Obstructive sleep apnoea and obesity

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CPD

Background

Obstructive sleep apnoea (OSA) and obesity are two common conditions affecting the Australian population; obesity is the major risk factor for OSA.

Objectives

The objectives of this article are to review the interactions between obesity and OSA, including the increased cardiovascular risk, and highlight the importance of using OSA diagnosis as a critical time to address obesity itself and other cardiovascular risk factors.

Discussion

Snoring and symptoms of OSA frequently worsen during periods of rapid weight gain. Obesity and metabolic factors (eg hypertension, hyperlipidaemia, insulin resistance) are commonly present at the time of OSA diagnosis. Severe OSA is an independent risk factor for cardiovascular disease and stroke. Continuous positive airway pressure (CPAP) treatment is safe and effective, reduces sleepiness, and improves mood and quality of life; however, the cardiovascular benefits of CPAP are uncertain. Weight loss leads to variable improvement in OSA, is most effective in milder OSA, and has a greater benefit on cardiovascular risk than CPAP.

Obstructive sleep apnoea (OSA) and obesity are very common and intrinsically linked health problems that affect millions of Australians, and place a huge burden on our healthcare system. In 2014–15, 27.9% of adult Australians were obese (body mass index [BMI] ≥30 kg/m^2), with a further 35.5% being classified as overweight (BMI = 25–29.9 kg/m^2).[1]

OSA is one of the most common medical disorders in the general population. Prevalence in adults ranges from 9% to 38% (higher in men and older people) when OSA is defined as disordered breathing present on a sleep study, although prevalence is in the range of 4% to 6% when OSA on sleep study is combined with symptoms of excessive daytime sleepiness.[2,3] Among health professionals, it is common knowledge that weight gain is the most important risk factor for developing OSA. However, it is not as commonly known that there is mounting evidence for the existence of a bidirectional relationship between obesity and OSA, with OSA potentially leading to more rapid weight gain, and the entrainment of a vicious cycle of increasing weight and worsening OSA.[4] As such, the treatment of both conditions is necessary to improve patient outcomes.

Recent evidence suggests that the putative cardiovascular benefits of continuous positive airways pressure (CPAP) treatment may be overstated. The emphasis for clinicians has now shifted to not only treating OSA symptoms,[5] but also aggressively addressing obesity and the cardiometabolic comorbidities inherent in this group of patients. In this article, we take the opportunity to review the epidemiology of, and bidirectional relationship between, OSA and obesity; discuss the recent evidence regarding the use of CPAP therapy in OSA; and highlight the absolute necessity to check for, and actively manage, obesity and cardiometabolic comorbidities.

Bidirectional relationship between obesity and OSA

Obesity is the strongest risk factor for developing OSA. Several large epidemiological studies have demonstrated a strong association between weight gain and an increase in the odds

of developing OSA. It is estimated that 58% of moderate-to-severe OSA is due to obesity.[6–8] Nevertheless, clinicians need to be aware of other risk factors, such as increasing age, male gender, perimenopausal or postmenopausal status in women and craniofacial abnormalities (eg retrognathic jaw).

More recently, clinicians are recognising that the development of OSA and its subsequent sleep fragmentation may contribute to accelerated weight gain. Many patients report rapid increases in weight in the year prior to OSA diagnosis.[9] This rapid weight gain is frequently associated with increases in snoring intensity and OSA symptoms such as tiredness and daytime sleepiness. The exact mechanisms underlying this reciprocal relationship have not been fully elucidated. Mechanistic support for the concept largely comes from data showing that sleep deprivation states are associated with increases in commonly recognised appetite hormones, with subsequent altered eating patterns, including a preference for calorie-dense foods.[4,10,11] This is not directly comparable to the complex physiological disturbance seen in OSA, and the area requires further research. Regardless of the potential mechanism, there is a window of opportunity to intervene and prevent the rapid weight gain associated with OSA. Recognition of this opportunity may have important flow-on benefits in preventing the worsening of snoring and OSA and the associated obesity-related comorbidities (eg hyperlipidaemia, hypertension, insulin resistance).

Association between obesity, OSA and cardiovascular disease

Obesity and OSA share common cardiometabolic risks. There is very strong evidence linking OSA as an independent causative factor in the development of hypertension, with the risk increasing with OSA severity.[12–14] Severe OSA (apnoea–hypopnoea index [AHI] ≥30 events/hour) has also been strongly associated with an increased risk of stroke, ischaemic heart disease, atrial fibrillation and excess mortality.[15] By contrast, mild OSA (AHI = 5–15 events/hour) has not been clearly established as an independent cardiovascular risk factor, beyond the risk imposed by obesity itself. The data for moderate OSA (AHI = 15–30 events/hour) yield conflicting results, although the strongest signal is for a potential increased risk for stroke.[16] The potential cardiometabolic benefits of OSA treatment are controversial and will be discussed in subsequent sections; however, there is no doubt that severe OSA is an important biomarker of increased cardiovascular and cerebrovascular risk.

Treatment of OSA

CPAP therapy

For many years, the mainstay of treatment for OSA has been CPAP therapy. CPAP devices generate positive air pressure that pneumatically splints the upper airway open. The treatment requires the patient to wear a mask at night when asleep to transfer the air pressure from the CPAP unit to the upper airway. CPAP is a wonderful treatment in that it is safe and highly efficacious. Snoring is universally resolved and, in most cases, the OSA is effectively treated, with many studies demonstrating reductions in daytime sleepiness and depression scores, and improvement in quality of life.[17] However, CPAP is relatively poorly tolerated, with approximately 50% of patients unable or unwilling to use the treatment in the long term.[18,19] Alternative treatments to CPAP (eg mandibular advancement splints, upper airway surgery) may be effective, but there are no good predictors of response and response rates in patients who are morbidly obese (BMI >35 kg/m^2) are very poor. In the past, one of the main motivating tools used to improve patient compliance with CPAP therapy was encouragement based on the idea that increased CPAP usage would result in improved energy levels, and an ability to exercise, eat better and lose weight. However, there is no evidence that CPAP itself promotes weight loss, and indeed, there is mounting evidence that the initiation of CPAP therapy may lead to a small amount of weight gain in a proportion of patients.[20] The observation that CPAP therapy itself does not help weight loss serves to emphasise the importance of addressing obesity itself. There is good evidence that weight-loss interventions remain successful when administered concurrently with CPAP therapy.[21]

One of the potential benefits of CPAP therapy is a reduction in cardiovascular disease, arrhythmias (eg atrial fibrillation) and stroke. There is good evidence that treating OSA with CPAP or mandibular advancement splints can lead to small improvements in blood pressure.[22] The benefit is particularly strong for those with more severe hypertension or OSA at baseline. The effect size with CPAP is smaller than that seen with antihypertensive medication, but there is likely to be a synergistic benefit when the two are used together.[23] The benefit of CPAP for other cardiovascular diseases is less clear. Many observational cohort studies have found that in severe OSA, adherent CPAP usage (average use >4 hours/night) is associated with a lower likelihood of stroke, fewer cardiovascular events, reduced atrial fibrillation burden (particularly following cardioversion or trans-catheter ablation) and improved survival.[15]

However, two recently published large randomised controlled trials failed to demonstrate an improvement in the risk of cardiovascular disease or stroke with CPAP therapy.[5,24] It must be emphasised, however, that these studies excluded patients who were severely sleepy (Epworth Sleepiness Score ≥16) and those with severe oxygen desaturation. These studies were also not designed to assess the effect of CPAP on atrial fibrillation. The trials also reiterated the symptomatic benefits of CPAP therapy, with CPAP improving quality of life and reducing sleepiness and depression, even in those who did not rate themselves as excessively sleepy (based on the ESS) prior to therapy.[5] It also is unclear from these trials whether the lack of benefit was due to poor CPAP adherence, as there was a suggestion in one study of cardiovascular benefit in those who used CPAP for >4 hours/night.[24]

Table 1. Comparison of effectiveness between CPAP and weight loss for the treatment of obstructive sleep apnoea

	CPAP	Weight loss
Success at normalising AHI	Very high	Low
Long-term adherence	~50%	~25%*
Daytime symptoms	↓ ↓ ↓	↓
Snoring	↓ ↓ ↓	↓
Hypertension	↓	↓
Cardiovascular risk	?†	↓
Stroke risk	?†	?
Diabetes control	?	↓
Mortality	?†	↓

**Data from Look AHEAD study where 26.7% of subjects undergoing intensive lifestyle intervention maintained ≥10% weight loss at eight years[29]*
†Possible benefits for adherent users >4 hours/night with severe obstructive sleep apnoea
AHI, apnoea hypopnoea index; CPAP, continuous positive airway pressure

The take-home message from these results is that there should be a low threshold for a trial of CPAP therapy in moderate-to-severe OSA, or in OSA of any severity that is associated with significant symptoms. If individual patients do not experience symptomatic benefit and struggle to use the treatment, they should be referred to a sleep specialist or clinic experienced in troubleshooting CPAP and other sleep-related problems. A proportion of patients with OSA will continue to struggle and will stop CPAP, without excessive concern from a cardiovascular-risk perspective, as long as other risk factors are being addressed. Importantly, this does not relate to patients with superimposed complex comorbidities, such as congestive heart failure or obesity hypoventilation syndrome with associated respiratory failure. These patients require ongoing management via specialised clinics.

Management of obesity and metabolic comorbidities

Given that CPAP neither contributes to weight loss nor convincingly improves cardiovascular morbidity, aggressive management of obesity is crucial in patients with OSA. The benefits of weight loss on improving blood pressure, insulin resistance, lipid profile and vascular inflammation are well established.[25] Furthermore, a recent randomised controlled trial demonstrated that weight loss leads to greater cardiovascular risk factor reduction than CPAP therapy, highlighting the importance of combining the two therapies (Table 1).[26]

Weight loss as a treatment for OSA

The effectiveness of weight loss on OSA itself is critically dependent on the severity of the underlying OSA at diagnosis. In patients with mild-to-moderate OSA, medical weight loss leading to approximately 10% excess weight reduction frequently leads to symptomatic and metabolic improvements. AHI often improves significantly, although OSA is only 'cured' (AHI <5 events/hour) in a minority of patients.[27]

Given that mild OSA is not established as an independent cardiovascular risk factor, whether the residual, mild OSA requires any further treatment depends on the extent and severity of ongoing symptoms of tiredness and sleepiness, and whether there is ongoing disruptive snoring. However, in those with severe OSA at baseline, the benefits of weight loss with respect to the OSA itself are less clear. Weight loss (either through medical or surgical means) has an unpredictable effect on OSA.[27,28] Some patients will experience significant or even substantial improvements in AHI; however, for the majority, there is ongoing moderate-to-severe OSA and most will still require CPAP therapy.

Nevertheless, weight loss commonly leads to sleep-related symptomatic improvements that are independent of the change in AHI.[28] This improvement in quality of life, and the well-established cardiovascular benefits of weight loss, highlight the importance of actively targeting obesity at the time of OSA diagnosis.

Conclusion

OSA diagnosis in patients who are obese (particularly when actively gaining weight) is a critical time for intervention – for the obesity and OSA. CPAP (and other treatments such as mandibular advancement splints) are effective at safely improving symptoms, quality of life and mood and, overall, lead to a small improvement in blood pressure. Adherent CPAP usage (>4 hours/night) may improve cardiovascular and stroke risks in those with severe OSA. However, overall, there is currently no convincing evidence that CPAP independently modifies cardiovascular risk. Therefore, addressing obesity with a dedicated weight-loss intervention is

crucial to improve cardiometabolic health. In particular, patients with severe OSA should have aggressive cardiovascular risk factor management, given the strong association between severe OSA and cardiovascular disease. Finally, although not supported by any direct evidence, we believe that intervening with lifestyle measures early in the weight-gain trajectory, before weight and OSA become too severe, is a common-sense approach to helping deal with these two common and important problems.

Key points

- Obesity and OSA are among the most common problems likely to be encountered in general practice, given their extraordinarily high prevalence in the general population.
- Rapid weight gain should be a trigger to look for symptoms of OSA.
- Severe OSA is a marker of increased risk for cardiovascular disease, atrial fibrillation and stroke, and should trigger aggressive risk-factor management.
- OSA diagnosis in a patient who is overweight or obese is a critical window of opportunity to implement a weight-loss intervention to improve OSA and cardiovascular risk profile.
- Severe OSA needs treatment with CPAP to reduce symptoms and improve quality of life, and weight loss to reduce cardiovascular and stroke risk. Weight loss alone leads to unpredictable improvements in OSA severity in a given patient.

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