Studies examine CPAP treatment and cardiovascular outcomes in adults with obstructive sleep apnea

May 22 2012

Two studies that included adults with obstructive sleep apnea examined the effectiveness of reducing the risk of cardiovascular outcomes, including high blood pressure, by treatment with continuous positive airway pressure (CPAP), according to the articles in the May 23/30 issue of *JAMA*.

Obstructive sleep apnea (OSA) affects 3 percent to 7 percent of the general population and is caused by the collapse of the upper airway during sleep, which leads to transient asphyxia, according to background information in the first study. Studies have shown an association between OSA and hypertension and cardiovascular diseases. First-line treatment for patients with symptomatic OSA is CPAP, which acts as a pneumatic splint to keep the upper airway open during sleep and corrects the obstruction.

Ferran Barbé, M.D., of the Institut de Recerca Biomedica, Lleida, Spain, and colleagues conducted a study to evaluate the effect of CPAP treatment on the incidence of hypertension or cardiovascular events in 723 patients with OSA without daytime sleepiness. The randomized controlled trial was conducted in 14 teaching hospitals in Spain between May 2004 and May 2006, with follow-up through May 2009. Patients were allocated to receive CPAP treatment or no active intervention. All participants received dietary counseling and sleep hygiene advice. The primary outcomes measured for the study were the incidence of either

systemic hypertension (taking antihypertensive medication or blood pressure greater than 140/90 mm Hg) or cardiovascular event.

The patients in the study underwent followup for a median (midpoint) of 4 years; 357 in the CPAP group and 366 in the control group were included in the analysis. A total of 147 patients with new hypertension and 59 cardiovascular events were identified. In the CPAP group, there were 68 patients with new hypertension and 28 cardiovascular events (17 hospitalizations for unstable angina or arrhythmia, 3 nonfatal stroke, 3 heart failure, 2 nonfatal heart attack, 2 transient ischemic attack, 1 cardiovascular death). In the control group, there were 79 patients with new hypertension and 31 cardiovascular events (11 hospitalizations for unstable angina or arrhythmia, 8 nonfatal heart attack, 5 transient ischemic attack, 5 heart failure, 2 nonfatal stroke). Analysis of the data indicated that treatment with CPAP compared with usual care did not result in a statistically significant reduction in the incidence of hypertension or cardiovascular events.

However, the authors note that their study may have limited power to detect a significant difference, and that a larger study or longer follow-up might have been able to identify a significant association between treatment and outcome. "A post hoc analysis suggested that CPAP treatment may reduce the incidence of hypertension or cardiovascular events in patients with CPAP adherence of 4 hours/night or longer."

Treatment of Obstructed Sleep Apnea With CPAP Therapy Associated With A Lower Risk Of Hypertension

In the second study, José M. Marin, M.D., of the Hospital Universitario Miguel Servet, Zaragoza, Spain, and colleagues examined whether CPAP therapy is associated with a lower rate of new-onset hypertension

in patients with OSA. "Although treatment of OSA with CPAP therapy is associated with decreased overall cardiovascular risk, its efficacy in preventing new-onset hypertension is unknown," the authors write. "Short-term studies indicate that CPAP therapy reduces blood pressure in patients with hypertension and OSA."

The study included 1,889 participants without hypertension who were referred to a sleep center for nocturnal polysomnography between January 1994 and December 2000. Incident hypertension was documented at annual follow-up visits up to January 2011. Multivariable models adjusted for confounding (factors that can influence outcomes) factors, including changes in body mass index during the study, were used to calculate hazard ratios of new hypertension in participants without OSA (controls), with untreated OSA, and in those treated with CPAP therapy according to national guidelines.

The average follow-up of the study was 11.3 years (median 12.2 years). During follow-up, 705 patients (37.3 percent) developed incident hypertension. After including change in body mass index as a covariate in the fully adjusted model, the hazard ratios (risk) for incident hypertension remained 33 percent greater among patients with OSA who were ineligible for CPAP therapy; the risk was nearly twice as great among patients with OSA who declined CPAP therapy; and about 80 percent greater among patients with OSA who were nonadherent to CPAP therapy, compared with controls without OSA. In patients with OSA who were treated with CPAP therapy, the risk of new-onset hypertension was 29 percent lower than in controls.

"Although CPAP therapy was not allocated randomly to our patients, the associated lower excess risk of hypertension strongly suggests that OSA may be an independent modifiable risk factor for development of new-onset hypertension. The observed correlation between severity of OSA and the magnitude of risk for hypertension further supports OSA as a

major contributor to cardiovascular risk. In conclusion, compared with participants without OSA, untreated OSA was associated with an increased risk of new-onset hypertension, whereas treatment with CPAP therapy was associated with a lower risk of new-onset hypertension," the authors write.

"Our observational findings suggest that OSA appears to be a modifiable risk factor for new-onset hypertension. Such findings are clinically relevant considering that OSA, despite a high prevalence in Western populations, remains overwhelmingly unrecognized and untreated."

In an accompanying editorial, Vishesh K. Kapur, M.D., M.P.H., and Edward M. Weaver, M.D., M.P.H., of the University of Washington, Seattle, write that "although these studies significantly advance the understanding of the positive relationship between OSA and incident hypertension and the benefit of CPAP therapy, many questions remain regarding OSA, hypertension, and treatment.

"What are the susceptible and responsive subgroups (e.g. OSA severity subgroups, sleepy vs. nonsleepy, and demographic subgroups)? How much CPAP use is necessary for an important treatment effect? What are the effects of other OSA treatments? These questions will require randomized controlled trials when feasible, subgroup analyses within these trials, and well-controlled observational studies. Novel approaches are needed, such as treatment withdrawal protocols."

More information:

JAMA. 2012;307[20]:2161-2168.
JAMA. 2012;307[20]:2161-2168.
JAMA. 2012;307[20]:2197-2198.