A Randomized Trial of Continuous Positive Airway Pressure Therapy, Weight Loss, or Both for Obese Adults with Obstructive Sleep Apnea

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Background: Obesity and obstructive sleep apnea (OSA) tend to co-exist and are associated with inflammation, insulin resistance, dyslipidemia and hypertension. The causal effect of OSA vs. obesity on these cardiovascular risk factors is unclear and cannot be confidently discerned in cross-sectional studies. We designed this mechanistic randomized trial to assess the incremental effect of combination therapy (weight loss and CPAP) over each individual therapy in obese patients with OSA.

Methods: We randomly assigned 181 subjects with obesity (body mass index >30 kg/m²), moderate-to-severe OSA (Apnea-Hypopnea Index >15), and a C-reactive protein (CRP) level >1.0 mg/L to undergo one of 3 interventions for 24 weeks: (1) Continuous positive airway pressure (CPAP); (2) Weight Loss; (3) Both CPAP therapy and weight loss. We assessed the effect of these interventions on C-reactive protein levels, insulin sensitivity (assessed with a frequently-sampled intravenous glucose tolerance test), fasting lipid parameters and blood pressure in both intent-to-treat analyses and pre-specified analyses including only compliant subjects.

Results: A total of 136 subjects completed the study. Weight loss, but not CPAP therapy, resulted in a sustained reduction in CRP, insulin resistance, LDL-cholesterol, LDL-particle concentration, apoprotein B and a sustained increase in LDL-particle size at 24-weeks (all \(P<0.05\)). For these endpoints, changes in the combination arm were significantly greater than those observed in the CPAP-only group (all \(P<0.05\)), without significant differences between the combination arm and the weight-loss only arm. In contrast, both weight loss and CPAP therapy resulted in significant sustained reductions in systolic and mean arterial pressure (\(P<0.0001\)). For these endpoints, changes in the combination therapy arm were significantly greater than both monotherapy arms. In pre-specified per-protocol analyses including only adherent subjects, combination therapy was associated with a much larger effect on systolic BP (14.1 mmHg-reduction) than that the effect associated with either CPAP monotherapy (3.0 mmHg-reduction; \(P\) vs. combination therapy arm <0.0001) or weight loss monotherapy (6.8 mmHg-reduction; \(P\) vs. combination therapy arm = 0.02).

Conclusions: Among obese patients with moderate-to-severe OSA, combination therapy with CPAP and weight loss is superior to either therapy alone to improve the cardiovascular risk profile. Our results suggest an important causative role for OSA on high blood pressure, whereas obesity is the predominant causative factor related to inflammation, dyslipidemia and insulin resistance.