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Obstructive sleep apnoea in adults

Identifying risk factors and tailoring therapy

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Obstructive sleep apnoea is increasingly being recognised as a significant health problem. Diagnosis is based on clinical assessment and objective testing and there are now several treatment options that can be tailored to each affected patient.

Key points

- Left untreated, obstructive sleep apnoea (OSA) may contribute to several health-related adverse outcomes.
- Diagnosis is based on clinical history, physical examination and objective findings during laboratory polysomnography or on a portable device.
- Behavioural modification is indicated in most patients with OSA. Weight loss should be attempted in overweight or obese patients.
- Positive airway pressure (PAP) therapy remains the first-line treatment, particularly in moderate to severe OSA.
- Mandibular advancement splints are an alternative first-line treatment, particularly in mild to moderate OSA or when PAP therapy is refused or fails.
- Surgery is considered first-line treatment only when there is an identifiable cause for OSA that can be surgically corrected. It is otherwise reserved for selected patients who have failed or are not suitable for PAP or therapy with an oral device.
- Optimal outcomes require skilled personnel, coupled with education and monitoring within a clinical context.

Obstructive sleep apnoea (OSA) is a common disorder that is characterised by repetitive upper airway collapse during sleep, resulting in apnoeas (complete cessation of airflow) and/or hypopnoeas (reduced airflow). The physiological sequelae include intermittent hypoxia, hypercapnia, increased sympathetic activity and marked swings in intrathoracic pressure.[1] This in turn results in sleep fragmentation and several associated adverse consequences, including excessive daytime sleepiness, neuro-cognitive impairment, mood disturbance, increased cardiovascular morbidity, increased risk of motor vehicle accidents and overall mortality.[2] OSA is increasingly being recognised as a serious public health issue. The total healthcare cost of diagnosed OSA in Australia in 2010 was estimated at $597 million, although such estimates exclude the significant proportion of symptomatic OSA that remains undiagnosed.[3]

The prevalence of OSA varies according to gender, age and body mass index (BMI). Men have twice the risk of developing the condition than women and the prevalence increases with age until the age of 65 years, after which it reaches a plateau.[4] Postmenopausal women have a higher risk of developing OSA than premenopausal women, suggesting that

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hormonal factors may also contribute to its pathogenesis.

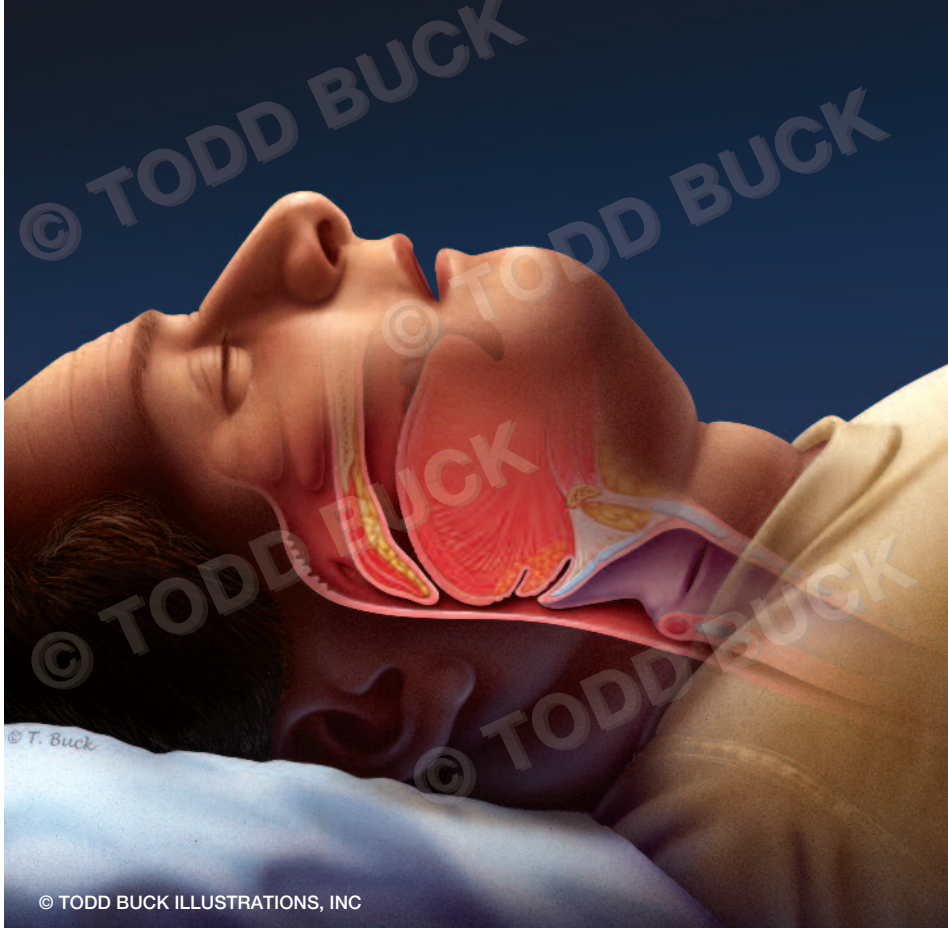
HEALTH IMPACTS

The neurocognitive and neurobehavioural consequences of OSA are well established and include: impaired daytime functioning, memory, mood and work performance; increased risk of driving and occupational accidents; and poorer quality of life.[5] Sleepiness is the most common neurobehavioural consequence. There is also a strong association between untreated OSA and hypertension, most likely related to sympathetic activation. More recently, a link between cardiovascular morbidity and mortality (myocardial infarction and stroke) and untreated OSA has been demonstrated, largely in population-based epidemiological studies.[6]

OBESITY AND OSA

In Australia, obesity is perhaps the most common and important risk factor for the development of OSA. It has been shown to increase the likelihood of OSA by 10- to 20-fold compared with normal-weight individuals.[7] Furthermore, a weight gain of 10% in patients with previously documented mild OSA significantly increases the risk of disease progression (about a sixfold increase).[4] Over the past 20 years there has been a steady rise in the average BMI of people in Australia. The most recent Australian Bureau of Statistics data estimate that 62.8% of men and 47.6% of women are either overweight or obese.[8] It is very likely that with rising rates of obesity, the prevalence of OSA will continue to climb. As such, it will become increasingly important at a primary care level to recognise this condition and pursue diagnosis and treatment.

It is important to note, however, that the absence of obesity in an individual with symptoms or other risk factors for OSA should not preclude the diagnosis. This is particularly evident among certain ethnic groups such as the Chinese, in whom the association between OSA and BMI has been shown to be weaker compared with matched groups of Caucasian subjects.[9] Differences in craniofacial features between ethnic groups may explain this observation.[10]



DIAGNOSIS

Most patients with OSA will first present to their GP with a complaint about snoring or some other sleep disturbance; however, the diagnosis should also be considered in those who are asymptomatic but at high risk for having the condition (see the boxes on page 16).[1] Patients in whom the consequences of excessive sleepiness may put themselves and others at risk of significant harm (e.g. commercial drivers, pilots) should also be prioritised for early recognition.

Symptoms suggestive of OSA that should be sought are summarised in the box on page 16.[3] The key symptoms of OSA are snoring, excessive daytime sleepiness (EDS) and deficits in neurocognitive function.[5] Daytime sleepiness in particular is an important feature of OSA; however, it is not always recognised by the patient because it is often longstanding and insidious in onset. It may sometimes be described as 'fatigue' and can be masked by activity, particularly in the workplace. Sleepiness is often more marked in passive or monotonous situations (e.g. watching television, reading and driving). The Epworth Sleepiness Scale is a simple, rapid screening test that assists in the identification and quantification of EDS (Table 1).[11] Although this instrument is not specific for OSA, a score

COMMON RISK FACTORS FOR OSA

- Male gender
- Middle age (over 40 years)
- Family history
- Obesity, increased neck circumference
- Nasal obstruction
- Enlarged tonsils, adenoids, macroglossia
- Craniofacial abnormalities
- Ethnicity (e.g. Asian, Polynesian)
- Alcohol, smoking, sedatives
- Menopause
- Chronic sleep deprivation

MEDICAL CONDITIONS ASSOCIATED WITH OSA

- Treatment-refractory hypertension
- Atrial fibrillation
- Nocturnal dysrhythmia
- Type 2 diabetes
- Stroke
- Cardiac failure
- Gastro-oesophageal reflux
- Acromegaly
- Hypothyroidism
- Congenital disorders (e.g. Down syndrome, Marfan's syndrome)

COMMON SYMPTOMS OF OSA

- Snoring
- Excessive daytime sleepiness
- Witnessed apnoeas
- Gasping, choking at night
- Unrefreshing sleep
- Sleep fragmentation, maintenance insomnia
- Morning headaches
- Poor concentration
- Memory loss
- Nocturia
- Diaphoresis
- Reduced libido, impotence

of 11 or greater is considered to be clinically significant. Higher scores have been associated with increased severity of OSA.[12]

The most common features of OSA on physical examination are obesity (BMI of 30 kg/m^2 or more) and a crowded and inflamed oropharynx (Figure 1).[1] A neck circumference of more than 43 cm in men and more than 40 cm in women has been shown to correlate with an increased risk of OSA.[13] Other anatomical factors known to predispose to OSA may be present, for example, tonsillar enlargement, nasal deviation or polyps, macroglossia and certain craniofacial features, such as retrognathia, overbite or overjet, high-arched palate and a narrow maxilla and mandible (Figures 2a to c). Co-existent hypertension and other consequences of OSA should be sought.

For patients who are asymptomatic and with no clearly identifiable risk factors for OSA, screening questions should be included as part of a routine health maintenance evaluation. Questions to be asked include a history of snoring and daytime sleepiness as well as evaluation for the presence of anatomical factors that may contribute to increased risk. Any positive findings on this screen should prompt a more comprehensive sleep history and physical examination.

TABLE 1. EPWORTH SLEEPINESS SCALE[11]

Situation	Chance of dozing (score of 0 to 3)*
Sitting and reading	
Watching television	
Sitting inactive in a public place (e.g. a cinema or meeting)	
As a passenger in a car for more than one hour	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to a companion	
Sitting quietly after an alcohol-free lunch	
In a car, while stopped briefly in heavy traffic	
Total Epworth sleepiness score The higher the score, the higher the person's level of daytime sleepiness.	

* Score: 0 = no chance of dozing; 1 = slight chance of dozing; 2 = moderate chance of dozing; 3 = high chance of dozing.

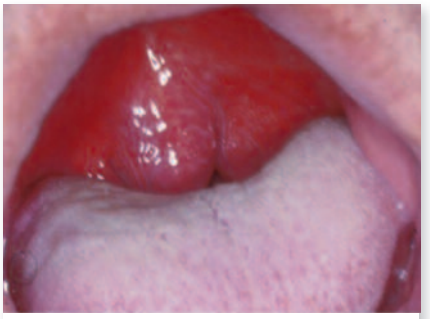
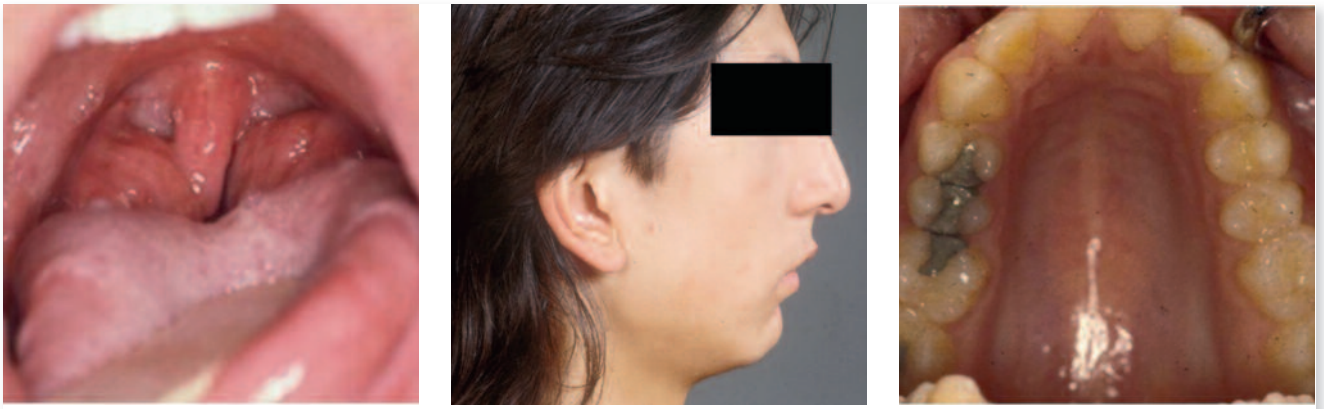


Figure 1. Intraoral photograph showing marked pharyngeal inflammation and airway crowding.



Figures 2a to c. Anatomical factors predisposing to OSA. a (left).Tonsillar hypertrophy causing airway narrowing. b (middle). Retrognathia. c (right). High-arched palate.

A useful tool that may facilitate identification of patients at risk of OSA in primary care is the Berlin questionnaire.[14] This comprises a set of questions specifically selected to elicit factors that have been demonstrated in the literature to be consistently associated with the presence of OSA. The tool has been validated for use in the primary care setting and encompasses symptoms, risk factors and physical findings.[14]

After a history has been taken and a physical examination performed, patients may be stratified according to their risk of having OSA. However, numerous studies indicate that the sensitivity and specificity of clinical assessment alone in diagnosing OSA is only about 60% each.[5] Objective testing is therefore required to establish a diagnosis and there are several methods by which this may be achieved. Discussion with a sleep physician at this point allows for appropriate test selection, which has the potential to expedite treatment in some instances.

THE OTHERWISE HEALTHY SNORER

The scenario of a healthy, otherwise asymptomatic snorer with no identifiable risk factors for OSA presents a particularly difficult management challenge because the role of objective testing remains unclear in this situation. It is important to be aware that this presentation may, in some instances, be related to a patient's misperception of symptoms (in particular, daytime sleepiness), and careful history taking and examination are essential in this regard. If there is no suggestion of occult symptoms, patients may be able to proceed directly to treatment aimed at ameliorating snoring, such as oral appliances or ENT surgery; however, the decision to proceed down this path should be evaluated on a case-by-case basis.

OBJECTIVE TESTING

Full-night supervised, in-laboratory polysomnography (PSG) remains the gold-standard investigation to establish a diagnosis of OSA. This involves the recording of multiple physiological signals during the sleep period, which typically include:

- sleep staging parameters – electro - encephalogram (EEG), electro-oculogram and electromyogram
- cardiorespiratory parameters – oronasal airflow, ribcage and abdominal motion (respiratory effort), oxygen saturation, diaphragm electromyogram and electrocardiography.

For the diagnosis of OSA, the key variables derived from a PSG include:

- measures of sleep architecture (total sleep time and proportion of time spent in each sleep stage) and fragmentation (arousals per hour of sleep)
- number of complete (apnoeas) and partial (hypopnoeas) obstructions per hour of sleep – known as the apnoea–hypopnoea index (AHI); this index is used to categorise severity (Table 2)
- oxygen saturation variables (baseline, mean and minimum).

Analysis of data obtained from a PSG has been simplified over the years by advances in computer technology. However, the technique remains very labour intensive and the costs of equipment and personnel are high. Demand for testing continues to outstrip supply, with some patients and primary care practitioners facing great difficulty in accessing timely services, particularly in regional Australia. This has resulted in the development of portable devices aimed at simplifying diagnosis and improving cost effectiveness.

Although there has been a growing move towards the use of portable devices for the diagnosis of OSA in recent years, guidelines for their appropriate use in clinical practice are still in evolution. Available devices range from those that measure all sleep parameters (including EEG), through to those that monitor only three or four parameters (limited

monitoring), to simple oximetry alone. Use of devices may be attended (in sleep laboratory or hospital) or unattended (at home). Current research suggests that attended monitoring with measurement of airflow, respiratory effort and blood oxygenation at a minimum provides the most consistent, high quality data to confirm a diagnosis of OSA.[1]

At present, the use of portable devices is most appropriate for ruling in the diagnosis of OSA in the setting of a high pretest probability. There are a number of potential pitfalls in the interpretation of portable sleep studies, depending on the type of device used, and hence a skilled reporting physician and appropriate clinical follow up are critical to the process. Such studies should not be used in patients with comorbidities that predispose them to non-OSA sleep-disordered breathing (e.g. heart failure and Cheyne–Stokes respiration) or when another sleep disorder is suspected.[15] A negative portable test in patients with a high pretest probability should be followed by an in-laboratory PSG.

TABLE 2. STRATIFICATION OF OSA SEVERITY

Severity	Apnoea–hypopnoea index (events/hour)
Mild	5 to 15
Moderate	15 to 30
Severe	Over 30

MANAGEMENT

The management of OSA usually starts with definitive diagnosis and assessment of its underlying severity. Ideally, objective test results should be reviewed by a sleep physician together with the patient to consider the need for treatment and the pros and cons of the various modalities. Patient education and engagement in the treatment process are critical to the outcome. Factors that guide management include severity of OSA, underlying symptoms, comorbidities and the risk of adverse outcomes. The severity of OSA at the time of diagnosis also forms the baseline from which treatment efficacy can be evaluated. It may also be important to counsel patients about the risks

BEHAVIOURAL MODIFICATION FOR PATIENTS WITH OSA

Weight loss
- Weight loss is advised in all overweight or obese patients
- Weight loss is associated with improvement in overall health, quality of life, reduction in apnoea–hypopnoea index and possibly daytime somnolence
- Bariatric surgery may be considered in morbidly obese patients

Change of sleep position
- Change of sleep position is advised for patients with OSA occurring predominantly or exclusively in the supine position
- Posture alarms or positional devices can be used to discourage sleep in the supine sleep position (e.g. belt with attached tennis ball pocket posteriorly or ball sewn onto back of pyjama shirt)
- Nonsupine sleep may improve or resolve OSA
- Limited long-term compliance is the main drawback of changing sleep position

Avoidance of alcohol
- Excessive alcohol intake can cause CNS depression with worsening OSA (it may also contribute to weight gain)
- Consumption of alcohol should be avoided both day and night

Avoidance of certain medications
- Pharmacological agents with inhibitory effects on the CNS can worsen obstructive events and exhibit different effects on sleep quality and architecture – these agents include benzodiazepines, barbiturates, antiepileptics, antidepressants, antihistamines and opioid analgesics
- Some medications are associated with weight gain (e.g. corticosteroids, some antidepressants)
- Risk–benefit ratio needs to be thoroughly assessed in patients with OSA before initiation; treatment must be carefully titrated and closely monitored

of driving or operating machinery while feeling sleepy. In particular circumstances, this can have legal implications regarding a patient's ability to practice their occupation if it involves, for example, driving a commercial vehicle (for more information on OSA and driving see: www.austroads.com.au/assessing-fitness-to-drive).

In most patients, OSA should be regarded as a chronic disease that often requires long-term interdisciplinary models of care. This may involve the patient's primary care provider, a sleep physician and in some cases an ENT surgeon, a dentist, a therapist specialising in continuous positive airway pressure (CPAP) therapy or a dietician.

The clinical benefits of treatment in patients with OSA may include reduced daytime tiredness, improved quality of life and control of hypertension,[16-20] as well as a decrease in the costs and use of healthcare services.[21,22] Furthermore, there is evidence to suggest a possible reduction in mortality.[23]

Behavioural modification

All patients diagnosed with OSA and who have a modifiable risk factor should receive behavioural modification advice, as appropriate (see the box on this page). The indication for further OSA-specific treatment should be tailored to the particular clinical situation.

Although obesity is generally recognised as the major risk factor for OSA, there is growing evidence that craniofacial features play a significant role not only in the aetiology but also potentially in the management and prevention of the disorder.[24] As such, phenotyping is becoming increasingly important in the diagnosis and management of OSA and in the future it may enable specific therapeutic targeting of the various mechanisms contributing to OSA in individual patients (i.e. personalised medicine).[25]

OSA-specific treatment

Although professional organisations vary in their treatment thresholds there is some consensus that OSA-specific treatment should be considered in patients who have an AHI of five obstructions or more per hour with accompanying symptoms or significant cardiovascular or metabolic comorbidities. In the absence of symptoms and risk factors, an AHI of 10 obstructions or more per hour could be considered as a threshold, although this will vary from case to case.

Treatment specifically targeted at OSA includes the administration of positive airway pressure (PAP) during sleep, the use of an oral appliance and/or specific upper airway surgery. The first of these two treatment modalities will be the appropriate initial form of specific OSA management in most patients.[17]

Positive airway pressure treatment

PAP remains the mainstay of treatment for people with OSA since its first report 30 years ago. It works by splinting the upper airway open, thereby preventing upper airway collapse. CPAP is the most commonly used method of PAP therapy and delivers either a fixed or automatically varying pressure throughout the respiratory cycle (see the box on page 22 for further details of different PAP modalities).[26] More sophisticated forms of PAP

DIFFERENT POSITIVE AIRWAY PRESSURE (PAP) MODALITIES

Continuous PAP (CPAP)
- Delivers fixed amount of pressure constantly throughout respiratory cycle

Auto-set/auto-titrating PAP
- Can alter amount of applied PAP according to detected changes in upper airway resistance
- Sometimes preferred over a fixed pressure device due to increased comfort perception from varying pressure levels throughout different sleep phases and positions
- Associated with higher equipment costs, but may not be associated with better compliance[26]

Bi-level PAP
- Has fixed higher level of inspiratory PAP than expiratory PAP
- Mainly used for management of patients with respiratory failure caused by concomitant or overlapping syndromes (e.g. obesity hypoventilation)

Adaptive servoventilation
- Delivers variable level of inspiratory PAP and a fixed lower level of expiratory PAP
- Can be used in patients with cardiac failure, Cheyne–Stokes respiration or complex sleep apnoea

TABLE 3. ENT SURGICAL PROCEDURES FOR THE TREATMENT OF SNORING AND OSA

Surgical procedure	Indications
Nasal reconstruction	Correction of nasal septal and/or bony deviation, collapse of alar valve or rim, turbinate hypertrophy
Adenoidectomy and/or tonsillectomy	Adenoidal and/or tonsillar hypertrophy
Uvulopalatopharyngoplasty (UPPP)	Enlargement of collapsible retropalatal space by removal of swollen and elongated uvula and posterior soft palate including reconstruction of lateral pharyngeal pillars
Mandibular osteotomy with genioglossus muscle advancement; hyoid myotomy suspension; surgery of base of tongue (by laser or radiofrequency techniques or linguoplasty)	Correction of tongue base (hypopharyngeal space) by advancement of tongue or supporting structures or direct tongue tissue volume reduction
Maxillomandibular advancement osteotomy	Frank mandibular deficiency or significant OSA in patients with treatment intolerance or noncompliance
Tracheotomy	Severe OSA unresponsive to other treatment modalities

include bi-level PAP and adaptive servo - ventilation, which are used in more complex forms of sleep-disordered breathing.

There is a wide selection of mask interfaces available, ranging from full-face masks covering the nose and mouth to nasal masks or nasal pillows with or without the use of an additional chinstrap. Nasal masks are the most commonly used. Heated humidification can be added to the PAP circuit to help with mouth dryness if needed. Patients should be assisted in selecting the optimum PAP interface for their individual needs. Education about equipment function and maintenance should also be provided to ensure maximum treatment tolerance and efficacy. PAP therapy should be followed up closely by adequately trained healthcare personnel, particularly during the first few weeks of treatment but also in the long term, with monitoring of objective usage data and assessment of symptom control at regular intervals.

Oral appliances

Oral appliances continue to emerge and gain importance as an alternative treatment for OSA. A wide variety of oral devices is now available in various designs. Most oral appliances work by protruding the mandible and are called mandibular advancement splints (MAS). Although they are generally recommended for the treatment of mild-to-moderate OSA, they can also provide effective treatment for some patients with severe OSA. MAS are preferred by many patients because they are easier to use and transport compared with PAP therapy and do not require an electricity supply. The evidence base supporting their clinical use is now strong, and the health outcomes of treatment appear to be similar to CPAP.[27,28] Successful treatment requires an interdisciplinary care model, involving a dentist with appropriate training and experience.

Nasal management

Nasal dilators that are placed on the nostrils are not endorsed for the treatment of snoring, the improvement of sleep architecture or sleep disordered breathing in patients with OSA.[29] However, since the side effect profile and cost of nasal dilators are low, many patients will undertake a trial, and a small subset may derive benefit.

Although short-acting nasal decongestants are not endorsed for the management of OSA, topical nasal corticosteroids

may be helpful in reducing obstructive events in patients with coexisting rhinitis.[1]

A novel approach to the treatment of OSA involves the application of high expiratory resistance valves to both the nostrils to create expiratory positive airway pressure (EPAP). Early clinical data demonstrate benefit in selected patients.[30]

ENT surgery

The principle of surgery for patients with OSA is to correct or bypass the site(s) of anatomical airway obstruction. Interventions are often combined and performed in stages addressing the relevant nasal, retropalatal or retrolingual level of upper airway narrowing.[31] Careful preoperative assessment of the airway is critical to selecting the appropriate patient and surgical procedure(s).

Although adenoidectomy and/or tonsillectomy have been shown to be effective OSA treatment modalities, other surgical therapies should be regarded as a last resort for patients who have either declined or failed treatment with an oral appliance or PAP, or who are snorers with minimal OSA. (See Table 3 for more details regarding different upper airway surgical procedures for the treatment of snoring and OSA.) Surgery can also play an important adjunctive role in facilitating use of CPAP therapy.

Bariatric surgery

Bariatric surgery has been proven to result in substantial weight reduction and is indicated in morbidly obese patients whose BMI is 40 kg/m^2 or more, or 35 kg/m^2 or more with significant comorbidities and previous failed weight loss attempts with diet. It may be considered in addition to other first-line treatment modalities for OSA in patients who qualify for it.[32,33]

Other treatment approaches

Patients with residual excessive daytime tiredness may be treated with stimulant medications (e.g. modafinil). The use of stimulant medications should only occur after confirmation of optimal OSA-specific treatment compliance and effectiveness, as well as a thorough exclusion of other conditions causing persistent sleepiness, such as inadequate sleep, poor sleep hygiene, periodic limb movement disorder, depression or underlying narcolepsy.[1]

No pharmacological agent is currently available to effectively treat patients with OSA, although research continues in this area. Other areas of active research include electrical pacing of upper airway muscles (e.g. hypoglossal nerve stimulation) and oral exercises.

ROLE OF THE GP

The role of the GP in managing patients with OSA includes:

- awareness/clinical suspicion of OSA, especially in patients with known risk factors and comorbidities
- appropriate referral of patients for further specialist investigation and management
- ongoing supervision of behavioural modifications (e.g. weight loss).

CONCLUSION

OSA is a condition with significant health impacts and a rising prevalence. GPs are ideally placed to identify those at higher risk, to refer these patients for further investigation and to institute treatment in collaboration with sleep specialists. There are now several OSA-specific treatment options, the choice of which depends on disease severity, symptoms and patient characteristics and preferences. Behavioural modification addressing modifiable risk factors is an essential component of management in many instances and GPs play an important role in this regard. MT

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COMPETING INTERESTS: Professor Cistulli has contributed to the development of an oral appliance for the treatment of OSA that is being commercialised by SomnoMed Ltd and he previously served on their Medical Advisory Board. His department has received financial and equipment support for the conduct of investigator-initiated and/or sponsored clinical studies from SomnoMed Ltd and ResMed Inc. He is a consultant for Exploramed Inc, a medical device incubator developing a novel treatment for OSA. Drs Palnitkar and Zimmermann do not have any competing interests.

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