Management of obstructive sleep apnoea syndrome

PRASHANTHI RATNAKUMAR AND ARI MANUEL

Obstructive sleep apnoea (OSA) describes the pathological narrowing and collapse of the upper airway in recurrent episodes during sleep. This can result in a variety of symptoms that markedly affect quality of life. In addition, other chronic complications, most significantly the development of long-term cardiovascular disease, are increasingly becoming recognised.

Obstructive sleep apnoea (OSA) is already a staunch contributor to the national burden of respiratory disease and this burden is growing rapidly. Healthcare professionals are now increasingly aware of presenting symptoms such as snoring, ‘choking’ episodes during sleep and excessive daytime somnolence. When excessive daytime sleepiness is present, the condition is referred to as obstructive sleep apnoea syndrome (OSAS).

This review explores current knowledge regarding the epidemiology, pathogenesis, diagnosis and treatment of OSAS, as well as looking in more detail at the links between OSAS and other common co-morbidities – an area of growing research interest that may provide alternative targets for therapeutic intervention.

Epidemiology

Although OSAS was first described in the 1970s, epidemiological figures are a relatively recent work in progress, only stretching back over the last 15 to 20 years. Estimates of prevalence vary, most likely due to a combination of differences in methodological assessment. Ideally, diagnosis of OSAS requires polysomnography conducted during an overnight sleep study; a time-consuming and expensive measure with limited patient compliance.

At present, OSA is thought to affect approximately 10–17 per cent of men and 3–9 per cent of women aged 30–70 years. These figures are primarily based on data from the Wisconsin Sleep Cohort, a prospective community-based study ongoing since 1988, which has used relatively rigorous methods of polysomnography and ongoing assessment to follow its study population. However, although current UK guidance uses these estimates, more recently, the HypnoLaus study conducted in Switzerland4 surveyed over 2000 individuals and recorded prevalences of 49.7 per cent in men and 23.4 per cent in women. It is also important to recognise that there is likely to be a high prevalence of patients with undiagnosed...
THERAPY FOCUS | Obstructive sleep apnoea

Pathogenesis
The underlying pathogenesis of OSA is multifactorial. In normal physiology, the nasal passages and hard palate at the upper end of the pharynx have bony and cartilaginous foundations, providing a relatively fixed diameter for airflow. At the lower boundary, the trachea is structured in a similar fashion. The portion of the airway between these two regions is highly dependent on pharyngeal muscle activity and tone, as well as the balance of intraluminal against extraluminal pressure. Ordinarily, this flexibility is key to the pharynx’s role in complex actions such as speech and swallowing.

However, where the pressure outside the pharynx (extraluminal) is greater than the intraluminal pressure, the airway narrows or collapses. During wakefulness, our conscious neuromuscular control assists with overcoming this; however, during deep sleep, the loss of conscious control facilitates varying degrees of obstruction, and subsequent hypopnoea or apnoea. This finding in association with OSA was first characterised in 1978 by Remmers et al. Additional factors contributing to airway collapse have been widely studied since, including the concept that anatomically narrower airways may be more prone to collapse and the role of instability of ventilatory feedback systems, which respond to low oxygenation and raised carbon dioxide to resolve obstruction.

As the upper airway obstructs, sympathetic nervous activity to increase respiratory drive, which eventually restores breathing patterns and reopens the airways. In patients with OSAS, this can occur many times a night, and the intermittent cycles of hypoxaemia and periodic states of arousal play a key role in driving many of the co-morbidities associated with OSAS.

Risk factors
Classically, risk factors for the development of OSAS include age, male gender and obesity. Of these, obesity is certainly one of the most commonly highlighted risk factors, as well as one of the most modifiable. Obesity can result in biomechanical imbalances due to the increase in adipose tissue exerting extraluminal pressure on the pharynx, causing a pressure imbalance, as described above. Numerous studies have shown that obesity, and particularly neck circumference, are independent predictors of OSAS. Weight gain can increase the severity of OSAS; conversely, weight loss can moderately decrease severity.

The association with obesity is also more pronounced in men than in women. Studies consistently demonstrate a higher prevalence of OSAS in men compared with women, and suggest that in women, OSAS severity is linked to a higher degree of obesity than the corresponding severity in men. Various mechanisms have been postulated to explain this, including different distributions of fat deposition in men and women, and hormonal influences related to testosterone levels (it is notable that OSAS in women is more commonly found post-menopause).

One of the largest cohort studies conducted in Pennsylvania demonstrated a notable increase in the prevalence of OSAS with increasing age, quoted as being two to three times greater in the 65-year-plus age group compared with those aged 30–64 years. This may be a consequence of age-related increases in fat deposition, particularly around the pharynx, as well as changes in the structure and elasticity of the pharyngeal muscles with time.

In addition to age, sex and weight, many other risk factors have now been identified. Differences in craniofacial anatomy, such as maxillary and mandibular lengths, as well as characteristics such as enlarged tonsillar tissue are recognised as mechanical contributors. Ethnicity is thought to play a role; although many of the studies on OSAS have been carried out on North American or European populations with a large Caucasian component, there is now more data emerging suggesting that patients of Asian origin have higher rates of OSAS for a given level of obesity, which may relate to possible differences in craniofacial anatomy. In addition, familial predisposition and genetics are increasingly recognised as important factors, with a higher risk in first-degree relatives.

Table 1 summarises the key risk factors involved in the development of OSAS.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Possible associations with smoking and increased alcohol intake</th>
<th>Possible associations with asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age</td>
<td>Male gender</td>
<td>Asian ethnicity</td>
</tr>
<tr>
<td>Obesity (BMI &gt;30)</td>
<td>First-degree relatives with OSAS</td>
<td>Craniofacial anomaly, eg tonsillar hypertrophy, retrognathia</td>
</tr>
</tbody>
</table>

Patients who may be suffering from OSAS commonly present with symptoms associated with fragmented sleep and repeated arousals, as a result of recurrent airway obstruction. Table 2 summarises the common presenting symptoms. Excessive daytime sleepiness is a cardinal feature, although not always part of the initial presentation. Determining the degree to which daytime sleepiness occurs, and its impact on both quality of life and safety, eg when driving or at work, is extremely important, and can help guide decisions regarding treatment.

Often, patients present in conjunction with partners or other family members, Table 2. Symptoms of obstructive sleep apnoea syndrome (OSAS)

- Snoring
- Sleep fragmentation – waking frequently throughout the night
- Excessive daytime sleepiness: falling asleep during conversation or meals, or during periods of low activity, eg sitting in traffic
- Feeling unrefreshed on waking
- Poor concentration during the day, irritability, mood swings
- Early morning headaches – due to increasing hypercapnia overnight
- Nocturia or nocturnal sweating
- Decreased libido

Table 1. Risk factors for the development of obstructive sleep apnoea syndrome (OSAS)
who have noticed heavy snoring with characteristic pauses, followed by a gasp or choking sound as an arousal state triggers reopening of the obstructed airway. For this reason, collateral histories are often very useful. The role of GPs and community health professionals in eliciting such histories and considering a diagnosis of OSAS is therefore invaluable.

Differential diagnoses to consider are listed in Table 3, as well as being summarised in the 2015 NICE guidance. The NICE guidance also provides a helpful summary of ‘red flag’ symptoms; the most concerning differential diagnosis is that of upper airway obstruction secondary to an upper airway malignancy. Features such as recurrent epistaxis, change in voice or swallowing, or increasing severity of symptoms that are not accompanied by concomitant weight gain should be treated with more suspicion.

Further assessment of possible OSAS includes physical examination, looking particularly at parameters such as BMI, neck circumference and features of craniofacial anatomy, for example enlarged tonsils. Basic biochemical tests, including thyroid function tests, should also be carried out.

Using written tools to help evaluate the severity of symptoms, such as the Epworth Sleepiness Scale (ESS) score or the STOPBang questionnaire, is also extremely useful in quantifying the impact on life. The ESS is a well-validated scoring system, with a specificity quoted at 80 per cent in detecting excessive daytime sleepiness (defined as a score of greater than 10/24 on the questionnaire).

In addition, enquiring about any problems with sleepiness while driving, operating heavy machinery or during occupational responsibilities is important for patient and public safety. It may be necessary to discuss the involvement of employers or the DVLA where safety is at risk. Urgent referral for assessment may be necessary, warning patients not to drive or undertake high-risk jobs, eg operating heavy machinery, until they have been assessed and symptoms are adequately controlled with treatment (see Table 4).

### Table 3. Key differential diagnoses of obstructive sleep apnoea syndrome (OSAS)

#### Diagnosis
Where OSAS is suspected, patients should be referred for assessment in a sleep medicine unit with overnight sleep studies using polysomnography, if available. This consists of a series of measurements to assess various physiological parameters such as oxygenation, thoracic wall movement, airflow and breathing patterns. Ideally, this is conducted in an overnight sleep centre with trained technicians, but there is now increasing use of overnight polysomnography assessment at home, which can provide sufficient information to diagnose OSA with considerably less logistical inconvenience to patients.

Diagnosis is based on the number of apnoea/hypopnoea events per hour, creating an apnoea-hypopnoea index (AHI) figure. Under five events per hour is considered normal, with AHI scores of 5–14, 15–29, and greater than 30 being graded mild, moderate and severe OSA respectively.

When polysomnography is not available, alternative diagnostic studies utilising respiratory variables (limited sleep study) or oximetry may be helpful in supporting the diagnosis.

#### Treatment
In mild sleep apnoea, lifestyle considerations should be addressed as part of management. Weight loss, aiming for a BMI of less than 25, is recommended. Other therapies should ideally be considered alongside this, as there is evidence to suggest that weight loss can decrease the severity of OSAS, but it may not reverse the pathophysiology completely owing to the multifactorial nature of the disease. Advice should also be given about changing sleeping position, eg advising a patient to sleep on their side rather than on their back, and on avoidance of alcohol or stimulants prior to bedtime.

In moderate to severe OSAS, or where the impact on daily life is significant, the mainstay of therapy is the use of positive pressure ventilation at home, via a continuous positive airways pressure (CPAP) machine. The patient is provided with a small device and a mask, which they wear over their nose and mouth overnight. The machine produces a continuous positive filtered airflow, which splints the upper airways open, allowing the patient to breathe spontaneously but preventing upper airway narrowing or collapse. The pressures can be altered to meet the needs of individual patients.

A 2006 Cochrane meta-analysis by Giles et al. evaluating 36 studies, concluded that CPAP was a highly effective intervention, decreasing AHI by up to 80%.
Patients with excessive daytime sleepiness, regardless of cause or a formal diagnosis of OSAS, should not drive if sleepiness occurs to a degree that could impact on the ability to drive safely, eg ability to complete an emergency stop.

Where a diagnosis of OSAS is suspected or made, medical professionals are obligated to inform patients of their responsibilities with regard to the DVLA.

If OSAS is suspected or diagnosed, patients are responsible for notifying the DVLA and completing the relevant paperwork. They may then be asked to refrain from driving until they have received treatment and symptoms are adequately controlled.

Once symptoms are controlled, patients may be allowed to return to driving if deemed safe to do so following ongoing assessment and liaison with the DVLA.

### Table 4. DVLA guidance on obstructive sleep apnoea syndrome (OSAS)

<table>
<thead>
<tr>
<th>Points</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Points with excessive daytime sleepiness, regardless of cause or a formal diagnosis of OSAS, should not drive if sleepiness occurs to a degree that could impact on the ability to drive safely, eg. ability to complete an emergency stop.</td>
<td></td>
</tr>
<tr>
<td>• Where a diagnosis of OSAS is suspected or made, medical professionals are obligated to inform patients of their responsibilities with regard to the DVLA.</td>
<td></td>
</tr>
<tr>
<td>• If OSAS is suspected or diagnosed, patients are responsible for notifying the DVLA and completing the relevant paperwork. They may then be asked to refrain from driving until they have received treatment and symptoms are adequately controlled.</td>
<td></td>
</tr>
<tr>
<td>• Once symptoms are controlled, patients may be allowed to return to driving if deemed safe to do so following ongoing assessment and liaison with the DVLA.</td>
<td></td>
</tr>
</tbody>
</table>

Complications and future prospects

Alongside our increasing understanding of OSAS as a disease is a growing body of knowledge about its associated co-morbidities. More importantly, we are increasingly recognising that controlling the pathological processes underpinning OSAS may also help control such co-morbidities, and vice versa.

Perhaps the most well-established link is between OSAS and vascular risk, in particular a connection with resistant hypertension (defined as blood pressure >140/90mmHg despite the use of three or more antihypertensive agents). The recurrent arousals during episodes of apnoea in OSAS and associated sympathetic surges drive adrenaline release, resulting in highly fluctuating blood pressure, which can in turn cause arterial wall shear stress and endothelial cell dysfunction, leading to the development of hypertension over time.

A meta-analysis by Iftikhar et al. in 2014 looked at six studies that assessed hypertension pre- and post-intervention with CPAP for the treatment of OSAS, and found an overall mean net change of -7mmHg in systolic blood pressure over 24-hour monitoring in patients using CPAP: a modest improvement. Another meta-analysis conducted by Schein et al. looked at 16 randomised controlled trials and found similar modest improvements in blood pressure following OSAS treatment. However, what is not yet well characterised is how well treatment of OSAS protects against vascular-related morbidity and mortality, and various prospective studies are ongoing to assess this. The link between coronary heart disease (for which vascular disease can be considered a surrogate marker) and OSAS is also being investigated.

Similarly, a high prevalence of type 2 diabetes in patients with OSAS is also recognised. OSAS and the spectrum of co-morbidities comprising metabolic syndrome, diabetes, and fatty liver disease share common features of high levels of fat deposition and insulin resistance in peripheral tissues, and so it is unsurprising that these diseases often co-exist. However, studies to date suggest that CPAP is of limited benefit in reducing insulin resistance.

### Conclusion

OSAS continues to be a significant and underdiagnosed respiratory cause of morbidity. The condition is often identified in the primary care setting, and may present via a collateral history from a bed partner rather than the patient themselves. Formal diagnosis requires overnight sleep studies, usually carried out at tertiary sleep units.

The mainstay of therapy for moderate or severe OSAS continues to be CPAP initiated with the support of a multidisciplinary sleep and ventilation team. It is becoming increasingly recognised that OSAS can exist in parallel with, and contribute to, a number of other medical conditions, and control of OSAS via conservative and medical therapies may potentially assist in the management of these conditions.

### References

Obstructive sleep apnoea l THERAPY FOCUS  ■


Declaration of interests
None to declare.

Prashanthi Ratnakumar is a core medical trainee in Oxford Deanery and Ari Manuel is a consultant at Cheltenham General Hospital