Recent advances in the sleep apnoea/hypopnoea syndrome

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This review highlights some of the advances in sleep apnoea/hypopnoea syndrome made over the last few years, particularly in diagnosis and treatment. Recent evidence of the controversial associations of sleep apnoea/hypopnoea syndrome with increased morbidity and mortality, particularly from cardiovascular disease, is presented.

Sleep apnoea/hypopnoea syndrome (SAHS) occurs when episodes of partial or complete obstruction of the pharyngeal airway occurs during sleep. This characteristically causes repetitive apnoeas (arbitrarily defined as cessation of airflow for more than 10 seconds) and hypopnoeas (50% reduction in airflow for more than 10 seconds), loud snoring and excessive daytime somnolence. The latter is caused by fragmented sleep because of arousals resulting from the increased respiratory effort needed to overcome the obstructed upper airway.

SAHS is caused by a combination of decreased muscle tone of the upper airway which occurs during sleep and predisposing structural factors that result in a reduced cross-sectional area of the upper airway. The most common factor is obesity, but others include retrognathia, macroglossia or tonsillar hypertrophy.

The prevalence of SAHS is about 4% in men and 2% in women, which is similar to other diseases perceived as being common such as diabetes and asthma (Young et al, 1993). It becomes commoner with increasing age. Recent work has suggested that the condition still goes unrecognized and underdiagnosed (Kramer et al, 1999). The sex difference may be the result of several factors such as higher airway muscle tone in women related to female hormones, more soft tissue volume in the neck of men and a greater proportion of fat in the neck of males compared to their bodies as a whole (Schwab, 1999).

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ASSOCIATIONS OF SAHS

Cardiovascular disease

SAHS has been linked to increased morbidity and mortality, particularly from coronary heart disease and stroke. The association is controversial (Wright et al, 1997) and the mechanisms of any association are yet to be fully established. Recent studies have strengthened the case for an association between SAHS and systemic hypertension (Young et al, 1997).

A recent prospective study has also demonstrated increased mortality (relative risk 2.2), particularly from cardiovascular causes, in 'sleepy snorers' under the age of 60 years, even with confounding factors such as obesity, hypertension and diabetes corrected for (Lindberg et al, 1998). Another study has confirmed a two-fold increased risk of stroke in patients with SAHS (Quereshi et al, 1997).

The definitive answer as to whether SAHS causes cardiac events, stroke, hypertension and increased all-cause mortality should be answered by The Sleep Heart Health Study, a multicentre prospective study, sponsored by the United States National Heart, Lung and Blood Institute, which is currently in progress (Quan et al, 1997). However, it should be noted that treatment of SAHS is designed to improve the sometimes disabling symptoms of the condition and not long-term survival.

Road traffic accidents

There is evidence that patients with SAHS have between three and four times increased risk of road traffic accidents than those without SAHS (Teran-Santos et al, 1999). This relationship is significant even when confounding factors such as alcohol, sleep schedule and history of traffic accidents are adjusted for. Treatment with nasal continuous positive airway pressure (CPAP) has been shown to improve simulated driving performance (George et al, 1997) and its use may therefore reduce the risk of accidents in patients with

SAHS. The standards of fitness to drive issued by the Driver and Vehicle Licensing Agency states that patients with SAHS should not drive if they continue to suffer from excessive awaketime sleepiness. However, driving can be resumed once sleepiness is corrected even if subjects are reliant on nasal CPAP.

DIAGNOSIS

The diagnosis rests on the frequency of hypopnoeas and apnoeas demonstrated (apnoea/hypopnoea index (AHI), also called the respiratory disturbance index (RDI)) in patients with appropriate symptoms. The AHI required to make a diagnosis has not been standardized but levels of more than 15/hour are usually considered sufficient to warrant treatment and greater than 30/hour represents severe disease.

The severity of symptoms, in particular daytime somnolence, is of major importance in the decision to implement treatment. This can be quantified using the Epworth sleepiness scale, an 8-item self-administered questionnaire that has been validated against the multiple sleep latency test which measures the speed of onset of sleep and is a useful predictor of SAHS (Pouliot et al, 1997) (*Figure 1*). This lack of definitive criteria for commencing treatment reflects a spectrum of disease severity causing excessive daytime sleepiness from 'simple' snoring through the upper airways resistance syndrome (UARS) to severe SAHS.

UARS is diagnosed by using oesophageal manometry during sleep to demonstrate excessive negative intrathoracic pressures. These pressures are associated with transient arousals not sufficient to cause apnoeas or hypopnoeas but enough to result in sleep fragmentation (Guilleminault et al, 1993). Oesophageal manometry may also be useful in distinguishing central sleep apnoea/hypopnoea, in which there is a failure of ventilatory drive, from SAHS, particularly when recordings of thoracic or abdominal movements have been unhelpful or suboptimal.

Home diagnosis

The gold standard for diagnosis of SAHS is inpatient overnight polysomnography. This involves measuring oximetry, oral and nasal airflow, ribcage and abdominal movements as well as electroencephalography, electromyography and electro-oculography. Most laboratories now use simpler sleep monitoring systems, reserving full polysomnography for cases in which the diagnosis of the sleep disorder is unclear. However, with increasing recognition of SAHS, demands on most sleep laboratories are high and there has been interest in diagnosing or excluding SAHS at home. There are now several portable sleep systems available that have been validated against polysomnography in a sleep laboratory, and studies have validated their use for home studies (Whittle et al, 1997). These usually measure oximetry, thoracic and abdominal movements and oronasal airflow only. As well as being more convenient for the patient and freeing up sleep laboratory time they offer considerable cost savings, being about a quarter of the cost of an inpatient study (Evans et al, 1997).

TREATMENT

Management of SAHS should always include general measures such as weight reduction, avoidance of alcohol and sedative drugs. The treatment of choice is nasal CPAP. Other options include surgery and oral appliances.

Auto-CPAP

Recent randomized placebo controlled trials have demonstrated improved daytime sleepiness and symptoms with CPAP in SAHS (Engleman et al, 1999; Jenkinson et al, 1999). It acts by providing positive intraluminal pressure at the site of airway collapse, usually the hypopharynx at the level of the posterior soft palate or in the oropharynx at the level of the base of the tongue (*Figure 2*).

The exact pressure for an individual is the lowest required to abolish apnoeas and arousals. Pressures of up to 20 cmH_2O are used but to find the correct pressure requires titra-

How likely are you to doze off or fall asleep in the following situations, in contrast to just feeling tired. Use the following scale to choose the most appropriate number for each situation: 0 = would never doze; 1 = slight chance of dozing; 2 = moderate chance of dozing; 3 = high chance of dozing

Situation	Chance of dozing
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g. a theatre or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in the traffic	_____

Figure 1. The Epworth sleepiness scale. When answers are added together the possible score is 0–24. Scores of up to 10 can be recorded in normal subjects. Scores of 16 or more indicate a high level of daytime sleepiness and are found in people with sleep apnoea/hypopnoea syndrome of at least moderate severity (apnoea/hypopnoea index > 15) or other conditions such as narcolepsy or idiopathic hypersomnia (see text).

tion which is usually performed by a sleep technician in a sleep laboratory and can therefore be time consuming, labour intensive and expensive. Other methods of determining the required pressure have been investigated such as a split-night protocol, home and partner titration or predictive formulas.

Auto titration of CPAP is a technique that has been validated against manual titration and is being increasingly used. 'Intelligent' CPAP machines find the therapeutic pressure required for long-term treatment or, in patients needing high or variable pressure, can continually adjust to a patient's requirements during the night on a long-term basis. They use feedback signals such as airflow or mask pressure (for apnoeas, hypopnoeas and flow limitation) and snoring to decide when to increase or decrease their pressure. Studies have confirmed its effectiveness and have shown that it can be performed outside the sleep laboratory and could be used in the home, ensuring its cost effectiveness (Lloberes et al, 1996; Bekani et al, 1998).

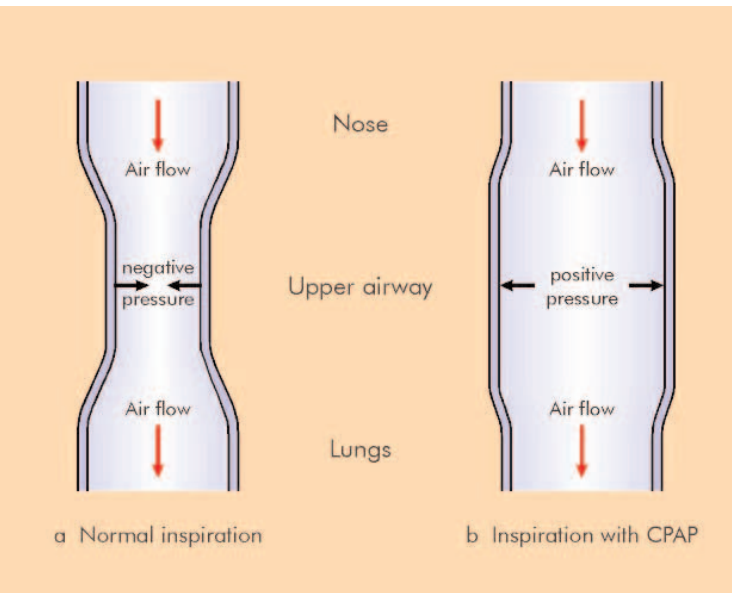

Figure 2. The effect of nasal continuous positive airway pressure (CPAP) on the upper airway. Positive intraluminal pressure generated by CPAP opposes the negative pressure in the upper airway created during inspiration. The airway is therefore prevented from collapsing and some dilatation may occur during expiration.

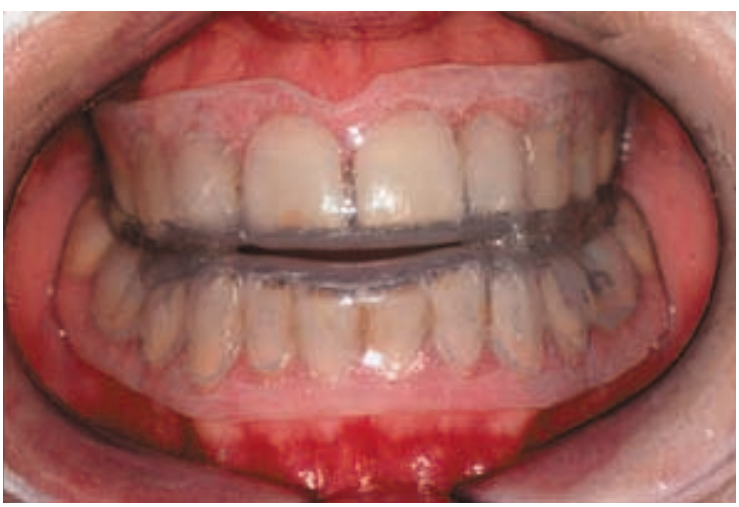

Figure 3. Patient wearing a mandibular advancement device.

Oral appliances

Side-effects of nasal CPAP are minor and mainly related to discomfort from the mask, the pressure itself, and nasal drying resulting in congestion and discomfort. Despite this CPAP is refused after a trial in up to 25% of patients and not tolerated in the long term by 20% of patients, although tolerance is even less in the more mild forms of SAHS (McArdle et al, 1999). As a result alternative treatments have been examined, the most promising of which has been oral appliances (*Figure 3*).

There are two main types of devices, the tongue-retaining device that advances the tongue and the mandibular advancement device. The latter device is used overnight and designed to attach to one or both dental arches and pull the mandible forward up to 75% of the maximum possible. This increases the anteroposterior diameter of the retroglossal space, thereby decreasing the degree of pharyngeal collapse.

Some of the newer devices are adjustable, which has the advantage of allowing additional jaw advancement if a patient's SAHS is undertreated or decreased advancement if the patient experiences excessive jaw pain. These devices are usually constructed by orthodontists using impressions and cost up to £400, although the price is falling as experience increases. There are now untested universal devices available over the counter costing around £40.

There have been several randomized crossover trials comparing mandibular advancement devices with nasal CPAP in patients with mild to moderate sleep apnoea (Ferguson et al, 1997). Reductions in AHI and daytime sleepiness have been demonstrated and although not as marked as with nasal CPAP these results suggest that mandibular advancement devices, particularly the adjustable ones, may be of benefit in patients with mild to moderate SAHS. It is not known if these devices will help patients with more severe SAHS and the effects of their long-term use on the temporomandibular joint requires further study.

Larger randomized multicentre studies are currently underway which will help define the role of these devices more clearly. Nasendoscopy can predict outcome of uvulopalatopharyngoplasty (UVPPP) in patients with SAHS. This may be useful in identifying the site of obstruction and therefore predict those patients more likely to achieve a successful outcome with mandibular advancement devices. Studies are required to confirm its place in the management of SAHS.

Pharmacological treatment

Drug treatment of SAHS has great appeal as it would be better tolerated than CPAP and oral appliances, increasing compliance and cost effectiveness, and potentially safer than surgery.

Protriptyline is a non-sedating tricyclic antidepressant that decreases the time spent in rapid eye movement (REM) sleep, which is the phase of sleep in which SAHS is usually worse. It decreases REM apnoeas, the severity of oxygen desaturation and daytime somnolence (Brownell et al, 1982). However, anticholinergic side-effects, particularly urinary hesitancy and impotence, are frequent which limits its use.

Fluoxetine is as effective and better tolerated. Medroxyprogesterone, a ventilatory stimulant, has been shown to be of no benefit in SAHS and acetazolamide, which can stimulate ventilation as a result of inducing a metabolic acidosis has been shown to worsen SAHS in some studies. Numerous drugs have been tried but as yet no universal panacea has been found (Hudgel and Thanakitcharu, 1998). HM

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KEY POINTS

- Sleep apnoea/hypopnoea syndrome (SAHS) is a common condition that remains under-diagnosed.
- Symptoms include snoring, excessive daytime sleepiness, poor concentration and nocturia. Apnoeas may be witnessed by a partner.
- There is increasing evidence of an association of SAHS with hypertension, ischaemic heart disease, stroke and an increased risk of road traffic accidents.
- Polysomnography is the gold standard for diagnosis. Home sleep studies are sufficient for most cases and are more cost effective.
- Nasal continuous positive airway pressure is the treatment of choice. Auto titration devices are a more efficient method of finding the required pressure for treatment.
- Oral appliances should be offered to patients intolerant of continuous positive airway pressure.