Obstructive sleep apnoea syndrome: treatment update

DSC Hui, DKL Choy, FWS Ko, TST Li, CKW Lai

Obstructive sleep apnoea syndrome is a common but underrecognised disorder with associated substantial morbidity and mortality. Excessive daytime sleepiness caused by the disorder leads to poor work performance and increases the risk of an individual having an automobile accident. The main objective of treatment for sleep apnoea is the relief of disabling daytime sleepiness and the improvement of quality of life. Conservative measures such as weight reduction and the avoidance of alcohol should be initiated when appropriate. Nasal continuous positive airflow pressure devices have remained the standard treatment since it was first introduced in 1981. Oral appliances provide an alternative treatment choice in mild-to-moderate cases, whereas surgery is useful in selected cases.

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Key words: Orthodontic appliances; Positive-pressure respiration; Sleep apnea, obstructive/therapy; Snoring/surgery

Introduction

Sleep-disordered breathing (SDB) represents a continuum ranging from simple snoring without sleepiness, upper-airway resistance syndrome, and obstructive sleep apnoea (OSA) syndrome, to hypercapnic respiratory failure. Apnoea is defined in general as the cessation of airflow of at least 10 seconds. Hypopnoea refers to a reduction in amplitude of airflow of $\geq 50\%$ of the baseline measurement that lasts for more than 10 seconds (Table 1).\(^1\) Sometimes, episodes of transient and partial airflow limitation, without apnoea or hypopnoea, occur with no significant oxygen desaturation resulting. However, the increasing respiratory efforts to overcome the upper-airway resistance result in frequent arousals and excessive daytime sleepiness (upper-airway resistance syndrome).\(^2\)

Obstructive sleep apnoea syndrome, defined as an apnoea/hypopnoea index (AHI) of 5 or more—that is, at least five apnoeic/hypopnoeic events per hour of sleep—plus reported sleepiness, is a common form of SDB. This condition affects 2\% to 4\% of adults aged from 30 to 60 years;\(^3\) prevalence increases with age.\(^4\) Repetitive episodes of obstructive respiratory events cause sleep fragmentation, hypoxia and, in more severe cases, hypercapnia. Excessive daytime sleepiness is a major complication of OSA and is the result of fragmented sleep and micro-arousals associated with obstructive respiratory events. Impaired alertness predisposes OSA patients to work-related or driving accidents and poor work and social functioning.\(^5\) People with OSA are involved in more motor vehicle accidents, with an accident rate seven times that of the general driving population.\(^6\) Preliminary evidence also suggests that patients with OSA are at increased risk of cardiovascular complications such as hypertension, cardiac arrhythmia,\(^7\) myocardial infarction,\(^8\) pulmonary hypertension,\(^9\) and stroke.\(^10\) The treatment objectives for OSA patients are to improve symptoms and quality of life, and to reduce mortality and morbidity. The treatment of sleep apnoea and its co-morbid conditions consists of conservative, medical, or surgical interventions (Table 2).

Conservative interventions

All patients with OSA should be warned regarding the increased risks of motor vehicle accidents, job-related injuries, and bodily impairment. Alcohol and sedatives such as benzodiazepines reduce the muscle tone in the upper airway and should be avoided. Sleep deprivation can increase upper-airway obstruction during sleep by reducing the muscle tone in the upper airway and by blunting arousals.\(^11\) Hence, it is
important to ensure that patients have an adequate amount of sleep. When an individual sleeps in the supine position, OSA occurs more often; sleeping in lateral positions can help ease the problem in mild cases. Smokers have more severe upper-airway oedema and it is advisable that smoking patients with significant OSA quit smoking. It is also important to look for and treat underlying causes such as hypothyroidism, acromegaly, and nasal obstruction, which may be associated with OSA. Weight reduction is effective in treating sleep apnoea and where appropriate, it should be encouraged. However, weight loss is difficult to achieve and maintain; other forms of treatment are often required.

Medical interventions

A number of medical interventions are available for the treatment of OSA. They include positive airway pressure devices, oral appliances, and certain medications.

Positive airway pressure devices

Nasal continuous positive airway pressure (CPAP) was introduced by Sullivan et al in 1981 as a pneumatic splint to prevent collapse of the pharyngeal airway and has become the first-choice therapy for OSA. There are now at least five randomised placebo-controlled studies that demonstrate significant improvement of symptoms and daytime function with the use of nasal CPAP in the treatment of OSA. The first was published in 1994; a group of 32 patients with moderate OSA and a mean AHI of 28 were studied. Compared with oral placebo, use of CPAP for a mean period of 3.4 hours per night resulted in significant symptom improvement, sleepiness (as measured by multiple sleep latency tests), and improved vigilance, cognitive function, quality of life, and mood. Similar improvements have been demonstrated recently in a group of 23 patients with severe OSA and a mean AHI of 43.

| Table 1. Definitions of terms used in obstructive sleep apnoea

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Apnoea</td>
<td>Cessation of airflow of at least 10 seconds</td>
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<tr>
<td>Hypopnoea</td>
<td>≥50% decrease in airflow amplitude of at least 10 seconds; or &lt;50% decrease in airflow amplitude associated with either an arousal or oxygen desaturation of ≥3%</td>
</tr>
<tr>
<td>Respiratory effort-related arousal</td>
<td>An event characterised by increasing respiratory effort for ≥10 seconds, leading to an arousal from sleep but which does not fulfill the criteria for a hypopnoea or apnoea</td>
</tr>
<tr>
<td>Apnoea/hypopnoea index</td>
<td>No. of apnoea + hypopnoea episodes per hour of sleep</td>
</tr>
<tr>
<td>Respiratory disturbance index</td>
<td>No. of apnoea + hypopnoea episodes + arousals per hour of sleep</td>
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| Table 2. Treatment options for obstructive sleep apnoea

<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Measure used</th>
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<tbody>
<tr>
<td>Conservative</td>
<td>Lose weight, sleep in lateral position, avoid alcohol</td>
</tr>
<tr>
<td>Medical</td>
<td>Use nasal continuous positive airway pressure, auto-continuous positive airway pressure, bilevel positive airway pressure, use oral appliances, give medication, treat associated diseases, eg hypothyroidism, acromegaly, allergic rhinitis</td>
</tr>
<tr>
<td>Surgical</td>
<td>Tracheostomy, nasal procedure, eg turbinectomy, polypectomy, septoplasty, uvulopalatopharyngoplasty, laser-assisted uvulopalatoplasty, maxillo-mandibular advancement</td>
</tr>
<tr>
<td>Experimental</td>
<td>Pharyngeal pacing, radio-frequency ablation, rapid maxillary expansion</td>
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Patients with mild OSA have also been helped by CPAP treatment. It has been shown to improve symptoms, mental flexibility, and mood when compared with oral placebo in a group of 16 OSA patients with AHI scores between 5 and 15. In a second study of 34 patients with mild OSA (defined as an AHI of 5-15 plus subjective sleepiness), Engleman et al again found an improvement in symptoms, subjective sleepiness, quality of life, and cognitive function, which was achieved by the use of CPAP for a mean of only 3.5 hours. Compared with the group receiving sham CPAP treatment (in which the pressure was
Jenkinson et al reported a greater improvement in both subjective and objective sleepiness when active CPAP was used for a mean of 5.3 hours. Thus, CPAP improves symptoms across the full range of OSA severity and confers more benefits in the moderate-to-severe groups.

In addition, two retrospective studies and one recent prospective study show that the use of nasal CPAP reduces driving accidents and naps during driving. The retrospective study showed that OSA patients treated with CPAP had significant improvement in subjective sleepiness, driving distance, concentration at work, and general health. The multicentre prospective study showed that the number of patients who had an accident decreased with CPAP treatment. The number of real and near-miss accidents declined (from 60 to 36 [P<0.01] and from 151 to 32 [P<0.01], respectively). The average number of accidents per patient also decreased significantly for real accidents and near-miss accidents. The result may have important implications for cost/benefit calculations made when treating OSA patients.

Although CPAP is an effective treatment for OSA, it is cumbersome and minor unpleasant side effects can occur (Table 3). The optimal duration of CPAP treatment is not known, and patients obviously have to tolerate discomfort for the benefits of the therapy. Nevertheless, most CPAP users derive benefits, with significant symptom improvement despite a mean CPAP use of less than 4 hours each night. In a recent study conducted at the Prince of Wales Hospital, patients were measured with an objective time-clock. The study revealed that the mean CPAP use among patients was 5.3 hours and 72% used CPAP for at least 4 hours each night for at least five nights weekly. This compliance rate compares favourably with the reported compliance rate of 46% for an American population.

**When should CPAP treatment be commenced?**

A retrospective study by He et al showed that patients with an apnoea index (number of apnoeic episodes per hour) of >20 without treatment had decreased survival, when compared with patients with an apnoea index less than this value. The same study also showed that patients with an apnoea index of >20 who were treated with nasal CPAP had improved survival compared with those who did not use CPAP. Most sleep disorder centres have been influenced by this study and, in the past, patients with an AHI of >20 were prescribed nasal CPAP. As our understanding of OSA has improved, it is now clear that AHI correlates poorly with subjective and objective measures of sleepiness, which is the main symptom of OSA. It is therefore inappropriate to select an arbitrary AHI value to define the severity of OSA and suitability for treatment.

Upper-airway obstruction during sleep often causes recurrent respiratory effort-related arousals without apnoea or hypopnoea, but which still fragment sleep. Sleep disruption has been shown to cause sleepiness, impaired cognition, and altered mood and to lead to a higher upper-airway collapsibility than does sleep deprivation. Sleep fragmentation is probably the most important predictor of daytime sleepiness and nowadays, the treatment threshold should be much lower, with more emphasis placed on symptoms rather than the respiratory disturbance index. For symptomatic patients with pre-existing hypertension, ischaemic heart disease, or cerebrovascular disease, especially in the presence of significant oxygen desaturation (arterial oxygen saturation <85%) during the obstructive respiratory event, a trial of nasal CPAP treatment should be offered early—even if the respiratory disturbance index falls in the mild category.

**Table 3. Side effects and problems related to use of continuous positive airway pressure**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients, n=112 No. (%)</th>
<th>Significant problem</th>
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<tbody>
<tr>
<td>Nasal blockage/dryness</td>
<td>52 (46)</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Sore nasal bridge</td>
<td>52 (46)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Increased tossing and turning</td>
<td>40 (36)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Sleep disruption</td>
<td>37 (33)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Facial irritation due to mask</td>
<td>36 (32)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Trouble putting on mask</td>
<td>36 (32)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Difficulty operating device</td>
<td>30 (27)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Poor-quality sleep</td>
<td>30 (27)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Embarrassment</td>
<td>29 (26)</td>
<td>0</td>
</tr>
<tr>
<td>Less intimacy with bed partner</td>
<td>25 (22)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

* Data from 3-month follow-up at the Respiratory Clinic, Prince of Wales Hospital, 2000
It is important for medical staff to educate patients and spouses about CPAP regarding its effects and potential side effects. It is essential that the nasal mask is selected and fitted carefully; a variety of nasal masks from different manufacturers are available for use. A short daytime trial of CPAP helps patients to acclimatise. Overnight CPAP titration is essential to determine an optimal pressure for the patient. Automatic CPAP titration with intelligent devices such as the AutoSet (Resmed, Sydney, Australia) and De Vilbiss Horizon (Sunrise Medical, Colorado, United States) systems have been shown to be as good as manual titration.

**Strategies to improve compliance**

If there are problems with CPAP use, it is important to change the nasal mask until the patient feels comfortable. Nasal pillows provide an alternative for patients with claustrophobia. Most patients who are affected by chronic nasal congestion and/or dryness benefit from attempts to reduce mouth leakage with chin straps or by the addition of a humidification system to their CPAP circuit. A delay-timer with a ramp allows the pre-set pressure to be gradually increased, thereby facilitating sleep onset. For patients who have difficulty exhaling against a high expiratory pressure, a bilevel positive airway pressure (BiPAP) device can be used. However, BiPAP has not been shown to improve compliance in patients with OSA.

**New devices**

‘Smart’ CPAP devices such as the Virtuoso (Respironics, Murrayville, United States), De Vilbiss Horizon, Tranquility (Healthclyne Technologies, Georgia, United States) and AutoSet systems have recently become available for the treatment of OSA. These are intelligent devices that can monitor the state of the upper airway and make automatic pressure adjustments during sleep according to the episodes of snoring, apnoea, and hypopnoea. In the case of the Resmed AutoSet, airflow limitation is also detected and pressure adjusted pre-emptively to prevent upper-airway obstruction. These intelligent self-adjusting devices can potentially eliminate the need for a CPAP titration study and have been shown to be as reliable as the conventional fixed-pressure CPAP device, while giving better sleep quality and patient compliance results. Although these automatic CPAP devices hold promise for the future, more data are needed before their cost-effectiveness can be established.

**Oral appliances**

There is growing interest in the use of oral devices to SDB. The initial reports of a potential role for oral appliances in the treatment of OSA were in relation to the tongue-retaining device; subsequent interest focused on the mandibular advancement splint. Oral appliances work by pulling the genioglossus muscle forward; this action increases the dimensions of the upper airway. More than 40 oral devices have been developed in North America, but the efficacy of different oral appliances is quite variable. Side effects are common, especially in the initial phase of use, and include temporo-mandibular joint discomfort, dental misalignment, increased salivation, and gum irritation. The mandibular advancement splint effectively decreases apnoea and improves sleep quality, especially in those with mild-to-moderate OSA. In a randomised crossover study of an oral appliance versus CPAP in patients with mild-to-moderate OSA, the oral appliance was shown to be effective in treating mild-to-moderate cases and achieved greater patient satisfaction. There is also objective evidence that mandibular advancement can significantly reduce the amount of snoring.

**Fig 1. Oral appliances prescribed by the Dental Clinic, Prince of Wales Hospital**

(1a) Mandibular advancement splint; (1b) Casts of dental and jaw structure of patient that are used to make the splint.
that occurs.\textsuperscript{39} Currently, the American Sleep Disorders Association recommends oral appliances as an alternative treatment for snoring and mild OSA, following confirmation by diagnostic sleep study. In addition, for patients with moderate-to-severe OSA who cannot tolerate CPAP treatment, oral appliances provide an alternative therapy; however, the efficacy must be confirmed by a follow-up sleep study.\textsuperscript{39} At the Prince of Wales Hospital, more than 70 mandibular advancement devices have been prescribed by dentists for patients who have had difficulty tolerating CPAP treatment (Fig 1).

\section*{Medication}

In general, medications play a limited role in the treatment SDB. Protriptyline and fluoxetine suppress rapid eye movement (REM) sleep and may reduce apnoea in some cases, but the side effects outweigh the marginal benefits.\textsuperscript{43} Nasal steroids and decongestants are effective in reducing nasal symptoms. Other medications such as progesterone, theophylline, and acetazolamide are not recommended.\textsuperscript{42} The administration of supplementary oxygen does not improve daytime sleepiness and may prolong apnoea in some cases. However, supplementary oxygen can reduce the degree of oxygen desaturation and arrhythmia that develop during obstructive respiratory events.\textsuperscript{43}

\section*{Surgical treatments}

\subsection*{Tracheostomy}

A tracheostomy bypasses the site of the upper-airway obstruction. It is the most effective surgery available for OSA and has been shown to improve survival.\textsuperscript{44} It is seldom performed, however, because of its complications (eg stoma and airway infection, and granuloma formation) and functional limitations (eg difficulty with speech) that require ongoing care.

\subsection*{Nasal surgery}

For patients with nasal septal deviation, bulky nasal turbinates or nasal polyps, procedures such as septoplasty, turbinatectomy, and polypectomy are helpful in removing the mechanical obstruction and can facilitate the use of nasal CPAP. Young children with bulky tonsils and adenoids benefit from having an adenotonsillectomy.

\subsection*{Uvulopalatopharyngoplasty}

Uvulopalatopharyngoplasty (UPPP) was introduced by Fujita in 1981 as a treatment for OSA.\textsuperscript{45} It is associated with significant postoperative discomfort and can result in palatal incompetence, nasal regurgitation on swallowing, and nasal speech. Early studies\textsuperscript{46,47} defined success as a reduction in the AHI by 50%, which was an inadequate result. By reducing AHI from 60 to 30, for example, the result is obviously still unacceptable. A more recent meta-analysis by Sher et al\textsuperscript{48} has shown that there is only a 41% chance of achieving an AHI of <20 following UPPP. Moreover, UPPP did not modify long-term mortality.\textsuperscript{26}

\subsection*{Laser assisted uvulopalatoplasty}

Laser assisted uvulopalatoplasty (LAUP) has been introduced recently as a surgical procedure for the treatment of SDB.\textsuperscript{49} The current indication for this procedure is for snoring alone and not for OSA. It is essential that patients who undergo LAUP to treat snoring also undergo a preoperative diagnostic sleep study to exclude any possibility of concomitant apnoea. Otherwise, the elimination of snoring by the procedure, which is the main symptom of OSA, could result in a delay in the diagnosis of OSA.\textsuperscript{50} A retrospective analysis has shown that LAUP has a success rate of 90% over 5 years in patients who have undergone the procedure for snoring.\textsuperscript{51} More data are needed to evaluate the long-term efficacy of LAUP.

\subsection*{Palatal surgery}

Many techniques have been tried to predict whether or not palatal surgery would be successful. These include the Mueller manoeuvre,\textsuperscript{52,53} cephalometry,\textsuperscript{53} computed tomography,\textsuperscript{54} and endoscopy of the upper airway.\textsuperscript{55} A study investigating sleep endoscopy suggests that if the site of obstruction is exclusively at the level of the nasopharynx, then palatal surgery is more likely to succeed at 4 months but the result is not sustained at 14 months following UPPP.\textsuperscript{55} Overall, the predictability of these techniques is poor. Upper-airway obstruction involves more than one specific site of the upper airway in the majority of patients with sleep apnoea, and obstruction at lower levels of the upper airway is more likely to be observed during REM sleep.\textsuperscript{56} Morrison et al\textsuperscript{57} found that only 18% of OSA patients with sleep endoscopy had airway obstruction limited to the soft palate. The remainder of the patients had multiple sites of airway obstruction. As a result, single-site surgery may not be sufficient to eliminate OSA.

\subsection*{Staged surgical protocol}

Realising the limitation of single-site surgery in the treatment of OSA, Riley et al\textsuperscript{58} have proposed a staged surgical protocol for patients with significant OSA who cannot tolerate CPAP treatment (Fig 2).\textsuperscript{59} Phase I surgery consists of UPPP for retropalatal obstruction and genioglossal advancement for retroglossal obstruction. If obstruction at both sites is found, then both
procedures are performed. Polysomnography is repeated 6 months postoperatively and, if significant OSA persists and patients have abnormal craniofacial structures such as micrognathia and/or retrognathia, then a phase 2 procedure with maxillo-mandibular advancement is performed. Reports indicate that results are comparable to those when CPAP is used, with a >90% response rate and a low complication rate.\(^5^8,^5^9\) The results have been replicated in Germany,\(^^6^0\) with postoperative success maintained over a 2-year period. However, long-term follow-up data are still pending.

**Experimental treatments**

**Electrical pacing**

Electrical pacing using the submental approach was initially attempted by a Japanese group, which showed favourable results in a small number of OSA patients.\(^6^1\) Guilleminault et al\(^6^2\) attempted electrical stimulation using the submental and sublingual approaches in seven patients and found that both approaches did not produce any significant change in AHI, obstructive duration, or the lowest oxygen saturation level. In addition, alpha-electroencephalography arousals were seen secondary to electrical stimulation when breaks of apnoea occurred. Schwartz et al\(^6^3\) attempted pacing of the soft palate with a lower voltage and managed to abolish snoring, but they were unable to consistently stop apnoea. Hence, there is currently no convincing support for the use of electrical stimulation to treat OSA.

**Radio-frequency ablation**

Radio-frequency ablation has been used experimentally for cranial nerve problems, cancer, the Wolff-Parkinson-White syndrome, and prostate hypertrophy for the past two decades. Using a radio-frequency generator, low-level energy is generated producing temperatures around \(80^\circ\)C. Because human protein denatures at approximately \(46^\circ\)C, the radio-frequency energy produces tissue necrosis, scar formation, and a reduction in tissue volume. Using this approach, Powell et al\(^6^4\) were able to achieve a volume reduction of 26% in pig’s tongue. Radio-frequency ablation of the soft palate has been attempted in a small group of humans with simple snoring, upper-airway resistance syndrome, or mild OSA. The participants showed significant reduction in soft palate size, subjective snoring, scores on the Epworth sleepiness scale, and excessive daytime sleepiness. However, there was worsening of AHI 2 to 3 days postoperatively due to oedema, which subsequently subsided and caused the AHI to return to the baseline value.\(^6^5\) More data are needed before any conclusion can be drawn from this procedure.

**Rapid maxillary expansion**

Cistulli and Sullivan\(^6^6\) have reported that patients with Marfan’s syndrome have a high OSA prevalence of 64%. Anatomical abnormalities in patients with Marfan’s syndrome, such as high-arched palate, maxillary constriction, and collapsible upper airway, are believed to contribute to upper-airway obstruction. The degree of OSA in this group of patients has been shown to correlate with maxillary measurement.\(^6^7\) Maxillary
constriction is associated with increased nasal resistance and low tongue posture, which can predispose to retroglossal obstruction.

Rapid maxillary expansion (RME) is an orthodontic procedure in which a fixed orthodontic device is attached to the upper posterior teeth with adjustable tension. The apparatus causes gradual opening of the mid-palatal suture and subsequent maxillary expansion. The full course of maxillary expansion with the orthodontic device takes 3 to 6 months, with active expansion in the first 3 weeks and passive retention during the following 3 to 6 months, when reossification occurs. After the age of 25 years, the mid-palatal line has fused and surgical assistance by way of maxillary osteotomy is needed to facilitate maxillary expansion.

In a group of patients without Marfan’s syndrome but with OSA, high-arched palate, and maxillary constriction, Cistulli et al. used the RME approach and managed to improve significantly the AHI (19 [standard deviation, 4] versus 7 [standard deviation, 4]; P<0.05) and symptoms in patients with mild-to-moderate OSA. Maxillary expansion results in improved nasal airflow and tongue posture as well as improved retroglossal dimensions. Thus, RME may be a useful alternative treatment for selected patients with OSA.

Conclusion

In summary, conservative measures such as weight loss, reduction of alcohol intake, and cessation of smoking should be initiated when appropriate in patients with OSA. In most cases, more definitive treatment is needed. Nasal CPAP remains the treatment of choice for OSA, more than a decade after its use was first reported. While it is undoubtedly an effective therapy, it is not curative, and the search for a simple and curative treatment continues. Oral devices provide useful alternative treatments for those with mild-to-moderate OSA and surgery is useful in some selected cases.

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