ADVANCES IN SLEEP MEDICINE

M El-Nazer, Consultant Physician
Furness General Hospital

INTRODUCTION

Sleep medicine is a new area in respiratory clinical practice, particularly in the UK. This review highlights the recent advances made in sleep apnoea/hypopnoea syndrome (SAHS) over the last few years, particularly in diagnosis and treatment, and its well-established role as a cause of impaired daytime performance and road traffic accidents, in addition to the associated increased risk of morbidity and mortality from cardiovascular disease.

BACKGROUND AND DEFINITIONS

Some degree of SAHS is present in 5-20% in adult men but symptomatic SAHS occurs in approximately 1-4% of middle aged men and in half as many women⁽¹⁾.

“Apnoeas are classified as obstructive ‘when the upper airway narrows or closes repeatedly during sleep’, and central ‘when the drive to breathe is reduced periodically’.”

Apnoeas are classified as obstructive ‘when the upper airway narrows or closes repeatedly during sleep’, and central ‘when the drive to breathe is reduced periodically’. This review is confined to the obstructive sleep apnoea/hypopnoea syndrome (SAHS) which is far more common than central apnoea.

SAHS is a result of decreased tone of the upper airway dilating muscles which occurs during sleep producing a reduced cross-sectional area of an already narrower than normal upper airway. This is due to pre-disposing structural factors, the most common being obesity (50% have a body mass index of >30) thought to be due to increased adipose tissue loading in the neck resulting in narrower throats⁽²⁾. Other factors include retrognathia, macroglossia, or tonsillar hypertrophy, or alcohol and sedatives.

Recent studies suggest that in thin patients the syndrome tends to run in families with shortened mandibles⁽³⁾. An apnoea is defined arbitrarily as ‘cessation of breathing for 10 seconds or more’ while hypopnoea refers to a reduction in airflow for similar duration.

Many authorities describe this sleep abnormality in terms of the apnoea/hypopnoea index (AHI) or respiratory disturbance index (RDI), ie the average number of periods of apnoea and/or hypopnoea per hour of sleep. However opinions recently moved away from rigid definitions and for practical purposes, SAHS requires the presence of demonstrable apnoea, hypopnoea or flow limitation (‘upper airway resistance syndrome’) (UARS) during sleep in the context of appropriate clinical presentation.

UARS (a controversial entity) is daytime sleepiness as a

result of increased flow limitation insufficient to cause apnoeas or hypopnoeas leading to recurrent transient arousals evident by excessive negative intrathoracic pressure on oesophageal manometry⁽⁵⁾.

Daytime sleepiness is a result of nocturnal sleep disruption as each apnoea or hypopnoea is terminated by a transient arousal which restores the tone in the muscles surrounding the pharynx, allowing the airway to re-open. This occurs hundreds of times each night and, as a result, patients with obstructive sleep apnoea essentially suffer from sleep deprivation.

It is thought that SAHS is part of a spectrum of disease ranging from simple snoring and UARS to advanced disease hypoventilation in obesity described as Pickwickian Syndrome. These stages are considered to be the result of a very slow progression over the years⁽⁴⁾ which can be reversed as shown in Figure 1⁽¹⁾.

Figure 1 Sleep-disordered breathing: a spectrum of abnormality

ASSOCIATIONS OF SAHS

Road traffic accidents

There has been increasing evidence over recent years that SAHS predisposes patients to being involved in road traffic accidents. Epidemiological studies have investigated the risk in subjects from the general population with disordered breathing and those with AHI >15 were found to have a seven-fold increase in the risk of being involved in multiple road traffic accidents in the recent past⁽⁶⁾. Even more challenging is a driving simulator study carried out in Canada that suggested sleepiness due to SAHS is associated with a marked driving impairment comparable to that produced by a blood alcohol level above the legal limit for driving⁽⁷⁾. This impairment is shown to respond to nasal continuous positive airway pressure therapy (nCPAP) in a controlled study⁽⁸⁾.

In the UK the DVLA regulations state that driving must cease if the driver is excessively sleepy from any cause.

Group 1 drivers (ordinary licence holders) with a diagnosis of SAHS should notify the DVLA, but can drive provided their sleepiness is controlled by treatment.

Group 2 drivers (public service and heavy goods vehicles) should cease driving until the DVLA has received confirmation by a specialist that their condition is adequately treated.

CARDIOVASCULAR DISEASE

A rise in BP is a normal accompaniment to arousal from sleep from any cause and SAHS causes recurrent arousal as a result of frequently increasing respiratory efforts with consequent rises in the nocturnal BP⁽⁹⁾. It is unproven whether the increases in nocturnal BP can lead to sustained systemic hypertension as patients with SAHS have a high prevalence of systemic hypertension due to other confounding factors such as obesity and smoking, hence the controversy regarding the association⁽¹⁰⁾. Recent studies have strengthened the case to associate SAHS with systemic hypertension following a prospective study that has demonstrated increased mortality (relative risk 2.2), particularly from cardiovascular causes in ‘sleepy snorers’ under the age of 60 years, with confounding factors such as obesity, hypertension and diabetes corrected for⁽¹¹⁾. Another study has confirmed increased risk from stroke in patients with SAHS⁽¹²⁾.

More recent epidemiological studies controlling for as many confounding factors as possible now strongly suggest beyond any reasonable doubt that SAHS is an independent risk factor for daytime hypertension with a four-fold increase in the group with AHI>15/h compared to AHI=0/h (with odds ratio of 2.89 compared to 1.42 respectively)⁽¹²⁾. The results of a large prospective multicenter study (The Sleep Heart Health Study) currently in progress should give a definitive answer as to whether SAHS causes cerebrovascular diseases, cardiovascular diseases and increased all-cause mortality⁽¹⁴⁾.

Early reports indicate that those with AHI values of >30/h are 1.37 times more likely to have hypertension (>140/90) or be on antihypertensives after allowing for confounders.

DIAGNOSIS

The diagnosis of SAHS rests on the frequency of hypopnoeas and apnoeas as demonstrated in patients with appropriate symptoms. The AHI has been divided into three stages: mild (5-15), moderate (16-30), severe (>30)⁽¹⁵⁾. Even though not standardized, a level above 15/hour is considered sufficient to warrant treatment for daytime sleepiness.

The severity of symptoms has been quantified by using the Epworth sleepiness scale, an eight-item questionnaire which asks patients to estimate the likelihood of falling asleep in a variety of different situations (Figure 2).

The gold standard for diagnosis of SAHS is by inpatient overnight polysomnography using a variety of physiological signals measuring oximetry, oral and nasal airflow, ribcage and abdominal movements as well as electroencephalography, electromyography and electro-oculography. Most laboratories use simple sleep monitoring systems, reserving full polysomnography for cases in which the diagnosis remains unclear. Recently there have been high demands on sleep laboratories due to increasing interest in and recognition of SAHS. Portable sleep systems (Figure 3) have

Name .....

Date .....

Your age (Yr) ..... Your sex ☐ Male ☐ Female

How likely are you to doze off or fall asleep in the situations described in the box below, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently, try to work out how they would have affected you.

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 (eg 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 lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	

Figure 2 The Epworth sleepiness scale

become available and are more utilized after being validated by studies in their use at home⁽¹⁶⁾. The use of these systems is considered more cost-effective and convenient for the patients.

TREATMENT

The main clinical indication for treating SAHS is to reduce daytime sleepiness and improve quality of life. Management should always include general measures such as weight reduction and avoidance of alcohol and sedative drugs, but such advice is often disregarded.

The treatment of choice is nasal continuous positive airway pressure (nCPAP) which is by far the most effective treatment⁽¹⁷⁾. It immediately and completely corrects upper airway obstruction (snoring, hypopnoea and apnoea) and the consequent sleep disruption. Evidence of its benefit is now overwhelming, both from uncontrolled studies^(18,19,20) and, more recently, controlled studies⁽²¹⁾ (Table1).

Recent development in dental appliances⁽²²⁾ or mandibular advancement devices (Figure 4) has provided an alternative

	Placebo	nCAP	p value
Change in ESS	-2	-7	<0.0001
Change in MWT (min)	0	6.75	0.005
SF-36 mental component summary (effect size)	0.4	1.02	<0.0001
SF-36 energy and vitality dimension (effect size)	0.97	1.68	0.002
Effect size is calculated by dividing the mean change in the variable by the baseline standard deviation (0.50 = moderate effect size; 0.80 = large effect size).			
ESS = Epworth sleepiness score (subjective measure of sleepiness); MWT = maintenance of wakefulness test (objective measure of sleepiness); SF-36 = short form 36 quality of life questionnaire.			

Table 1 Change in sleepiness and quality of life after placebo continuous positive airway pressure (CAP) and real nasal CPAP (nCPAP) at one month⁽²¹⁾

Figure 3a Recording before sleep

Figure 3b Recording during sleep showing obstructive sleep apnoea

treatment option for patients with mild to moderate SAHS whose symptoms are not severe enough to warrant nCPAP⁽²³⁾. If worn overnight these devices open the retroglossal space by holding the tongue and/or mandible forward. Most appliances can be fitted by a maxillofacial surgeon working with the respiratory sleep clinic.

The alternative surgical option may be appealing to young patients as a single treatment, compared to the possible need for a lifetime of nCPAP. It is, however, not uniformly successful and should only be considered in a minority of carefully selected non-obese cases. Uvulopalatoplasty (UPPV) is designed to increase the volume of the pharynx by resecting the pharyngeal wall tissue and the soft palate. It has significant morbidity, particularly perioperative pain, and nasal fluid regurgitation in up to 20% of patients with occasional mortality⁽²⁴⁾. There is insufficient data on its effect in SAHS.

Recent data⁽²⁵⁾ suggest that in a minority of thin young patients major reconstructive surgery to the jaw (mandibular advancement osteotomy) can result in just as satisfactory an outcome as nCPAP therapy.

Other advances in maxillofacial surgical techniques are still awaiting assessment.

CONCLUSION

SAHS causes daytime sleepiness with significant impairment of work performance and quality of life. It also contributes to

Figure 4 Mandibular repositioning appliance. This mandibular repositioning oral appliance is manufactured in a laboratory from dental impressions (Klearway appliance, Great Lakes Orthodontics, Inc, Tonawanda, NY)

many road traffic accidents and an increased risk of cardiovascular morbidity.

The condition is common, occurring in perhaps 1-4% of the middle aged population, with serious side effects, yet a recent survey⁽²⁶⁾ suggests that it is still not taken seriously by purchasing authorities in the UK.

REFERENCES

- 1 Davies RJO, Stradling JR. The epidemiology of sleep apnoea. *Thorax* 1996; 51(suppl. 2):565-70
- 2 Mezzanote WS, Tangel OJ, White DP. Waking genioglossal electromyogram in sleep apnoea: patients versus normal controls (a neuromuscular compensatory mechanism). *J Clinical Investigations* 1992;89:1571-9
- 3 Marhur R, Douglas NJ. Family studies in patients with the sleep apnoea/hypopnoea syndrome. *Ann Intern Med* 1995;122:174-8
- 4 Lindberg *et al.* Is sleep apnoea a slowly progressive disorder? *Am J Respir Crit Care Med* 1999;159:2024
- 5 Guilleminault C, Stoohs R, Clerk A *et al.* A cause of excessive daytime sleepiness: the upper airway resistance syndrome. *Chest* 1993;104:781-7
- 6 Young T, Bhistein J, Finn L, Palta M. Sleep disordered breathing and motor vehicle accidents in a population based sample of employed adults. *Sleep* 1997;20:608-13
- 7 George CFP, Bondreau AC, Smilie A. Simulated driving performance in patients with obstructive sleep apnoea. *Am J Respir Crit Care Med* 1996;154:175-81
- 8 Hack MA, Davies RJO, Mullins R, Stradling JR. Randomised, sham placebo, controlled study of nasal continuous positive airway pressure (CPAP) on simulated steering in obstructive sleep apnoea (OSA). *Am J Respir Crit Care Med* 1999;159:A429

- 9 Davies RJ, Vardi-Visy K, Clarke M, Stradling JR. Identification of sleep disruption in sleep disordered breathing from the systolic blood pressure profile. *Thorax* 1993; 48:1242-7
- 10 Wright J, John R, Watt I *et al*. The health effects of OSA and the effectiveness of treatment with continuous positive airways pressure: a symptomatic review of the research evidence. *Br Med J* 1997;314:851-60
- 11 Lindberg E, Janson C, Svardsudd K *et al*. Increased mortality among sleepy snorers: a prospective population based study. *Thorax* 53:1998;631-7
- 12 Quereshi AL N, Giles WH, Croft JB *et al*. Habitual sleep patterns and risk for stroke and coronary heart disease: a 10 year follow up from NHANES I. *Neurology* 1997;48:904-11
- 13 Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep disordered breathing and hypertension N England J Med 2000;342:1378-84
- 14 Ruan SF, Howard BV, Iber C *et al*. The Sleep Heart Health Study: design, rationale and methods. *Sleep* 1997;20:1077-85
- 15 Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medical Task Force. *Sleep* 1999;22(5):667-89
- 16 Whittle AT, Finch SP, Mortimore IL *et al*. Use of home sleep studies for diagnosis of the sleep apnoea/hypopnea syndrome. *Thorax* 1997;52:1068-1070
- 17 Sullivan CE, Issa FG, Berthon-Jones, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1981;i:862-5
- 18 Hardinge FM, Pitson DJ, Stradling JR. Use of the Epworth sleepiness scale to demonstrate response to treatment with nasal continuous positive airway pressure in patients with obstructive sleep apnoea. *Respir Med* 1995;89:617-20
- 19 Smith IE, Shneerson JM. Is the SF sensitive to sleep disruption? A study in subjects with sleep apnoea. *J Sleep Res* 1995;4:183-8
- 20 Jenkinson C, Stradling J, Peterson S. Comparison of three measures of quality of life outcome in the evaluation of continuous positive airway pressure therapy for sleep apnoea. *J Sleep Res* 1997;6:199-204
- 21 Jenkinson C, Davies RJO, Mullins R, Stradling JR. Comparison of therapeutic and sub-therapeutic nasal continuous positive airway pressure of obstructive sleep apnoea: a randomised prospective parallel trial. *Lancet* 1999;353:2100-5
- 22 Schmidt-Nowara W, Rowe A, Wiegand L, Cartwright R *et al*. Oral appliances for the treatment of snoring and obstructive sleep apnoea: a review. *Sleep* 1995;18:501-10
- 23 Ferguson KA, Ono T, Lowe AA *et al*. A short term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. *Thorax* 1997;52:362-8
- 24 Fujita S, Conway W, Zorick F, Roth T. Surgical correction of anatomic abnormalities in obstructive sleep apnoea syndrome: uvulo palato-pharyngoplasty. *Otolaryngol Head Neck Surg* 1981;89:923-34
- 25 Conrad TR, Hochban W, Heitmann J *et al*. Sleep fragmentation and daytime vigilance in patients with OSA treated by surgical maxilla mandibular advancement compared to CPAP therapy. *J Sleep Res* 1998;7:217-23
- 26 Gibson GJ, Douglas NJ, Stradling JR *et al*. Sleep apnoea: clinical importance and facilities for investigation and treatment in the UK. *J R Coll Phys Lond* 1998;32(6):540-44