

The complex relationship between weight and sleep apnoea

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Obesity has long been recognised as the most important reversible risk factor for obstructive sleep apnoea (OSA). Analyses from the Wisconsin Sleep Cohort Study suggest that 41% of adult OSA cases, including 58% of moderate-to-severe cases, are attributable to overweight or obesity.¹ As such, weight loss has long been recommended as an ancillary treatment for OSA. Longitudinal analyses from the Sleep Heart Health Study support the notion that weight loss is associated with improvements in OSA severity.² However, the beneficial impact of weight loss was much less than the adverse effect of the same amount of weight gain in that study suggesting that the relationship between obesity and OSA is more complex than can be explained by an acute (and reversible) unidirectional causal model.

Given evidence that short sleep durations and poor quality sleep predict an increased rate of weight gain,^{3,4} many have postulated that OSA may itself predispose to obesity. Retrospective data indicate that those with recently diagnosed OSA are more likely to have had recent weight gain.⁵ These findings have been used to support the contention that OSA causes weight gain but of course, this may simply reflect the impact of weight gain on OSA risk. An association between OSA and elevated leptin levels, which fall with CPAP therapy, suggests that an effect of OSA on weight gain may be mediated by leptin resistance whereby improvements in leptin resistance with OSA treatment would produce weight loss.⁶ Uncontrolled studies have reported that initiation of CPAP therapy is associated with induction of mild weight loss.⁷ However, given that most patients are educated on the association between obesity and OSA at the time of CPAP prescription, whether these observations were due to CPAP itself or due to concomitant weight loss attempts by the patient was never clear. Nevertheless, many clinicians have continued to counsel

their patients that use of CPAP might help them in losing weight.

More recently, analyses from the Apnea Positive Pressure Long-term Efficacy Study (APPLES) have lain to rest the myth that CPAP causes weight loss. In that 6-month trial, patients randomised to CPAP gained weight, whereas those randomised to sham lost weight (presumably due to concomitant weight loss attempts). The difference between groups (~1.0 kg) was small but statistically significant.⁸ Furthermore, a dose-response relationship was identified, whereby increased CPAP adherence was associated with greater weight gain. In this issue of *Thorax*, Drager *et al*⁹ have now confirmed the APPLES findings by conducting a meta-analysis including 25 well-designed randomised controlled trials (RCTs) enrolling over 3000 patients with OSA. Across studies ranging from 1 to 48 months in duration, they report that CPAP is associated with a 0.5 kg weight gain compared with control therapy. The authors are to be congratulated in making use of existing data from a large number of prior RCTs. Almost every OSA trial measures weight at baseline and follow-up, so the data were readily available even if not previously reported. Given that weight was not a key outcome in any of these trials, the likelihood of publication or other selection biases in the identification of data for this meta-analysis is low. Although the meta-regression analyses did not reveal any sources of heterogeneity in the weight-promoting effects of CPAP, these analyses were hampered by the substantial similarity in the populations recruited across trials (middle-aged, predominantly men with severe OSA). Thus, further research is needed to test for effect modification in important subpopulations. Nevertheless, the findings strongly confirm that CPAP therapy for OSA produces a small increase in weight and definitely does not lead to weight loss.

The cause of this weight gain is not yet clear. The reduction in leptin levels associated with CPAP therapy may result in increased hunger if the degree of leptin resistance does not change. Another explanation is that CPAP leads to reduced energy expenditure during sleep,¹⁰ as work of breathing is reduced due both to

a patent upper airway as well as lung volumes rising to a more efficient point on the pressure-volume curve. Removal of the anorectic effects of hypoxia also may play an important role.¹¹

Where the additional weight from CPAP goes is also not yet known. A number of trials have demonstrated no substantial impact of CPAP on visceral fat volume,¹² although the imaging methods used may not be sensitive enough to exclude the small magnitude of weight gain observed. Improvements in growth hormone and insulin-like growth factor 1 signalling with CPAP might result in increased muscle mass.¹³ Further studies are clearly needed to determine whether CPAP-induced weight gain represents increases in fat, lean body or water compartments.

In understanding the impact of CPAP, it is important to note that increases in weight are also observed in overweight children with OSA following adenotonsillectomy,¹⁴ suggesting that weight gain is an effect of eliminating OSA rather than an effect specific to CPAP. Closer evaluation of the effects of other OSA therapies such as oral appliances would be helpful in establishing that the effect is not CPAP specific. Just as with CPAP, these data almost certainly already exist from prior RCTs and are ripe for meta-analysis.

Some readers may wonder if treatment recommendations for OSA should be altered in light of this identified adverse effect of CPAP therapy. The impact of 0.5 kg weight gain on health outcomes is fairly minimal and so should not change decision making regarding the use of CPAP in symptomatic OSA. However, it does give one pause regarding the use of CPAP in asymptomatic OSA where a cardiovascular benefit of CPAP has yet to be definitively established and makes more urgent the need for RCTs adequately powered to assess meaningful outcomes in this population.

These findings also highlight the need for the regular use of weight loss therapies in conjunction with CPAP in all overweight and obese patients with OSA. Although CPAP does not facilitate weight loss, it does not make weight loss strategies less effective either. The amount of weight loss achieved is no different in patients with OSA randomised to CPAP plus weight loss compared with weight loss alone.^{15,16} In one small trial, the weight loss achieved with a dietary intervention was correlated to level of CPAP adherence suggesting that similar traits (eg, level of self-efficacy) predict the effectiveness of both interventions.¹⁷

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Dietary intervention trials have demonstrated an improvement in both OSA severity and OSA-related symptoms with weight loss.^{18–19} However, some have argued that because weight regain is common with such lifestyle interventions, there may be little long-term benefit on OSA. In fact, several studies have now established that despite some weight regain, the improvements in OSA severity are durable.^{20–21} Furthermore, a recent RCT demonstrated greater benefit in a wide range of cardiovascular risk factors obtained by combining CPAP with aggressive behavioural weight loss than CPAP alone.¹⁶ Thus, there is fairly strong evidence that intensive behavioural weight loss interventions are beneficial in overweight/obese patients with OSA. Implementation research is now sorely needed to determine how best to incorporate these lifestyle interventions into routine OSA care.

Further investigation into the role of pharmacological and surgical weight loss treatments in OSA management is another research priority. Although a recent trial found no additional benefit of gastric banding surgery over behavioural weight loss in OSA,²² more aggressive bariatric options such as gastric bypass or sleeve gastrectomy are clearly more effective at weight loss than gastric banding and probably more effective at treating OSA as well.^{23–24} No RCTs have yet evaluated the efficacy of these procedures on OSA.

Despite the limitations in current knowledge, it is clear that clinicians need to pay more than lip service to weight loss counselling. Although practice guidelines on OSA treatment uniformly recommend weight loss be encouraged,^{25–27} clinicians need to do more than just encourage. The evidence base for intensive lifestyle interventions combining diet, activity and behavioural support in producing long-term weight loss and improved health outcomes is strong,²⁸ but the tools are currently unfamiliar to most who treat OSA. Just as respiratory physicians treating COPD need to be adept with evidence-based methods for smoking cessation, those treating sleep apnoea need to be trained in best practices for achieving weight loss.

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