Alcohol use before sleeping
Night-time nasal congestion

Risk Factors

Review of published literature suggests that several risk factors are associated with the development of OSA[4,6,7,9-13]. These are listed in Table 2.

PATHOGENESIS: NEWER INSIGHTS

Recurrent occurrence of upper airway occlusion during sleep produces OSA[14]. This is thought to be the result of a variety of physiological characteristics[15]. Patients with OSA have an anatomically small upper airway with augmented pharyngeal dilator muscle activation maintaining airway patency while awake, but not during sleep. Variation in the individual phenotypic characteristics in the upper airway anatomy; the ability of upper airway dilator muscles to respond to rising intrapharyngeal negative pressure and increasing carbon dioxide during sleep; arousal threshold in response to respiratory stimulation, and ventilatory control instability are the factors that are thought to determine the development and severity of OSA in the individual patient[14,15].

Molecular Basis of Somnogenesis

Accumulating evidence also points to the bi-directional, feed forward, pernicious association between sleep apnea, sleepiness, inflammation, and insulin resistance—all promoting atherosclerosis and cardiovascular disease[14,15]. Data are available linking circulating nuclear factor - κB (NF-κB)–dependent genes, tumor necrosis factor - α (TNF-α), and interleukin-8 (IL-8) to OSA[16,17]. Evidence is available suggesting that the pro-inflammatory cytokine TNF-α is somnogenic and is independently associated with daytime sleepiness[15-17]. Patients with OSA have elevated circulating levels of TNF-a and it has also been demonstrated that OSA is associated with the TNF-α (-308A) gene polymorphism, which results in increased TNF-α production[18]. In a recently published study[17], it was reported that, on multivariate analysis, TNF-α was independently associated with the desaturation index ($p<0.001$), Epworth Sleepiness Score ($p=0.005$); and CPAP therapy lowered TNF-α levels ($p=0.004$).

CLINICAL MANIFESTATIONS

Historical Perspective

References to OSA have been found in the Hippocratic Corpus (V-IV century BC). The Roman author Pliny the Younger (79 AD) reported the death of a man with obesity, sleepiness, and snoring. The account of "Fat Joe", the famous character of Charles Dickens's Pickwick Papers, an obese person who fell asleep during daytime while performing even extremely simple tasks is a lucid description of a person affected by OSA. Distinguished personalities such as Emperor Napoleon Bonaparte, Queen Victoria, and President Franklin D. Roosevelt were victims of this malady[19].

Since the pathophysiological consequences of OSA can virtually affect almost every organ system in the body, it is not surprising that patients with OSA present to several specialists and clinicians. Patients with OSA present with daytime and night-time symptoms

Table 3: Clinical manifestations in patients with obstructive sleep apnea

Daytime symptoms	Nocturnal symptoms
Excessive daytime sleepiness	Snoring
Cognitive and memory impairment, intellectual deficiency	Nocturnal polyuria
Irritability, changes in personality	Choking
Morning headache	Gasping
Dry mouth	Profuse body sweating
Sexual dysfunction	Restless sleep
Gastroesophageal reflux	

(Table 3)[4,7,13,20]. Bed partners of patients with OSA often provide useful information regarding the nocturnal symptoms. Snoring is the most frequently reported nocturnal symptom. It is usually loud and intermittent with periods of silence (apnea) despite the ventilatory efforts of the chest and abdomen. Prevalence of OSA has been reported to be 35 to 64% in habitual snorers[4,6,7,9]. Nocturnal polyuria is frequent—may be the result of increased atrial natriuretic peptide secretion due to increased stretch on the right atrial wall due to swings in negative intrathoracic pressure.

Excessive daytime sleepiness, the principal symptom in patients with OSA, appears to result from sleep fragmentation due to recurrent central nervous system arousals in response to disordered breathing events. Morning headaches may reflect hypercapnia and the consequences of obesity hyperventilation syndrome. Altered levels of sexual hormones and pudendal neuropathy may result in sexual dysfunction. High negative intrathoracic pressures during apnea, and effect of hypoxia on the gastro-esophageal sphincter may result in increased occurrence of gastro-esophageal reflux.

Driving is considered to be a complex task involving distinct cognitive, perceptual, motor, and decision making skills. Driving not only involves ensuring speed and lane control, but also monitoring the speed. To safely do this requires careful attention and alertness which can be problematic for patients with OSA. It is not surprising therefore that OSA patients have an increased rate of automobile accidents[4,21].

Consequences of OSA

The tremendous impact of the cardiovascular and neurocognitive pathophysiological consequences of OSA is increasingly being recognized. The consequences of OSA are being increasingly understood and are listed in Table 4, and recent evidence regarding some of them are discussed hereinafter.

Table 4: Consequences/associations of obstructive sleep apnea

Cardiovascular
Hypertension
Left ventricular hypertrophy
Nocturnal angina
Myocardial infarction
Arrhythmias, particularly bradyarrhythmias
Heart failure
Cor-pulmonale
Increased pulmonary artery pressure
Sudden cardiac death
Endocrine
Hypothyroidism
Acromegaly
Diabetes mellitus
Neurobehavioral and cognitive
Refractory epilepsy
Stroke
Headache on waking-up in the morning
Depression
Anxiety
Behavioral problems
Acute delirium
Otorhinolaryngology
Snoring, sore throat
Hoarse voice
Urology
Nocturia
Impotence
Erectile dysfunction
Miscellaneous
Automobile accidents
Gastro-esophageal reflux disease
Polycythemia
Difficult intubation, sensitivity to opioid analgesia and sedation, witnessed apneas during recovery
Nocturnal dyspnea, Respiratory failure

Hypertension and Cardiovascular Disease

The strong association between OSA and hypertension, heart failure and cardiac arrhythmias is well known[1,22-25]. Recently, the term ''syndrome Z'' (hypertension, central obesity, insulin resistance, hyperlipidaemia, obstructive sleep apnea) has been coined to highlight the potential interaction between OSA and various risk factors for cardiovascular disease[25]. In addition, evidence is also available indicating that untreated OSA is associated with an additional

independent cardiovascular risk which is reduced by effective treatment of OSA[3,6,25]. In a recently published study[26], multivariate analysis revealed that untreated severe OSA significantly increased the risk of fatal (OR 2.87, 95% CI 1.17-7.51) and non-fatal (OR 3.17, 95% CI 1.12-7.51) cardiovascular events compared with healthy subjects. It was also observed that CPAP treatment reduced this risk.

Atherosclerosis

In patients with OSA, acceleration of atherosclerosis may result due to episodic hypoxemia, chronic sympathetic hyperactivity, elevated levels of fibrinogen and homocysteine, pulmonary hypertension and consequent risk for right heart hypertrophy and heart failure; increased risk of plaque ruptures and subsequent cardiovascular or cerebrovascular events[5,6,14].

Sudden Cardiac Death

Patients with OSA are known to have severe perturbations of autonomic, hemodynamic, humoral, and vascular regulation during sleep, and OSA is being recognized as an important treatable cause of sudden death. In the general population, the risk of sudden death from cardiac causes is significantly greater during the morning hours after waking (i.e. from 6 a.m. to noon), compared with the period during sleep from midnight to 6 a.m. In patients with OSA, the reverse was observed, and the relative risk of sudden death from cardiac causes from midnight to 6 a.m. was 2.57 (95% CI, 1.87 to 3.52) in a study carried out in OSA subjects from Minnesota[27].

Neurocognitive Dysfunction

Neurocognitive dysfunction is an important consequence of OSA. Magnetic resonance spectroscopy (MRS) has been applied for detecting abnormalities and their significance and correction with CPAP intervention[28].

Erectile Dysfunction

Erectile dysfunction, a common problem in patients with OSA has been shown to improve considerably over a short-term with CPAP treatment[29].

Sleep Deprivation

The consequences of sleep deprivation are a subject of investigation recently. Sleep deprivation, especially in working adolescents and young resident doctors is considered to be a hidden health hazard[30]. Sleep deprivation is also believed to worsen OSA. In a study published from Australia[31], subjects with OSA showed a lower minimum oxygen saturation following sleep deprivation. The authors reported that, while acute sleep deprivation did not worsen most OSA parameters as measured by PSG, a lower minimum oxygen saturation after sleep deprivation may be important in patients with mild OSA and significant cardiorespiratory disease. These issues merit further study.

DIAGNOSIS

The diagnosis of OSA is based on the characteristic clinical presentation together with objective demonstration of sleep disordered breathing.

Clinical Evaluation

A detailed history and thorough clinical examination is the initial step in the evaluation of a patient with suspected OSA. It should be remembered, however, that none of the common presenting clinical features alone has sufficient discriminatory value to make an accurate diagnosis, and combining constellations of symptoms can improve diagnostic accuracy[32]. Loud snoring and witnessed apneas have been reported to identify OSA with a sensitivity of 78% and a specificity of 67%[32]. Oropharyngeal and cranial anatomical abnormalities such as tonsillar hypertrophy, enlargement of soft palate, or tongue, retrognathia or micrognathia, should all alert the clinician towards the possibility of OSA. Current evidence does not mandate the use of routine upper airway imaging for the diagnosis of OSA. While obesity is an important risk factor for OSA, nearly half the patients with OSA may not be obese. Neck circumference (>43 cm in males and >41 cm in females) reflecting the upper body obesity has been associated with a high risk of OSA[4,7,32].

Assessment of Daytime Somnolence

Daytime somnolence has been studied using instrumental and non-instrumental tests. Commonly used instruments for the evaluation of daytime somnolence include multiple sleep latency test (MSLT), maintenance of wakefulness test (MWT), driving simulators, among others[33-37]. MSLT consists of a series of sleep recordings under standardized conditions that measure the latency of sleep onset and occurrence of REM sleep. In MWT, a series of sleep recordings are obtained under standard conditions while the subject attempts to stay awake in a quiet room. Non-instrumental test questionnaires such as the Stanford Sleepiness Scale (SSS)[36] and the Epworth Sleepiness Scale (ESS)[33],

administration of modified Berlin questionnaire prior to PSG study have been found to be useful in identifying high-risk subjects and in avoiding unnecessary PSG studies especially in resource-limited settings[38].

Prediction Models

Several prediction models have been developed to accurately predict OSA using self-reported symptoms combined with demographic and anthropometric data[11,39]. One such model has been developed and validated in overtly asymptomatic obese subjects from India[11]. In another study conducted by the authors' group[39], a diagnostic model for prediction of OSA was derived and validated in subjects presenting with non-sleep-related complaints at All India Institute of Medical Sciences (AIIMS), New Delhi. In this study, 102 subjects (group I, age range 31-70 years) presenting to the hospital with non-sleep-related complaints, none of whom had any significant co-morbid illness such as respiratory or congestive cardiac failure, underwent detailed evaluation. Using multivariate logistic regression analysis, a diagnostic model for prediction of OSA was derived. Subsequently, using similar selection criteria, another 104 subjects (group II, age range 32-68 years) were included for validation of the newly derived diagnostic model. BMI (kg/m^2) [OR (95% CI), 1.14(1.1-1.2)], male gender 5.0 (1.4-27.1), relative-reported snoring index (SI) 2.8 (1.7-5.0), and choking index (ChI) 8.1 (1.4-46.5) were found to be significant, independent predictors of OSA. The diagnostic model had an area under the receiver operator characteristics curve of 89.6%. A cutoff of 4.3 for the score was associated with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 91.3%, 68.5%, 70.5%, and 92.3%, respectively. Misclassification rate with the application of the diagnostic model on group II subjects was 13.5% (14/104). Sensitivity, specificity, PPV, and NPV of the model for predicting OSA in this group were 82, 90.7, 89.1, and 84.5%, respectively[39].

With increasing demand for diagnostic services, such models may help to select patients for further evaluation and may facilitate more efficient use of bed space in sleep laboratories. However, none of these models are a substitute for full PSG evaluation for the diagnosis of OSA.

Nocturnal Pulse Oximetry

Nocturnal pulse oximetry has been used to screen for OSA, and evidence is available suggesting that it may be useful in screening patients for PSG[11]. The sensitivity of nocturnal pulse oximetry in the diagnosis of OSA ranges from 31 to 98% and specificity from 41 to 100%[32].

Polysomnography

Several forms of PSG such as full, attended, in-laboratory PSG, unattended PSG, portable PSG, have all been variously used for the diagnosis of OSA. Presently, attended, in-laboratory overnight full polysomnography where monitoring of various parameters reflecting respiration and monitoring cortical brain activity to assess the presence or absence of sleep and its stage are studied is considered the gold standard in the diagnosis of OSA. PSG is performed overnight in a sleep laboratory with a trained technician constantly monitoring the patient.

Apnea is defined as a greater than 90% cessation of airflow for ten or more seconds. Hypopnea is defined as a 50 to 90% reduction in airflow or a fall in percentage oxygen saturation of three or more or an arousal evident on electroencephalographic (EEG) recording. A respiratory event related arousal (RERA) is defined as increasing respiratory effort required to maintain a normal airflow culminating in an arousal on EEG.

Sometimes, split-night PSG is performed during a single night in the sleep laboratory, especially if the patient manifests AHI greater than 40 in the first two hours of the study. In the split-study, the baseline diagnostic portion is followed by therapeutic continuous positive airway pressure (CPAP) titration. The guidelines proposed by the American Sleep Disorders Association (ASDA) and classification of severity of OSA is shown in Table 5[3].

Table 5: American Sleep Disorders Association (ASDA) classification of obstructive sleep apnea

Sleepiness
Mild: unwanted sleepiness or involuntary sleep episodes occur during activities that require little attention
Moderate: unwanted sleepiness or involuntary sleep episodes occur during activities that require some attention
Severe: unwanted sleepiness or involuntary sleep episodes occur during activities that require active attention
Sleep-related obstructive breathing events (apnea, hypopnea, and respiratory effort related arousals):
Mild: 5–15 events/hour of sleep
Moderate: 15–30 events/hour of sleep
Severe: > 30 events/hour of sleep

Source: Reference 3

Metabolic Abnormalities

Several metabolic abnormalities have been described in patients with OSA. Critical evaluation of published evidence, however, suggests that OSA has no independent association with lipid abnormalities, insulin resistance, serum leptin, adiponectin[40] and C-reactive protein measured by high sensitivity enzyme immunoassay (hs-CRP) levels[41]. Obesity, and not OSA, appears to be responsible for these metabolic abnormalities[40,41].

Differential Diagnosis

OSA must be distinguished from other conditions associated with excessive sleepiness such as narcolepsy, idiopathic hypersomnia, hypothyroidism, depression, limb movement disorders like periodic limb movement disorder, restless leg syndrome, alcohol, drugs like sedatives, hypnotics, antidepressants, anticonvulsants, antihypertensives. Other conditions such as insufficient sleep time, insomnia, environmental disturbances, and inadequate sleep hygiene must also be distinguished from OSA by diligent clinical examination and judicious use of investigations.

MANAGEMENT

Modifiable risk factors including recent weight gain, alcohol, sedative/hypnotic use, cigarette smoking, and chronic nasal obstruction should be identified and corrected. Co-morbid medical conditions including systemic hypertension, atherosclerotic disease, heart failure, hypothyroidism, chronic lung disease, and neuromuscular disease that may be worsened by OSA should be diligently searched for and managed appropriately[42,43]. An algorithm for treatment of OSA is shown in Fig. 1.

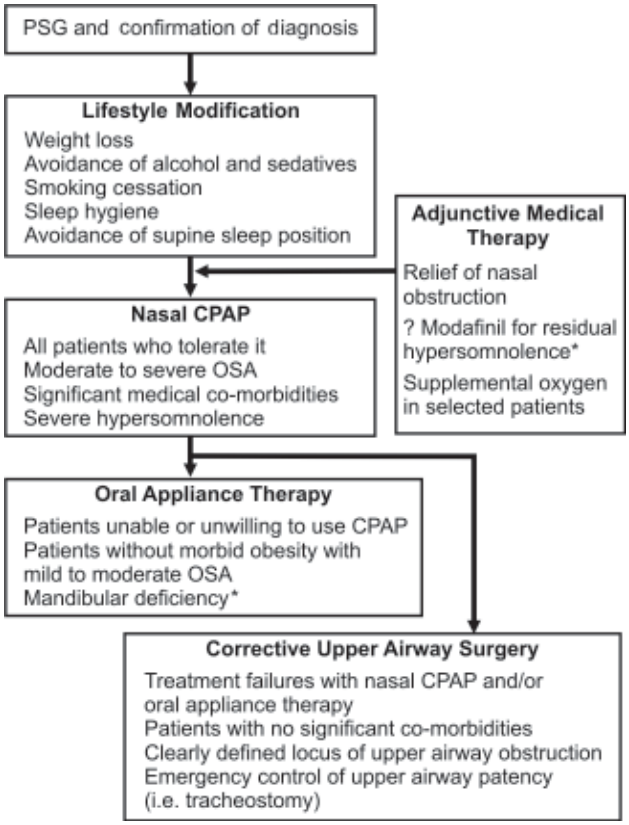

Fig. 1: Algorithm for the treatment of patients with obstructive sleep apnea. Bilevel positive airway pressure (BiPAP) is better tolerated by some patients and may facilitate therapeutic salvage of patients who are intolerant of CPAP or in whom CPAP is inadequately effective. PSG = polysomnography; CPAP = continuous positive airway pressure

* = potentially beneficial

Conservative Treatment

Lifestyle Modification

While there are no randomized controlled trials endorsing the utility of lifestyle modification in the management of OSA, enough rationale exists supporting the view that lifestyle modification may be beneficial at least to the co-morbid illnesses that usually accompany OSA[44-46].

Weight Reduction

Because a decrease in body weight of as little as 10% has been associated with clinically significant improvement in the AHI, weight loss should be recommended to overweight patients with OSA. Other potential benefits of weight loss include its favorable impact on co-morbid conditions such as hypertension, heart failure, respiratory failure, insulin resistance and dyslipidaemia[44-46].

Avoidance of Alcohol and Respiratory Depressants

Alcohol selectively suppresses upper airway dilator muscle activity, increases inspiratory resistance during wakefulness and sleep and predisposes to OSA. Avoidance of alcohol and drugs such as hypnotics and sedatives is helpful in amelioration of the symptoms of OSA[44-46].

Cessation of Cigarette Smoking and Sleep Hygiene

Patients with OSA who are current cigarette smokers should be counselled to quit smoking. Poor sleep habits (referred to as hygiene) are among the most common problems encountered in the modern society. These

include staying up too late and getting up too early, interrupting sleep with work, drugs, chemicals, and late-night activities such as movies and television among others. Measures to improve sleep hygiene such as avoidance of caffeine and other stimulants, regular sleep-wake schedule, creating a comfortable undisturbed sleep environment, and avoidance of daytime napping should be advocated[44-46].

Measures to Relieve Nasal Congestion

Measures to relieve nasal congestion include nasal corticosteroids, oral non-sedating antihistamines, and various surgical procedures too may contribute in the improvement of OSA especially when used under the supervision of an otorhinolaryngologist.

Pharmacological Treatment

While a wide range of pharmacological agents have been used earlier, currently available evidence does not support the use of pharmacological agents in the treatment of OSA. Recently published evidence[47] suggests that modafinil showed significant improvement in alertness and subjective and objective daytime sleepiness in patients with OSA who had residual sleepiness despite nasal CPAP therapy, thereby suggesting that this agent may have a role as adjunctive symptomatic therapy. These findings merit further detailed evaluation. As of now, there is insufficient evidence to recommend the use of drug therapy in the treatment of OSA[48].

Nasal Continuous Positive Airway Pressure (CPAP)

Nasal CPAP remains the most effective therapy for patients with OSA, especially those with daytime somnolence[4,49-51]. CPAP eliminates upper-airway flow limitation by acting as a mechanical stent of the upper airway, stabilizing the upper airway, augmenting the lung volume and eliciting a reflex which increases upper airway dilator muscle tone. The Amercian Academy of Sleep Medicine guidelines for CPAP therapy[3] recommend its use for patients with an apnea index (mean number of apneas per hour of sleep) of greater than 20 and for symptomatic patients with AHI or respiratory arousal index (mean number of arousals per hour of sleep) of greater than 10. A 'titration' study is performed over a single night with the therapeutic pressure determined as that which overcomes 90% or 95% of sleep-related events.

CPAP use has clearly been shown to have a favorable impact on daytime sleepiness in sleepy patients with OSAHS, driving performance as measured by driving simulators, and also accident rates. CPAP favorably modifies multiple factors at the neurophysiological and molecular levels which promote cardiovascular disease. Overall, about 70% of symptomatic patients use CPAP effectively and sufficiently to have a major impact on symptoms[4,49-51].

Bilevel Positive Airway Pressure (BiPAP)

Unlike CPAP which provides the same magnitude of pressure during the inspiratory and expiratory portions of the ventilatory cycle, bilevel positive airway pressure (BiPAP) permits independent adjustment of the inspiratory and expiratory positive airway pressures[49]. In BiPAP, the inspiratory positive airway pressure (IPAP) level is set to prevent upper airway closure and partial obstruction (hypopnea) during the inspiratory phase of breathing. The expiratory positive airway pressure (EPAP) is set to stabilise the upper airway at end-expiration, such that the airway remains sufficiently patent to permit the patient to trigger delivery of IPAP by generating low level inspiratory volume or flow during the subsequent effort. The benefits of BiPAP include: providing ventilatory assistance and improved patient comfort. Anecdotal evidence suggests that BiPAP is better tolerated by some patients and may facilitate therapeutic salvage of patients who are intolerant of CPAP or in whom CPAP is inadequately effective[4,49].

Others

In addition to the conventional fixed pressure CPAP (F-CPAP), autotitrating CPAP (A-CPAP) has recently been introduced. Unlike F-CPAP, which must remain throughout the night at a sufficiently high level to maintain upper airway patency, A-CPAP levels fluctuate to accommodate the physiological requirements to maintain upper airway patency[49]. The relative efficacy of these modalities of treatment merit further study.

Adverse effects of CPAP include those related to nasopharyngeal symptoms, those related to the interface or nasal route of delivery, and those specifically related to the magnitude of pressure. Nasopharyngeal symptoms are often amenable to local treatment measures. Interface-related problems can be resolved by careful and methodical assessment of all interface options and choosing the one that is most appropriately suited to the patient. Clinicians should be aware of the potential risk of raised intraocular pressure, barotrauma resulting in pneumothorax and pneumoencephalus[4,49].

Oral Appliance Therapy

Mandibular advancement devices that result in the protrusion of the mandible during sleep and thereby

reduce retroglossal airway collapse have been used in patients with mild apnea or non-apneic snoring and have been found to be beneficial. A multidisciplinary team approach including a dentist and/or orthodontist who understands the limitations of oral appliance therapy, is essential to facilitate the benefits associated with this form of treatment[49,52].

Surgery

Overall, the usefulness of surgery in the management of OSA remains ill-defined and is still controversial. Various surgical procedures aimed at relieving upper airway obstruction include: (i) resection of redundant soft tissue (nasal surgery, uvulopalatopharyngoplasty, laser assisted uvulopalatoplasty, midline glossectomy); (ii) induction of scar tissue formation (cautery or radio-frequency ablation of soft palate, tongue, or epiglottis); and (iii) displacement of bony and ligamentous attachments of upper airway soft tissue structures (maxillary and mandibular osteotomies, tongue and hyoid suspensions)[46,53]. In the emergency setting, tracheostomy may occasionally be required.

While specific obstructing lesions such as adeno-tonsillar enlargement should be surgically resected, the relative utility of these surgical procedures remains variable and should be confined to carefully designed clinical trials performed in centres with expertise in these complex surgical procedures.

Experimental Measures

Sleeping in lateral position has been recommended for mild positional OSA especially for patients who are not tolerating CPAP. Nocturnal electrical stimulation of the hypoglossal nerve by an implanted pace-maker has been attempted to prevent sleep related upper airway collapse by activating submandibular muscles[52]. Intriguingly, regular didgeridoo playing has been reported to be an effective alternative treatment in patients with moderate OSA[54]. Didgeridoo, classified by musicologists as an aerophone, is a wind instrument of the indigenous Australians of Northern Australia.

Conclusions

Early identification and treatment of OSA is associated with immense benefit to the patients. Education and sensitization of primary care physicians to screen for OSA is desired as it may facilitate referral to the specialist for PSG and diagnostic confirmation[55,56]. Further research is warranted into the natural history, causes, and consequences of OSA. This will facilitate interventions to reduce or reverse OSA progression before the development of significant morbidity.

REFERENCES

1. Guilleminault C, Tilkian A, Dement WC. The sleep apnea syndromes. Annu Rev Med 1976;27:465-84.
2. Gibson GJ. Obstructive sleep apnoea syndrome: underestimated and undertreated. Br Med Bull 2005;72:49-65.
3. American Academy of Sleep Medicine. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999;22:667-89.
4. Caples SM, Gami AS, Somers VK. Obstructive sleep apnea. Ann Intern Med 2005;142:187-97.
5. Stradling JR, Davies RJ. Sleep. 1: Obstructive sleep apnoea/hypopnoea syndrome: definitions, epidemiology, and natural history. Thorax 2004;59:73-8.
6. Ferini-Strambi L, Fantini ML, Castronovo C. Epidemiology of obstructive sleep apnea syndrome. Minerva Med 2004;95:187-202.
7. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002;165:1217-39.
8. Udwadia ZF, Doshi AV, Lonkar SG, Singh CI. Prevalence of sleep-disordered breathing and sleep apnea in middle-aged urban Indian men. Am J Respir Crit Care Med 2004;169:168-73.
9. Sharma SK, Kumpawat S, Banga A, Goel A. Prevalence and risk factors of obstructive sleep apnea syndrome in a population of Delhi, India. Chest 2006;130:149-56.
10. Davies RJ, Ali NJ, Stradling JR. Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnoea syndrome. Thorax 1992;47:101-5.
11. Sharma SK, Kurian S, Malik V, Mohan A, Banga A, Pandey RM, et al. A stepped approach for prediction of obstructive sleep apnea in overtly asymptomatic obese subjects: a hospital based study. Sleep Med 2004;5:351-7.
12. Sharma SK, Reddy TS, Mohan A, Handa KK, Mukhopadhyay S, Pande JN. Sleep disordered breathing in chronic obstructive pulmonary disease. Indian J Chest Dis Allied Sci 2002;44:99-105.
13. Sharma SK, Hira HS. Sleep apnoea syndrome. In: Sharma SK, Behera D, Mohan A,(Eds). Recent Advances in Respiratory Medicine. New Delhi: Jaypee Brothers Medical Publishers; 1998.p.52-72.
14. Sharma SK. Obstructive sleep apnea: Indian perspective. In: Sahay BK (Ed). Medicine update. Mumbai: Association of Physicians of India; 2006;16:605-15.
15. White DP. Pathogenesis of obstructive and central sleep apnea. Am J Respir Crit Care Med 2005;172:1363-70. Epub 2005 Aug 11.
16. Yamauchi M, Tamaki S, Tomoda K, Yoshikawa M, Fukuoka A, Makinodan K, Koyama N, Suzuki T, Kimura H. Evidence for activation of nuclear factor kappa B in obstructive sleep apnea. Sleep Breath 2006; [Epub ahead of print].

17. Ryan S, Taylor CT, McNicholas WT. Predictors of elevated nuclear factor-kappaB-dependent genes in obstructive sleep apnea syndrome. Am J Respir Crit Care Med 2006;174:824-30. Epub 2006 Jul 13.
18. Riha RL, Brander P, Vennelle M, McArdle N, Kerr SM, Anderson NH, Douglas NJ. Tumour necrosis factor-alpha (-308) gene polymorphism in obstructive sleep apnoea-hypopnoea syndrome. Eur Respir J 2005;26:673-8.
19. Conti AA, Conti A, Gensini GF. Fat snorers and sleepy-heads: were many distinguished characters of the past affected by the obstructive sleep apnea syndrome? Med Hypotheses 2006;67:975-9. Epub 2006 Jun 8.
20. Schlosshan D, Elliott MW. Sleep. 3: Clinical presentation and diagnosis of the obstructive sleep apnoea hypopnoea syndrome. Thorax 2004;59:347-52.
21. Hartenbaum N, Collop N, Rosen IM, Phillips B, George CF, Rowley JA, et al. American College of Chest Physicians; American College of Occupational and Environmental Medicine; National Sleep Foundation. Sleep apnea and commercial motor vehicle operators: Statement from the joint task force of the American College of Chest Physicians, the American College of Occupational and Environmental Medicine, and the National Sleep Foundation. Chest 2006;130:902-5.
22. Sharma SK, Mohan A. Sleep disordered breathing and hypertension: time to wake up! Indian J Chest Dis Allied Sci 2001;43:77-9.
23. Cormican LJ, Williams A. Sleep disordered breathing and its treatment in congestive heart failure. Heart 2005;91:1265-70.
24. Caples SM, Kara T, Somers VK. Cardiopulmonary consequences of obstructive sleep apnea. Semin Respir Crit Care Med 2005;26:25-32.
25. Wilcox I, McNamara SG, Collins FL, Grunstein RR, Sullivan CE. "Syndrome Z": the interaction of sleep apnoea, vascular risk factors and heart disease. Thorax 1998;53 (Suppl 3):S25-8.
26. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365:1046-53.
27. Gami AS, Howard DE, Olson EJ, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med 2005;352:1206-14.
28. Sharma SK, Sinha S, Jagannathan NR, Danishad KA, Misra H, Sharma H. Proton magnetic resonance spectroscopy of brain and cerebral metabolism in obstructive sleep apnea patients: A study in Northern Indian Asian subjects. Proc Am Thorac Soc (submitted).
29. Goncalves MA, Guilleminault C, Ramos E, Palha A, Paiva T. Erectile dysfunction, obstructive sleep apnea syndrome and nasal CPAP treatment. Sleep Med 2005;6:333-9.
30. Teixeira LR, Fischer FM, Lowden A. Sleep deprivation of working adolescents—a hidden work hazard. Scand J Work Environ Health 2006;32:328-30.
31. Desai AV, Marks G, Grunstein R. Does sleep deprivation worsen mild obstructive sleep apnea? Sleep 2003;26:1038-41.
32. Mattei A, Tabbia G, Baldi S. Diagnosis of sleep apnea. Minerva Med 2004;95:213-31.
33. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540-5.
34. Carskadon MA, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S. Guidelines for the multiple sleep latency test (MSLT): a standard measure of sleepiness. Sleep 1986;9:519-24.
35. Sangal RB, Thomas L, Mitler MM. Maintenance of wakefulness test and multiple sleep latency test. Measurement of different abilities in patients with sleep disorders. Chest 1992;101:898-902.
36. MacLean AW, Fekken GC, Saskin P, Knowles JB. Psychometric evaluation of the Stanford Sleepiness Scale. J Sleep Res 1992;1:35-9.
37. Thorpy MJ. The clinical use of the Multiple Sleep Latency Test. The Standards of Practice Committee of the American Sleep Disorders Association. Sleep 1992;15:268-76.
38. Sharma SK, Vasudev C, Sinha S, Banga A, Pandey RM, Handa KK. Validation of the modified Berlin questionnaire to identify patients at risk for the obstructive sleep apnea syndrome in North Indians. Indian J Med Res 2006 (in press).
39. Sharma SK, Malik V, Vasudev C, Banga A, Mohan A, Handa KK, Mukhopadhyay S. Prediction of obstructive sleep apnea in patients presenting to a tertiary care center. Sleep Breath 2006;10:147-54.
40. Sharma SK, Kumpawat S, Goel A, Banga A, Ramakrishnan L, Chaturvedi P. Obesity, and not obstructive sleep apnea, is responsible for metabolic abnormalities in a cohort with sleep disordered breathing. Sleep Med 2006 (accepted).
41. Sharma SK, Misra H, Sharma H, Goel A, Gulati V, Mohammed T. Obesity and not OSA is responsible for raised levels of serum hs-CRP. Sleep Med 2006 (submitted).
42. Jha A, Sharma SK, Tandon N, Lakshmy R, Kadhiravan T, Handa KK, Gupta R, Pandey RM, Chaturvedi PK. Thyroxine replacement therapy reverses sleep-disordered breathing in patients with primary hypothyroidism. Sleep Med 2006;7:55-61. Epub 2005 Sep 28.
43. Sharma SK, Mohan A. Sleep disordered breathing and hypertension: time to wake up! Indian J Chest Dis Allied Sci 2001;43:77-9.
44. Qureshi A, Lee-Chiong TL. Medical treatment of obstructive sleep apnea. Semin Respir Crit Care Med 2005;26:96-108.
45. Guilleminault C, Abad VC. Obstructive sleep apnea syndromes. Med Clin North Am 2004;88:611-30.
46. Ryan CF. Sleep 9: an approach to treatment of obstructive sleep apnoea/hypopnoea syndrome including upper airway surgery. Thorax 2005;60:595-604.
47. Kingshott RN, Vennelle M, Coleman EL, Engleman HM, Mackay TW, Douglas NJ. Randomized, double-blind, placebo-controlled crossover trial of modafinil in the treatment of residual excessive daytime sleepiness in the sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 2001;163:918-23.
48. Smith I, Lasserson TJ, Wright J. Drug therapy for obstructive sleep apnoea in adults. Cochrane Database Syst Rev 2006 Apr 19;(2):CD003002. Update of: Cochrane Database Syst Rev 2002;(2):CD003002.
49. Gordon P, Sanders MH. Sleep.7: positive airway pressure therapy for obstructive sleep apnoea/hypopnoea syndrome. Thorax 2005;60:68-75.

50. Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnoea in adults. Cochrane Database Syst Rev 2006;3:CD001106.
51. Veasey SC, Guilleminault C, Strohl KP, Sanders MH, Ballard RD, Magalang UJ. Medical therapy for obstructive sleep apnea: a review by the Medical Therapy for Obstructive Sleep Apnea Task Force of the Standards of Practice Committee of the American Academy of Sleep Medicine. Sleep 2006;29:1036-44.
52. Bloch KE. Alternatives to CPAP in the treatment of the obstructive sleep apnea syndrome. Swiss Med Wkly 2006;136:261-7.
53. Li KK. Surgical therapy for obstructive sleep apnea syndrome. Semin Respir Crit Care Med 2005;26:80-8.
54. Puhan MA, Suarez A, Lo Cascio C, Zahn A, Heitz M, Braendli O. Didgeridoo playing as alternative treatment for obstructive sleep apnoea syndrome: randomised controlled trial. BMJ. 2006;332:266-70. Epub 2005 Dec 23.
55. McNicholas WT, Ryan S. Obstructive sleep apnoea syndrome: translating science to clinical practice. Respirology 2006;11:136-44.
56. White DP. Sleep apnea. Proc Am Thorac Soc 2006;3:124-8.