

Metabolic abnormalities in obstructive sleep apnea: A double whammy

The global obesity epidemic continues to gain momentum, resulting in increased prevalence of obstructive sleep apnea (OSA). In India, a recent community-based survey reported prevalence of OSA as 9.3% and that of obstructive sleep apnea syndrome (OSAS) as 2.8%.^[1] The figures are similar to those reported in western population.^[2] These patients often have co-existent risk factors for cardiovascular disease such as obesity, hypertension, dyslipidemia, and impaired glucose tolerance. This clustering of risk factors is called metabolic syndrome. OSA has been shown to be independently associated with these risk factors including hypertension,^[3] dyslipidemia,^[4] and insulin resistance.^[5] Coughlin *et al.* demonstrated that OSA is independently associated with metabolic syndrome.^[4] The co-occurrence of OSA and metabolic syndrome, termed syndrome Z, acts synergistically to increase the risk for cardiovascular disease. The prevalence of syndrome Z in India ranges from 4.5% in population-based study^[6] to 79% among patients with OSA in hospital-based study.^[7] However, obesity acts as an important confounder in interpretation of the relationship between OSA and metabolic syndrome, due to its independent association with OSA and other cardiovascular risk factors.^[8] These patients are frequently prescribed multiple drugs to address individual components of the metabolic syndrome.

Continuous positive airway pressure (CPAP) is the first-line treatment for symptomatic OSA. However, the effect of CPAP on the metabolic syndrome is unclear. The most consistent effect reported is the reduction in blood pressure with CPAP therapy.^[9,10] It is also believed that pulmonary pressure elevation in sleep apnea patients usually settles down after initiation of CPAP treatment.^[11] The reports on effect on insulin resistance^[9,12] and lipid profile are discordant.^[9,13] Two studies assessing the effect of CPAP on metabolic syndrome in patients with obstructive sleep apnea gave divergent results.^[9,14] In a recent study by Sharma *et al.*,^[15] published in the December 15 issue of the *New England Journal of Medicine*, CPAP therapy has been shown to be associated with improvement in various

components of metabolic syndrome in patients with both OSA and metabolic syndrome. The authors of this study should be congratulated for giving convincing evidence in a double blind study design.

The study was a double-blind, placebo-controlled, randomized, crossover trial with 3 months of CPAP and 3 months of sham CPAP, and a 1-month washout period between the interventions. The crossover design obviated the need for a control group. Ninety patients with moderate to severe OSA and not on treatment for hypertension, diabetes mellitus, or dyslipidemia were randomized and 86 of them completed the study. The patients had a mean age of 45 years and all but 9 were males. Seventy-five of 86 patients (87%) had metabolic syndrome at the time of recruitment. At baseline, 47% of patients had hypertension, 49% had diabetes mellitus, and dyslipidemia was present in 84% of patients. The frequency of the metabolic syndrome decreased significantly after CPAP therapy as compared with sham CPAP. After CPAP therapy, 13% of the patients no longer met criteria for the metabolic syndrome compared to 1% of those with sham CPAP therapy. There was a significant reduction in systolic (3.9 mm Hg) and diastolic (2.5 mm Hg) blood pressure, glycated hemoglobin (0.2%), triglycerides (18.7 mg/dl), and low density lipoprotein (LDL) (9.6 mg/dl), non-HDL (13.3 mg/dl), and total cholesterol (13.3 mg/dl) as well as significant decrease in body mass index (BMI) and visceral and subcutaneous fat after CPAP therapy as compared with sham therapy. There was no effect on fasting blood glucose, fasting insulin, or insulin resistance. The magnitude of reduction in blood pressure and lipid indices appears small but may be important clinically. It has been shown that 5 mm reduction in blood pressure reduces the risk of coronary artery disease by 15% and risk of stroke by 42%.^[16] Similarly, 40 mg reduction in LDL cholesterol brings down the risk of stroke and coronary artery disease by 20%.^[17] The change in all these parameters with CPAP therapy is small but in the direction of improvement of metabolic syndrome which makes it more meaningful clinically.

The decrease in BMI and abdominal fat has been attributed to a decrease in daytime somnolence and a consequent increase in physical activity after CPAP use at night. The authors further speculate that a favorable effect on leptin levels with CPAP therapy may be responsible for the effect. Adherence was higher with CPAP than with sham CPAP. Better adherence was associated with greater improvement

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in metabolic parameters, as confirmed by a subgroup analysis of patients who used CPAP for at least 5 h per night compared to the overall population. Limitations of the study included the fairly short washout period of 1 month, which could not exclude carryover effect of treatment, the lack of ambulatory blood pressure measurement, and the absence of follow-up polysomnographic data.

Previous studies on effects of CPAP therapy on metabolic syndrome have yielded mixed results; most of them showing favorable effects on blood pressure, but data on insulin resistance and lipids have been inconsistent and even conflicting.^[9,11,18] The strengths of the current study includes large number of patients and a longer follow-up period, as well as being a placebo-controlled, double-blind, randomized, crossover study. The patients included in the study had more severe metabolic abnormalities at baseline, which may have been responsible for the better response to CPAP therapy. Longer term studies are required to study if the benefits are sustained, the effect of adherence to the therapy, and to see any significant effect on carotid intima-media thickness. The present study outcome supports the use of CPAP therapy as a modality of management of metabolic syndrome in patients with OSA in addition to lifestyle modification, weight reduction, and dietary modification. Early identification of metabolic syndrome in patients with OSA and prompt institution of CPAP therapy will help in decreasing the drug requirement for the individual components of metabolic syndrome and considerably decrease the risk factors for cardiovascular disease.

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