

Disordered Breathing Takes a Toll on Nighttime BP

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People with sleep-disordered breathing were less likely to experience a normal nighttime decrease in systolic blood pressure and were at increased risk of adverse cardiac and other outcomes, according to a new prospective study.

Data from a previous study showed that most people experience a 10%-20% dip in blood pressure at nighttime (Hypertension 1995;26:60-9). Other data have shown an association between sleep apnea syndrome and a failure to experience the beneficial nighttime decrease in blood pressure, but the evidence is limited to cross-sectional studies (Am. J. Hypertens. 2001;14:887-92; Chest 2002;122:1148-55).

The current study's findings are important because "nocturnal nondipping" associated with sleep-disordered breathing (SDB) has been linked in earlier studies to target organ damage and a poor cardiovascular prognosis (Can. J. Cardiol. 2007;23:132-8; JAMA 1999;282:539-46).

Dr. Khin Mae Hla and her associates of the departments of medicine and population health sciences at the University of Wisconsin, Madison, assessed 328 adults in the ongoing Wisconsin Sleep Cohort Study. Mean patient age was 49 years,

63% were men, and the mean body mass index was 29 kg/m². The subjects had a baseline polysomnography study and at least two 24-hour ambulatory blood pressure monitoring assessments during an average 7.2 years of follow-up. Of the total, 18% developed systolic nondipping, and 11% developed diastolic nondipping. No association was found between SDB and diastolic nondipping, but the longitudinal association with systolic BP alterations was significant (Sleep 2008;31:795-800).

The chances of developing systolic nondipping were significantly correlated with baseline SDB severity in a dose-response fashion. Patients scoring less than 5 on the Apnea-Hypopnea Index (no or minimal SDB) were used as a reference group. Those with mild SDB (score of 5 to 15) were three times as likely to develop systolic nondipping (adjusted odds ratio, 3.1), and those with moderate to severe SDB (score of 15 or greater) were more than four times as likely to develop systolic nondipping (OR, 4.4).

The researchers controlled for possible confounders, including age, gender, body mass index, smoking, and alcohol use. Use of continuous positive airway pressure (CPAP) by 11 patients, antihypertensive medication use (42 patients), and inclusion of 8 patients with a history of cardiovascular disease did not significantly alter the findings, though inclusion of the CPAP patients was a possible limitation of the study, said the researchers. Grants from the National Institutes of Health helped fund the study. ■

COPD May Point To Obstructive Sleep Apnea

BALTIMORE — Two measures of lung function—a higher forced expiratory volume in 1 second/forced vital capacity ratio and lower total lung capacity—may predict the presence of obstructive sleep apnea in chronic pulmonary disease patients, according to a poster presented at the annual meeting of the Associated Professional Sleep Societies

Dr. Ramez Sunna and colleagues at the University of Missouri, Columbia, reviewed all adult patients who underwent both pulmonary function testing and polysomnography between 2000 and 2007 at a tertiary care medical center.

Overall, 279 patients (61%) met the criteria for obstructive sleep apnea (OSA), 167 patients (37%) met the criteria for chronic obstructive pulmonary disease (COPD), and 11 patients (2%) did not have either condition.

A total of 101 patients (60%) had both COPD and OSA, but there was no significant correlation between the severity of the COPD and the severity of the OSA.

But the researchers analyzed the COPD patients independently and found that those with both COPD and OSA had a significantly higher forced expiratory volume in one second (FEV₁)/forced vital capacity (FVC) ratio, compared with COPD patients without OSA (61.03% vs. 54.61%), although both of these values fell below healthy levels. The association remained significant after controlling for variables.

—Heidi Splete



Indications and usage

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Levemir® is contraindicated in patients hypersensitive to insulin detemir or one of its excipients.

Hypoglycemia is the most common adverse effect of all insulin therapies, including Levemir®. As with other insulins, the timing of hypoglycemic events may differ among various insulin preparations. Glucose monitoring is recommended for all patients with diabetes. Levemir® is not to be used in insulin infusion pumps. Any change of insulin dose should be made cautiously and only under medical supervision. Concomitant oral antidiabetic treatment may require adjustment.

Inadequate dosing or discontinuation of treatment may lead to hyperglycemia and, in patients with type 1 diabetes, diabetic

ketoacidosis. Levemir® should not be diluted or mixed with any other insulin preparations. Insulin may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy. Dose and timing of administration may need to be adjusted to reduce the risk of hypoglycemia in patients being switched to Levemir® from other intermediate or long-acting insulin preparations. The dose of Levemir® may need to be adjusted in patients with renal or hepatic impairment. Other adverse events commonly associated with insulin therapy may include injection site reactions (on average, 3% to 4% of patients in clinical trials) such as lipodystrophy, redness, pain, itching, hives, swelling, and inflammation.

*Whether these observed differences represent true differences in the effects of Levemir®, NPH insulin, and insulin glargine is not known, since these trials were not blinded and the protocols (eg, diet and exercise instructions and monitoring) were not specifically directed at exploring hypotheses related to weight effects of the treatments compared. The clinical significance of the observed differences in weight has not been established.

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References: 1. Meneghini LF, Rosenber KH, Koenen C, Meriläinen MJ, Lüddeke H-J. Insulin detemir improves glycaemic control with less hypoglycaemia and no weight gain in patients with type 2 diabetes who were insulin naive or treated with NPH or insulin glargine: clinical practice experience from a German subgroup of the PREDICTIVE study. *Diabetes Obes Metab.* 2007;9(3):418-427. 2. Hermansen K, Davies M, Derezinski T, Ravn GM, Clauson P, Home P, for the Levemir Treat-to-Target Study Group. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naïve people with type 2 diabetes. *Diabetes Care.* 2006;29(6):1269-1274. 3. Klein O, Lyngø J, Endahl L, Damholt B, Nøse L, Heise T. Albumin-bound basal insulin analogues (insulin detemir and NN344): comparable time-action profiles but less variability than insulin glargine in type 2 diabetes. *Diabetes Obes Metab.* 2007;9(3):290-299. 4. Phillis-Tsimikas A, Charpentier G, Clauson P, Ravn GM, Roberts VL, Thorsteinsson B. Comparison of once-daily insulin detemir with NPH insulin added to a regimen of oral antidiabetic drugs in poorly controlled type 2 diabetes. *Clin Ther.* 2006;28(10):1569-1581. 5. Danne T, Endahl L, Haahr H, et al. Lower within-subject variability in pharmacokinetic profiles of insulin detemir in comparison to insulin glargine in children and adolescents with type 1 diabetes. Presented at: 43rd Annual Meeting of the European Association for the Study of Diabetes; September 17-21, 2007; Amsterdam, Netherlands. Abstract 0189. 6. Heise T, Nøse L, Ronn BB, et al. Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes.* 2004;53(6):1614-1620. 7. Data on file. NDA21-536. Novo Nordisk Inc, Princeton, NJ.



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