

Medical Management of Obstructive Sleep Apnoea

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Introduction

Untreated OSA has many potential consequences and adverse clinical associations, including excessive daytime sleepiness, impaired daytime function, metabolic dysfunction, and an increased risk of cardiovascular disease and mortality.

General Approach - The goals of OSA therapy are to resolve signs and symptoms of OSA, improve sleep quality, and normalise the apnoea-hypopnoea index (AHI) and oxyhaemoglobin saturation levels.

OSA should be approached as a chronic disease that requires long-term, multidisciplinary management. The potential benefits of successfully treating OSA include clinical improvement (e.g., less daytime sleepiness), reduced health care utilisation and costs, and, possibly, decreased cardiovascular morbidity and mortality.^{1,2}

Medical management of OSA

Education And Behaviour

Patient education - The management of a patient with OSA begins by firmly establishing the diagnosis and its severity. Disease severity guides management by identifying patients who are at greatest risk for adverse outcomes and by providing a baseline from which to measure the

effectiveness of treatment.¹

Once the diagnosis of OSA is confirmed and its severity determined, the results of all testing should be reviewed with the patient. The patient should be educated about the risk factors, natural history, and consequences of OSA.¹ All patients should be warned about the increased risk of motor vehicle accidents associated with untreated OSA and the potential consequences of driving or operating other dangerous equipment while sleepy.³ Patients should also be counselled to avoid activities that require vigilance and alertness, if sleepy.

Patients should be counselled that they should always inform their medical providers that they have sleep apnoea, especially, if they are to have surgery or to be started on opiate medications.⁴

Behaviour modification - Behaviour modification is indicated for all patients who have OSA and a modifiable risk factor. The types of behaviour modification that should be instituted depend upon the characteristics of the patient. Overweight or obese patients should be encouraged to lose weight. Patients with positional OSA should change their sleep position accordingly. All patients should be advised that alcohol and certain common medications, such as benzodiazepines, may worsen their OSA.

The American Academy of Sleep

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Medicine states that "medical cannabis and/or its synthetic extracts should not be used for the treatment of OSA due to unreliable delivery methods and insufficient evidence of effectiveness, tolerability, and safety".⁵ Thus, smoking cannabis should not be encouraged.

Weight loss and exercise - Weight loss and exercise should be recommended to all patients with OSA who are overweight or obese.^{1,2}

Rarely leading to complete remission of OSA, weight loss, including that from bariatric surgery, has been shown to improve overall health and metabolic parameters, decrease the apnoea-hypopnoea index, reduce blood pressure, improve quality of life, and probably decrease daytime sleepiness.^{6,7} Available strategies for weight loss include behavioural modification, dietary therapy, exercise, drug therapy and bariatric surgery.

The effects of weight loss on OSA were illustrated by a trial that enrolled 72 consecutive over-weight patients (mean BMI 32 kg/m²) with mild OSA (mean AHI 10 events per hour of sleep). The patients were randomly assigned to receive a single session of general nutrition and exercise advice versus a more intensive programme that included a low calorie diet for three months plus nutrition and exercise counselling for one year. Patients in the latter group had significantly greater weight loss (11 versus 2 kg), reduction in the AHI (mean change from baseline, -4 versus 0.3 events per hour), and

improvement in quality of life compared with the control group. Smaller studies that included patients with more severe OSA and more daytime sleepiness at baseline suggest that weight loss also improves daytime sleepiness.

Patients whose OSA improves or resolves after weight loss should strive to maintain their weight loss, since weight gain has been associated with worsening or recurrence of OSA.^{8,11}

In addition, CPAP therapy itself may be associated with weight gain.^{12,13} Counselling regarding ongoing diet modification and exercise, as well as referral to a nutritionist, may be beneficial.

Exercise may modestly improve OSA even in the absence of significant weight loss. In a 2014 meta-analysis that included five small randomised trials, a supervised exercise programme was associated with significantly improved AHI (mean change, 6 events/hour), sleep efficiency, subjective sleepiness, and cardiorespiratory fitness with minimal change in body weight.¹⁴

Sleep position - During the diagnostic sleep study, some patients will be observed to have OSA that develops or worsens during sleep in the supine position. Such patients tend to have less severe OSA, to be less obese, and to be younger than non-positional patients.¹⁵

Sleeping in a non-supine position (e.g., lateral recumbent) may correct or improve OSA in such patients and should be encouraged but not generally relied upon as the sole therapy.¹⁶

Several commercial devices are available that use vibratory feedback around the chest or neck to restrict supine sleep.^{17,18} However, sleeping in a non-supine position should not be used as the primary therapy unless normalisation of the AHI when sleeping in a non-supine position has been confirmed by polysomnography and adherence can be verified.

Alcohol avoidance - All patients with untreated OSA should avoid alcohol, even during the daytime, because it can depress the central nervous system, exacerbate OSA, worsen sleepiness, and promote weight gain. Acute alcohol consumption often worsens the duration and frequency of obstructive respiratory events during sleep as well as the degree of oxyhaemoglobin desaturation and snoring.¹⁹ In patients who snore but do not have OSA at baseline, alcohol consumption can prompt frank OSA.

Concomitant medications - Medications with inhibitory effects on the central nervous system should be avoided if reasonable alternatives exist. In particular, benzodiazepines should be avoided in untreated patients.

Other medications that may exacerbate OSA and worsen daytime sleepiness include benzodiazepine receptor agonists, barbiturates, other antiepileptic drugs, sedating antidepressants, antihistamines, and opiates. Antidepressants that cause weight gain (e.g., mirtazapine) might be particularly problematic in these

patients.

Positive Airway Pressure Therapy - Positive airway pressure therapy is the mainstay of therapy for adults with OSA.

Indications for treatment

- The American Academy of Sleep Medicine (AASM) recommends offering positive airway pressure therapy to all patients who have been diagnosed with OSA.^{1,20}

Patients with RDI ≥ 15 events per hour with or without symptoms, OR an obstructive RDI between 5 and 14 events per hour that is accompanied by any of the following: sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms; waking up with breath holding, gasping, or choking; habitual snoring and/or breathing interruptions; hypertension, mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes.²¹

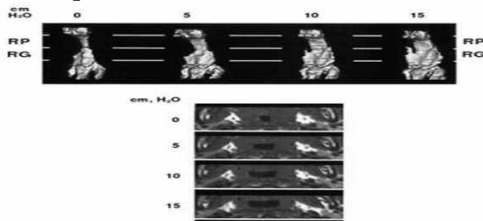
- Patients who perform mission critical work (e.g., airline pilots, air traffic controllers, locomotive engineers, bus and truck drivers) and have an AHI between 5 and 15 events per hour of sleep, even if there are no clinical or physiological symptoms attributable to OSA.
- Patients with an increased number of RERAs (e.g., ≥ 10 per hour) and excessive daytime sleepiness, even if the AHI is ≥ 5 events per hour.

Modes of administration - The most common modes of positive airway pressure administration include

continuous positive airway pressure (CPAP), bilevel positive airway pressure (Bi-PAP), and autotitrating positive airway pressure (APAP). CPAP is generally favoured as initial therapy because it is the most familiar and best studied.

The available modes of positive airway pressure therapy are summarised as follows¹:

- **CPAP** - delivers positive airway pressure at a level that remains constant throughout the respiratory cycle. The CPAP device produces continuous positive-pressure airflow. This airflow is usually applied at the nose and is then directed through the UA. CPAP increases the caliber of the airway in the retropalatal and retroglottal regions. It increases the lateral dimensions of the UA and thins the lateral pharyngeal walls, which are thicker in patients with obstructive sleep apnoea than in people without obstructive sleep apnoea. It maintains a positive pharyngeal transmural pressure so that the intraluminal pressure exceeds the surrounding pressure. CPAP also stabilises the upper airway through increased end-expiratory lung volume. As a result, respiratory events due to upper airway collapse (e.g., apnoeas, hypopnoeas) are prevented.



Top image is 3-dimensional surface renderings of the upper airway demonstrating the effect of progressive increase in continuous positive airway pressure (CPAP) from 0-15 cm of water on upper-airway volume in a patient with upper airway narrowing. CPAP significantly increases airway volume in the retropalatal (RP) and retroglottal (RG) regions. Bottom image is soft tissue images in the same patient in the RP region at analogous levels of CPAP. With increasing CPAP, the upper airway progressively enlarges, particularly in the lateral dimension. Note the progressive thinning of the lateral pharyngeal walls as the level of CPAP increases. Little movement occurs in the parapharyngeal fat pads, the white structures lateral to the airway. The first image in each series depicts the baseline upper airway narrowing present in this patient.

- **BPAP** delivers a preset inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP). The degree of pressure support and consequently tidal volume is related to the difference between the IPAP and EPAP. There is no proven advantage to using BPAP instead of CPAP for the routine management of OSA.
- **APAP** increases or decreases the level of positive airway pressure in response to a change in airflow, a change in circuit pressure, or a vibratory snore (signs that generally indicate that upper airway resistance has changed).

The degree of improvement of major outcomes conferred by APAP and CPAP is similar.

- **Adaptive servo-ventilation (ASV)** - provides a varying amount of inspiratory pressure superimposed on a low level of CPAP.

There is high quality evidence from randomised trials and meta-analyses that in most adults, including the elderly, positive airway pressure therapy reduces the frequency of respiratory events during sleep, decreases daytime sleepiness, improves systemic blood pressure, lowers the risk of crashes, and improves quality of life across a range of disease severities.^{22,23}

Alternative Therapies

Oral appliances - There are an increasing number of oral appliances that are designed to either protrude the mandible forward (i.e., mandibular advancement/repositioning splints, devices, or appliances) or hold the tongue in a more anterior position (i.e., tongue retaining devices, TRD). Either design holds the soft tissues of the oropharynx away from the posterior pharyngeal wall, thereby maintaining upper airway patency.

Oral appliances are an alternative therapeutic strategy in OSA that may be offered to patients with mild to moderate OSA who decline or fail to adhere to positive airway pressure therapy and who have a preference for such treatment.

Oral appliances have variable efficacy in patients with severe OSA and/or significant sleep-related hypoxaemia;

such patients are not good candidates for an oral appliance as first-line therapy and should be encouraged to use positive airway pressure therapy.

Contraindications for OA treatment include the following

Less than 6-10 teeth in each arch

Patient unable to protrude the mandible forward and open the jaw widely

Preexisting temporomandibular joint problems

Severe bruxism

Patient with full dentures (cannot use a mandibular repositioner, but could use a tongue retaining device)

Didgeridoo: Playing the didgeridoo strengthens and tones the tissues of the throat, and can also provide good exercise for the respiratory system, as well as a meditation aid. Regular playing of a didgeridoo reduces sleep apnoea and snoring in people with moderate obstructive sleep apnoea syndrome and also improves the sleep quality of partners.²⁴

Pharmacologic

Pharmacological therapy is rarely recommended in OSA treatment, but has been tried.

Intranasal steroids and antihistaminic: Nasal problems can include rhinorrhoea, nasal congestion, epistaxis, and nasal and/or oral dryness after using CPAP. Nasal congestion can be treated with antihistamines and/or topical corticosteroids. Nasal dryness can be treated with topical saline sprays or humidification. If the air generated by the

unit is too cold, the patient should use a heated humidifier.

A variety of pharmacologic agents have been investigated in randomised trials as primary therapeutic agents for the management of sleep-disordered breathing on OSA, with the goal of replacing the more burdensome therapies. This includes drugs that might act to stimulate respiratory drive directly (e.g., theophylline) or indirectly (e.g., acetazolamide) or drugs that reduce upper airway collapsibility (e.g., desipramine).^{25,26} However, no pharmacologic agent has proven to be sufficiently effective to warrant replacement of such therapies.²⁷

Oxybutynin and Atomoxetine: Combination of drugs under trial for treatment of OSA. Oxybutynin blocks receptors for acetylcholine on hypoglossal motor neurons, making the genioglossus muscle more responsive during REM sleep. Atomoxetine prevents norepinephrine from being reabsorbed by neurons that releases it, increasing its signal. In concert with oxybutynin it boosts responsiveness of the genioglossus in NREM sleep.

Persistent Sleepiness - Pharmacologic therapy (with agents such as modafinil or armodafinil) may be beneficial as adjunctive therapy for excessive daytime sleepiness that persists despite documentation of adequate and successful conventional therapy (e.g., positive airway pressure, oral appliances).^{1,28,29} Prior to initiating

pharmacologic therapy, adherence with conventional therapy should be confirmed and alternative causes of daytime sleepiness should be excluded.

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Feel the heat: a short history of body temperature

He showed that women have a slightly higher average temperature than men, and that old people have slightly lower temperatures than young people.

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