

Obstructive sleep apnoea: a review of current management

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INTRODUCTION

Sleep apnoea is a condition characterised by a temporary cessation of breathing during sleep. There are three types of sleep apnoea – central, obstructive, and mixed. Central sleep apnoea is defined as a sleep-related breathing disorder which occurs as a result of the respiratory centre in the *medulla oblongata* failing to send the appropriate signals to the respiratory muscles which initiate respirations. Obstructive sleep apnoea (OSA) occurs due to passive collapse of the pharyngeal airway during deep sleep, causing intermittent upper airway obstruction. Mixed sleep apnoea, as the name suggests, has manifestations of both central and obstructive sleep apnoea.

OSA affects approximately 1-2% of the population worldwide and is most common in overweight, middle-aged men but can present in all ages. Population studies have shown that OSA is becoming more and more prevalent in adults, in particular one in five adults are now thought to suffer from mild OSA.⁽¹⁾

The aetiology of OSA can be grouped according to the site of obstruction of the upper airway and associated reason for obstruction (see figure 1). It should be noted that other causes of obstruction that do not directly originate in the airway can also cause OSA. OSA has been linked to longterm health problems such as hypertension, cardiovascular disease, metabolic problems and neurocognitive dysfunction.⁽²⁾

Site	Cause of OSA
Nasopharynx	Nasal polyps Deviated nasal septum Rhinitis Adenoids
Oropharynx	Obesity Macroglossia Enlarged tonsils
Laryngopharynx	Obstructive lesions, eg tumour
Other	Respiratory depressant drugs, eg alcohol, sedatives Smoking Anthropometric (males, middle age, obesity) Mechanical factors (supine posture)

Figure 1 Aetiology of OSA

The pathophysiology of OSA is complex and is not fully understood but it is generally accepted that OSA occurs when the airway is sucked closed whilst breathing during sleep, causing hypopnoea (breathing that is shallower or slower than normal) or apnoea (where breathing stops completely). Apnoea is usually terminated by brief arousals which cause sleep fragmentation and change in sleep architecture; markedly reduced slow-wave sleep and rapid-eye-movement sleep. Patients are usually unaware of this; however, the changes in

sleep architecture contribute to chronic daytime sleepiness. When awake, the airway does not get sucked closed whilst breathing as the muscles of the upper airway (the genioglossus and palatal muscles) stop this from occurring. These muscles become hypotonic during sleep. The upper airway collapses when the force produced by these muscles is exceeded by the negative airway pressure generated by inspiratory activity of the diaphragm and intercostal muscles. Therefore, obstruction can occur if the suction pressure is too high or if the counteracting forces of the genioglossus and palatal muscles are too weak.⁽³⁾

The clinical features of OSA are summarised in figure 2. OSA is diagnosed by full history, examination and various investigations. By definition, OSA is the occurrence of 15 or more episodes of apnoea or hypopnoea during one hour of sleep. Investigations used to aid diagnosis include: overnight pulse oximetry; computed tomography; and, the 'gold standard' test, polysomnography. During polysomnography, the following are monitored: pulse oximetry; electrocardiogram; electromyography; and, abdominal/chest wall movement. A further invasive investigation that may help diagnose the level of obstruction is sleep nasendoscopy. This involves induction of deep sleep with an anaesthetic agent and nasendoscopy performed by an otolaryngologist.

Clinical features of OSA
Snoring Apnoeic episodes during sleep Nocturnal choking Daytime somnolence Restless sleep/poor sleep quality Morning headache Reduced libido Decreased cognitive performance

Figure 2 The clinical features of OSA

There are numerous conservative, medical and surgical treatment modalities currently available to manage OSA. These are summarised in figure 3. The treatment modalities will be discussed in the review of literature/discussion to include their efficacy and side effects. OSA can cause stigmatisation, embarrassment and marital issues in sufferers. Therefore, effective management is essential for this debilitating and socially embarrassing disorder.

DISCUSSION

Conservative management

Literature suggests that lifestyle changes such as weight loss in the obese, smoking cessation, reduced alcohol intake (<7 units per week), nasal dilating clips and sleeping in a non-supine position may improve symptoms.⁽⁴⁾

Conservative management	<ul style="list-style-type: none"> • Weight loss • Reduced alcohol consumption • Smoking cessation • Mandibular advancement splints/other mandibular advancement appliances
Medical management	<ul style="list-style-type: none"> • Various drugs • Positive airway pressure
Surgical management	<ul style="list-style-type: none"> • Uvulopalatopharyngoplasty • Laser assisted uvulopalatopharyngoplasty • Tonsillectomy and adenoidectomy • Tracheostomy • Inferior sagittal mandibular osteotomy and genioglossus advancement with hyoid myotomy and suspension (GAHM) • Laser midline glossectomy • Lingualplasty • Maxillo-mandibular osteotomy • Removal of other obstructing pathological lesions • Palatal implants
<i>Figure 3 Management modalities for OSA</i>	

Mandibular advancement splints (MAS) are increasingly being used as a conservative management modality in OSA (see figure 4).⁽⁵⁻⁷⁾ It should be noted that there are various types of MAS and the one below is an example of one particular type. Other oral appliances are also available for sleep apnoea, but most of the literature found reported the use of MAS. MAS are now considered as an alternative to continuous positive airway pressure (CPAP), which will be discussed later. MAS cause anterior displacement of the mandible and base of the tongue; thereby increasing the calibre of and preventing the collapse of the upper airway during sleep.⁽⁷⁾ The American Academy of Sleep Medicine suggests that MAS are appropriate for patients with mild-moderate OSA where CPAP is not appropriate, eg those that are unable to tolerate CPAP.⁽⁸⁾ Other literature also advocates that MAS are a good alternative to CPAP as the effectiveness of CPAP is often compromised by poor patient compliance.^(9,10) It should be noted that there are also compliance issues with MAS.

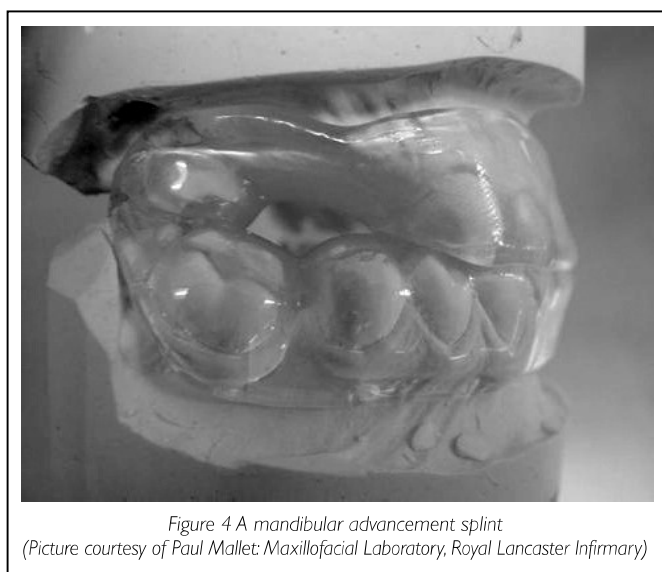


Figure 4 A mandibular advancement splint
(Picture courtesy of Paul Mallet: Maxillofacial Laboratory, Royal Lancaster Infirmary)

One particular randomised control trial (RCT) which trialled mandibular repositioning splints (MRS) – a type of MAS – and nasal CPAP reported that after completing the trial 40% of patients preferred MRS as their final treatment choice, 25% preferred nasal CPAP and 35% preferred neither.⁽¹¹⁾

At 12-month follow-up, the majority of patients were still compliant with the treatment option of their choice. A particular problem with the MRS was temporomandibular discomfort. This RCT used a very small cohort. Further larger RCTs are required to truly understand which treatment is preferred by patients.

Another RCT has shown that MAS are significantly effective in improving symptoms of OSA. Participants reported subjective outcomes using the Epworth Sleepiness Scale (see appendix) and objective improvement was reported using polysomnography. The results of the trial were very positive, stating a significant difference between the results of the intervention group and control group.⁽¹²⁾ Other similar studies have reported similar findings; predominantly significant improvements in OSA symptoms with MAS.^(13,14) The success rate of MAS can be high; however, side effects such as dental pain, excessive salivation and temporomandibular joint pain are regularly reported by patients which may limit their use.^(4,11) Although many RCTs exist regarding the efficacy of MAS, most have very small sample sizes, subsequently small cohorts and short follow-up.

A large meta-analysis consisting of 745 participants has shown that oral appliances such as MAS and tongue stabilising devices improve symptoms of OSA; however, there is no definite evidence to suggest that oral appliances are as effective as the 'gold standard' CPAP therapy.⁽¹⁵⁾

Medical management

Medications such as those which increase respiratory drive, eg cocaine and adrenaline, are not currently licensed to treat OSA in the UK. There is also no evidence to suggest that drugs reduce OSA morbidity and mortality.⁽¹⁶⁾

Positive airway pressure (PAP) is a treatment for OSA. There are three types of PAP:

- continuous positive airway pressure (CPAP)
- autotitration
- bi-level positive airway pressure (BiPAP)

Autotitration enables the minimum necessary pressure to be administered according to the patients need, and BiPAP is a variation of CPAP. For this review, the focus of PAP therapy was CPAP as this therapy is the form of PAP that is most commonly used to treat OSA.

CPAP is a ventilation therapy which is delivered to the airway. A flow of air is delivered at a constant pressure throughout the respiratory cycle so that the airway remains patent. CPAP therefore acts as a type of 'pneumatic splint'. It is indicated for patients who are able to initiate respirations but are not able to maintain adequate arterial oxygen levels without assistance; therefore, CPAP is an appropriate treatment modality for OSA. In patients with OSA, CPAP is usually administered using a nasal or oronasal mask; but can also be administered through an endotracheal tube or nasal cannula. In practice, most patients use CPAP for approximately four hours per night; others use it for part of the night or all of the night. Side effects are generally few, with the most common being nasal stuffiness.⁽¹⁶⁾

Numerous literature, including RCTs, have shown that CPAP is effective in improving the subjective and objective symptoms of OSA. These include improvement in sleep quality, reduction

of apnoea/hypopnoea episodes and reduction in daytime sleepiness.⁽¹⁷⁻¹⁹⁾

In 2009, a study reported on a meta-analysis of 48 clinical effectiveness trials (the majority being RCTs) for CPAP in the treatment of OSA.⁽²⁰⁾ The majority of studies used the Apnoea Hypopnoea Index to measure objective outcome (see figure 5). Results of the meta-analysis showed a statistically significant improvement in OSA symptoms, including daytime sleepiness with CPAP compared to controls.

Apnoeas/hypopnoeas per hour	Apnoea Hypopnoea Index
5-20	Mild
21-50	Moderate
>51	Severe

Figure 5 Apnoea Hypopnoea Index

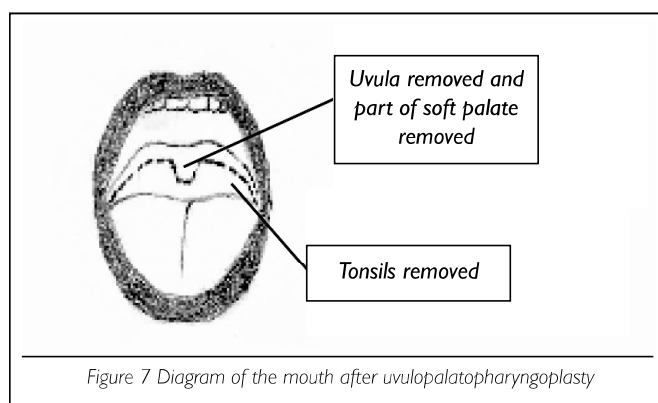
The 2009 study concluded that CPAP is effective in the management of OSA, although longterm follow-up was lacking. Furthermore, there was no difference between CPAP and dental appliances.⁽²⁰⁾

Unsurprisingly, CPAP is poorly tolerated and many patients do not comply. Compliance can be helped by group cognitive behavioural therapy.⁽¹⁹⁾

Surgical management

The surgical management techniques for OSA are summarised in figure 6. The literature search was restricted to uvulopalatopharyngoplasty (UPPP/UPPP) trials, as this is the surgical procedure most commonly used for OSA. It should be noted that some patient groups may benefit from other surgeries according to their anatomical features, eg tonsillectomy for enlarged tonsils. UVPP is a surgical procedure whereby the airway is widened by the removal of excess soft tissue including the uvula, tonsils and part of the soft palate. Removal of these tissues widens the airway, thus allowing air to move through more easily (see figure 7).

A recent non-randomised prospective case series reported on the outcome of UVPP conducted on patients with OSA.⁽²¹⁾ Using objective and subjective measures (including the



Epworth Sleepiness Scale and AHI) the study showed that UPPP was effective and safe in OSA patients that had previously failed non-surgical treatment. The success rate of UPPP varied between 54-64%, with the overall satisfaction rate being 88%. Limitations of this study were that there were no controls and the lack of a robust study design. Even so, the results of the trial were promising. Other small, similarly designed case series were found which report similar outcomes.^(22,23)

Two RCTs for UVPP with comparison to conservative/CPAP management were found. One reported a significant difference in daytime sleepiness symptoms in favour of UVPP with comparison to conservative measures, but no difference in objective measures was found.⁽²⁴⁾ Contrary to these findings, the other found that there was a significant difference in favour of oral appliance therapy compared with UVPP with regards to AHI outcome.⁽²⁵⁾ However, these two RCTs cannot be directly compared and used to create a conclusion due to the differences in the technique used to measure outcome. Both studies also had a very small sample size.

A recent review by the Cochrane Collaboration reported on findings from 12 RCTs of mixed quality.⁽⁵⁾ In total, the results from surgical procedures conducted on 709 participants with mild-moderate symptoms of OSA were analysed. In summary, the review concluded that there was insufficient evidence to support the widespread use of surgical procedures over conservative methods to treat OSA. Some RCTs included in

Surgical management technique	Description
Uvulopalatopharyngoplasty (UPPP)	The airway is widened by the removal of excess soft tissue including the uvula, tonsils, and part of the soft palate
Laser-assisted uvulopalatoplasty (LAUP)	A modification of UPPP. A laser is used to vaporise part of the uvula and soft palate as opposed to sharp dissection
Tracheostomy	A direct opening is created into the trachea, bypassing any obstruction completely. No longterm RCTs support this modality for OSA
Tonsillectomy and adenoidectomy	Commonly used to treat OSA in children
Inferior sagittal mandibular osteotomy and genioglossus advancement with hyoid myotomy and suspension (GAHM)	Soft tissue and bony advancement which subsequently enlarges the airway
Laser midline glossectomy	Stops the tongue from obstructing the airway
Lingualplasty	Enlarges the retrolingual airway
Maxillo-mandibular osteotomy	Enlarges the retrolingual and retropalatal airway by bony advancement
Removal of other obstructing pathological lesions	Increase the calibre of the airway
Palatal implants	Stiffen the soft palate tissue to reduce the flutter that causes obstruction of the upper airway

Figure 6 The surgical techniques currently available to treat OSA

	Advantages	Disadvantages
Conservative management <i>Lifestyle changes</i>	<ul style="list-style-type: none"> • No medical/surgical intervention required • No side effects 	<ul style="list-style-type: none"> • No disadvantages
<i>Mandibular advancement splints</i>	<ul style="list-style-type: none"> • Good alternative to CPAP in mild-moderate cases • Does not require invasive surgery 	<ul style="list-style-type: none"> • Longterm therapy required • Side effects • Compliance issues
Medical management <i>Drugs</i>	<ul style="list-style-type: none"> • No advantages 	<ul style="list-style-type: none"> • Numerous side effects
<i>Continuous positive airway pressure</i>	<ul style="list-style-type: none"> • Effective in improving symptoms in OSA • Side effects are generally few with the most common being nasal stuffiness 	<ul style="list-style-type: none"> • Compliance issues • Longterm therapy
Surgical management <i>Uvulopalatopharyngoplasty</i>	<ul style="list-style-type: none"> • Effective in treating OSA in some cases • One-off procedure 	<ul style="list-style-type: none"> • Numerous side effects
<i>Figure 8 Summary of advantages and disadvantages of management of OSA</i>		

the review showed some statistical differences between surgery versus conservative methods in favour of surgery; however, adequate controls were not of common practice and the complete exclusion of selection bias could not be excluded. There was also a distinct lack of longterm follow-up.

Longterm follow-up of patients is rare with regards to surgical treatment for OSA. However, during the literature search one retrospective cohort study was found which reported on the survival rates between patients treated with CPAP or UVPP for OSA. The study found that UVPP survival was better than CPAP survival. CPAP patients had a 31% greater mortality compared with UPPP patients. The study had a very large sample size; however, it did have limitations – only 10% of the cohort had UPPP, OSA severity was not noted and co-morbidities and confounding were not reported.⁽²⁶⁾

The literature found on UVPP for OSA suggests that in some cases UVPP is effective in reducing subjective and objective outcomes. However, there is a dearth in the literature. RCTs and other robustly designed studies are lacking.

As expected, the methodological challenge of designing appropriately controlled trials for surgery are huge. Patients with significant co-morbidities cannot ethically be subjected to sham operations or travel large distances to take part in large cohort studies or be followed up.

In summary, influential guidelines published in America and Scotland on the subject offer conflicting advice on the role of surgery.^(8,27)

CONCLUSION

Figure 8 summarises the advantages and disadvantages of conservative, medical and surgical management of OSA.

Conservative management of OSA includes lifestyle changes and the use of MAS and other oral appliances. There are compliance issues with MAS as patients are required to wear them every night, as is the case with CPAP. Overall, results of trials of MAS for OSA are promising, but much more research is required to support the efficacy of MAS as a comparable treatment to CPAP.

Unfortunately, no drugs currently exist that can be used as a treatment for OSA. The development of a drug to maintain

airway patency would be a real breakthrough in the treatment of OSA; however, due to the complex pathophysiology of OSA this is not likely.

A large amount of literature was found during the review that suggests that CPAP is an effective treatment for OSA. There is much robust RCT evidence that supports the use of CPAP in OSA; as a result of this CPAP is currently the 'gold standard' treatment modality in the management of OSA.

There is a succinct lack of RCT evidence to support the use of UVPP in OSA. The difficulties of RCT design make it difficult to make any conclusions. Numerous small case series have reported safe and effective outcomes of UVPP for OSA. A major difficulty in interpreting and comparing the results of any study is the lack of consistency of outcome measures. The Epworth and AHI scores, for example, are not consistently used. A standardised scoring system would be clearly useful in allowing future developments to be evaluated.

Given the obvious constraints imposed by the lack of RCT, the following tentative conclusions can be made:

MAS, CPAP and UVPP are effective treatments in improving symptoms of OSA. However, the level of evidence for each modality varies. The most robust evidence is in favour of management using CPAP, followed by the use of MAS. The least robust evidence was found in favour of UVPP. There is a dearth in the literature regarding surgical UVPP management. Further RCTs in larger populations with longer follow-up are required to ascertain if this management modality is safe and effective enough to compete with CPAP or MAS for the treatment of OSA.

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Appendix

Epworth Sleepiness Scale (ESS)

The ESS is an eight-question scale of sleep behaviour. The scale is scored according to the likelihood of 'dozing off' when sitting doing various activities such as reading, attending a meeting, travelling as a car passenger, resting after lunch, as a driver stuck in traffic, watching television or in a conversation. It also asks about the habit of taking an afternoon nap.

Readers who have struggled to get through this article can check their Epworth score online:

http://www.britishtsnoring.co.uk/sleep_apnoea/epworth_sleepiness_scale.php