

## Reducing complications from obstructive sleep apnoea



Obstructive sleep apnoea (OSA) is a chronic disorder affecting more than 12 million individuals in the USA. Untreated OSA has long-term negative health consequences; observational and clinical studies have shown that OSA is associated with increased risk for hypertension, diabetes, and cardiovascular morbidity and mortality.

Treatments for OSA are available, the most common and effective of which is continuous positive airway pressure (CPAP). A CPAP machine delivers air through a mask at a slightly greater than ambient pressure, thereby preventing airway collapse. However, consistent adherence to CPAP therapy is often less than optimal.

Researchers are investigating the OSA interventions that would best reduce the risks for complications from OSA, with the goal of mitigating or preventing the associated diseases. One measure of OSA severity used in these studies is the apnoea-hypopnoea index (AHI), ie, the number of occurrences of apnoea (temporary breathing cessation) and hypopnoea (abnormally shallow breathing) per hour of sleep. Studies have focused on the increased risk of diabetes, hypertension, and cardiovascular disease associated with OSA.

Richard Leung (University of Toronto, Toronto, ON, Canada) is senior author of a recent report on the risk of incident diabetes in 8678 patients with OSA who were followed up for a median of 67 months. "Our study—by far the largest of its kind—found that sleep apnoea, especially severe OSA [AHI >30], is a significant risk factor for developing diabetes. Patients initially free of diabetes underwent sleep studies... those with severe OSA were 30% more likely to develop diabetes in the next 5–10 years."

Leung continued, "We don't know the results of treating sleep apnoea on developing diabetes. At the least, patients with other risk factors for diabetes should be screened for

sleep apnoea, and if found to be severe, treatment should be strongly considered".

A clinical study of OSA therapy and hypertension enrolled 281 patients with moderate-to-severe OSA (AHI 15–50) who were already receiving medications for heart disease or multiple cardiovascular risk factors. Participants were randomly assigned to one of three treatment groups (all of which received healthy lifestyle and sleep education) for 12 weeks: no treatment, CPAP, or nocturnal supplemental oxygen. Compared with the control group, patients treated with CPAP had significant reduction in mean arterial blood pressure (–2.4 mm Hg;  $p=0.04$ ), whereas the group treated with supplemental oxygen did not (0.4 mm Hg;  $p=0.71$ ).

"Our results show that CPAP, which is standard therapy for OSA, lowers blood pressure in patients with sleep apnoea, and that overnight supplemental oxygen, which is sometimes used as salvage therapy, does not", commented first author Daniel Gottlieb (Brigham and Women's Hospital, Boston, MA, USA). "This tells us that factors other than hypoxaemia contribute to the hypertension from OSA, for example, increases in blood CO<sub>2</sub>, large changes in intrathoracic pressure, and arousal that restores normal breathing."

Gottlieb hopes that this study would "reduce reliance on oxygen as salvage therapy. Other therapies are available for sleep apnoea, such as surgery and oral appliances, that can be effective in appropriately selected patients".

Obesity and OSA frequently co-occur, and both are associated with development of cardiovascular disease. A recent clinical trial enrolled 146 obese patients with moderate-to-severe OSA (AHI  $\geq 15$ ) and raised concentrations of C-reactive protein (a marker of inflammation associated with cardiovascular risk). Participants were randomly assigned to one of three treatment groups for 24 weeks: CPAP, weight loss, or a combination of CPAP and weight loss.

Patients receiving weight loss therapy or a combination of weight loss plus CPAP therapy had reductions in C-reactive protein and lipid concentrations, insulin resistance, and blood pressure. Patients receiving CPAP alone had only blood pressure reduction.

"Weight loss is the essential component of reducing the burden of cardiovascular risk factors in patients with obesity and OSA. However, CPAP does provide an incremental benefit for blood pressure reduction among patients who adhere to therapy", summarised lead author Julio Chirinos (University of Pennsylvania, Philadelphia, PA, USA). Future research questions include, "How do we enhance CPAP adherence? How do we implement effective, low-cost weight loss to the population at large? How do we identify a priori the people who will benefit the most from blood pressure reduction due to CPAP intervention?" Chirinos added that, going forward, "I would hope that people would pay a lot more attention to the weight loss component for reducing cardiovascular risk among patients with obesity and OSA."

"These studies follow upon a lot of impressive evidence that has accrued about OSA", says Robert C Basner (Columbia University College of Physicians and Surgeons, New York, NY, USA). As for future directions, "There have been very few large randomised controlled trials to pinpoint what would really be the best treatment in the best settings. We need to have longer, larger, and more comprehensive studies...and we need to consistently consider OSA pathobiology, treatments, and outcomes, in its milieu of cardiovascular, cerebrovascular, metabolic, and ventilatory disorders. Treating OSA alone appears necessary, but not sufficient, for optimal outcomes in such vulnerable populations".

Judith A Gilbert



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*Lancet Respir Med* 2014

Published Online

June 20, 2014

[http://dx.doi.org/10.1016/S2213-2600\(14\)70110-9](http://dx.doi.org/10.1016/S2213-2600(14)70110-9)

For more on **obstructive sleep apnoea and cardiovascular disease** see *Lancet Respir Med* 2013; 1: 61

For **Richard Leung and colleagues' study** see

*Am J Respir Crit Care Med* 2014; published online June 4. <http://dx.doi.org/10.1164/rccm.201312-2209OC>

For the **OSA therapy and hypertension study** see

*N Engl J Med* 2014; 370: 2276–85

For **Julio Chirinos and colleagues' study on obesity**

and OSA see *N Engl J Med* 2014; 370: 2265–75