CPAP Aids Metabolic Syndrome in Apnea Patients

BY MARY ANN MOON

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

ontinuous positive airway pressure therapy improved several components of the metabolic syndrome along with obstructive sleep apnea in patients who had both disorders, according to researchers.

In most cases, only one component of the metabolic syndrome improved significantly after continuous positive airway pressure (CPAP), but that improvement was significant enough to "reverse" the syndrome, reported Dr. Surendra K.

Sharma of All India Institute of Medical Sciences, New Delhi, and his associates.

No particular component stood out as being the most responsive to CPAP; statistically significant improvements were seen in systolic BP, diastolic BP, total cholesterol, non-HDL cholesterol, LDL cholesterol, triglycerides, gly-

cated hemoglobin, weight, and visceral and subcutaneous fat.

"These results suggest a significant clinical benefit that will lead to a reduction in cardiovascular risk," the investigators noted.

To examine the effect of CPAP on

components of the metabolic syndrome, Dr. Sharma and his coinvestigators recruited 86 patients aged 30-65 years from the sleep laboratory at the institute who had obstructive sleep apnea that was moderate or worse in severity. All of the subjects reported excessive daytime somnolence.

A total of 75 study subjects (87%) had the metabolic syndrome, and the remainder had some of the components of the metabolic syndrome.

These patients were randomly assigned to undergo either CPAP or sham CPAP for 3 months, followed by a washout period of 1 month. They then



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crossed over to receive the other intervention for 3 months.

The sham CPAP was not discernible to the study subjects or the investigators.

The metabolic syndrome resolved in 14 (20%) of the study subjects after

Major Finding: The metabolic syndrome resolved in 11 of 86 patients after CPAP therapy, compared with 1 of those same patients after sham therapy. The treatment also significantly improved systolic and diastolic BP; total, LDL, and non-HDL cholesterol; triglycerides; glycated hemoglobin; weight; and visceral and subcutaneous fat.

Data Source: A double-blind, randomized trial involving 86 patients with moderate to severe obstructive sleep apnea and components of the metabolic syndrome who received 3 months of real and 3 months of sham CPAP therapy. **Disclosures:** This study was funded by Pfizer. All investigators reported having no financial conflicts of interest. The investigators received technical support from ResMed Corp. in designing a sham CPAP machine.

CPAP. This was attributed to decreased blood pressure in five; decreased fasting blood glucose in two; decreased triglycerides in two; increased HDL cholesterol in three; improved triglycerides plus HDL cholesterol in one; and improved triglycerides, HDL cholesterol, and fasting blood glucose in one, Dr. Sharma and his colleagues reported. Symptoms of the syndrome developed in three patients who did not have metabolic syndrome at the start of the study.

Overall, CPAP was associated with a mean decrease in systolic BP of 3.9 mm Hg, a mean decrease in diastolic BP of 2.5 mm Hg, a mean decrease in total cholesterol of 13.3 mg/dL, and a mean decrease in triglycerides of 18.7 mg/dL.

CT scans revealed a significant decrease in both visceral and subcutaneous fat, which was accompanied by a decrease in BMI, with CPAP therapy. "These findings could be secondary to a decrease in daytime somnolence and a consequent increase in physical activity after CPAP use at night," the researchers noted.

In addition, "we speculate that CPAP has a favorable effect on leptin levels,

which have been shown to be elevated in patients with obstructive sleep apnea and to normalize with CPAP therapy," the investigators said (N. Engl. J. Med. 2011;365:2277-86).

In a subgroup analysis involving only the 51 subjects who were most compliant with CPAP, with a mean use of at least 5 hours every night, the improvements in components of the metabolic syndrome were even greater. In particular, systolic BP decreased by 5.6 mm Hg and diastolic BP decreased by 3.3 mm Hg.

This subgroup of patients also showed significant improvement in carotid intima-media thickness, "suggesting a potential role for CPAP therapy in reversing endothelial damage due to obstructive sleep apnea and the metabolic syndrome," Dr. Sharma and his associates said.

Two patients could not tolerate CPAP and one could not tolerate sham CPAP within the first month of treatment, and they withdrew from the study. "Other adverse events reported included skin irritation (in 51% of all patients), nasal bridge discomfort (in 44%), nasal congestion (in 28%), headache (in 26%), and mask leaks (in 30%)."

High Systolic BP and LDL Predict Different Events

BY NASEEM S. MILLER

FROM THE ANNUAL SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION

ORLANDO – Although higher systolic blood pressure and LDL cholesterol are traditional risk factors for cardiovascular disease, each may have a different effect on the cerebrovascular and coronary systems.

Pooled analysis of three landmark studies done on the cholesterol-lowering agent atorvastatin in high-risk patients showed that higher baseline systolic blood pressure is predictive of a significantly higher risk of stroke. Meanwhile, higher baseline LDL cholesterol is predictive of a significantly higher risk of coronary events, the analysis showed.

The findings have implications on both research design and clinical practice, Dr. Prakash C. Deedwania, the study's lead author, said at the meeting.

Patients who might be at risk of both stroke and coronary events should be treated aggressively to reduce systolic blood pressure and LDL cholesterol, he said. (See video for more comments from Dr. Deedwania.)

Dr. Deedwania and his colleagues pooled data on 21,727 patients from three trials: Treating to New Targets (TNT), which compared 10 mg with 80 mg atorvastatin in patients with stable coronary heart disease and LDL levels below 130 mg/dL (N. Engl. J. Med.

2005;352:1425-35), Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL), which compared high-dose (80 mg) atorvastatin with normal-dose (20-40 mg) simvastatin in post-MI patients (JAMA 2005;294:2437-45), and the Collaborative Atorvastatin Diabetes Study (CARDS), which compared 20 mg atorvastatin with placebo in patients with type 2 diabetes and without established coronary heart disease (Lancet 2004;364:685-96).

Results showed that with each 10-mm Hg increase in baseline systolic blood pressure, the risk of a fatal or nonfatal stroke increased by 16%. Meanwhile, each 10-mg/dL increase in baseline LDL cholesterol increased the risk of coronary events by 5%.

Both differences were significantly different.

Dr. Deedwania said that the reduction in LDL cholesterol has been associated with a decrease in the risk of stroke, "but perhaps by a different mechanism."

The investigators also looked at a subgroup of patients with type 2 diabetes (5,408 patients from the three trials), and found results consistent with the larger cohort.

Although systolic blood pressure is known to be a powerful predictor of stroke, many clinicians may not



In a video interview, Dr. Deedwania discusses the way different factors affect stroke and coronary event risks. Scan the QR code (right) or go to www.clinicalendocrinologynews.com.



be aware that LDL cholesterol is not associated with an increased risk of stroke, said Dr. Deedwania. "What predicts baseline risk is different than what happens in treatment, so there are yet many lessons to be learned from these trials."

Dr. Deedwania has received research grants from Pfizer. He has been a consultant to and on the advisory boards of Pfizer and Novartis.