Assess and Treat Apnea In Diabetes Patients

BY MIRIAM E. TUCKER
Senior Writer

ST. LOUIS — Sleep apnea assessment and treatment should be considered an integral part of diabetes management, Susan M. LaRue, R.D., said at the annual meeting of the American Association of Diabetes Educators.

"Sleep apnea is highly prevalent in people with diabetes, people with hypertension and obesity, all of which we see in huge numbers in our patient population," said Ms. LaRue, a certified diabetes educator with Amylin Pharmaceuticals.

Because sleep apnea is so common among people with diabetes—concomitant with obesity and hypertension—the Scripps' Whittier Institute for Diabetes, La Jolla, Calif., has instituted a "best practice" in which every patient is screened for OSA.

In a study published by Whittier's Dr. Daniel Einhorn and his associates, 72% of 279 adults with type 2 diabetes were found to have some degree of sleep apnea, defined as an apnea-hypopnea index (AHI) of five events or more per hour. Over a third of the patients (36%) had an AHI of at least 15 events per hour, which was associated with a doubling of the risk for the development of hypertension after adjustment for comorbidities (Endocrine Practice 2007;13:355-62).

That study and the symposium in which Ms. LaRue spoke were both sponsored by the ResMed Corp., which manufactures continuous positive airway pressure (CPAP) devices for treatment of OSA.

Diabetes is among several cardiovascular-related conditions that are strongly associated with OSA. Data suggest that OSA is present in about 80% of individuals with drug-resistant hypertension (35% of all hypertension) and in 50% of those with atrial fibrillation.

The mechanism for the association is not known, but theories focus on the increased sympathetic nervous activity resulting from repeated apneas, said Ms. LaRue, formerly with the Whittier Institute.

Treatment with CPAP not only reduces apneic episodes and improves sleep quality, but also appears to improve the cardiovascular and metabolic abnormalities. In a German study of 60 patients with moderate to severe OSA, those given "therapeutic" levels of CPAP for an average of 9 weeks had a 95% reduction in apneas and hypopneas and a decrease in mean arterial blood pressure of 9.9 mm Hg.

That level of decline would be predicted to reduce coronary heart disease event risk by 37% and stroke risk by 56%, the investigators said (Circulation 2003;107:68-73). ■

Too Much, Too Little Sleep Doubles Risk of Death

BY BRUCE JANCIN
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COLORADO SPRINGS — Change in sleep duration during midlife is associated in a U-shaped fashion with risk for death more than a decade later, Dr. Francesco Cappuccio reported at a conference of the American Heart Association.

The major driver of increased mortality among individuals at the low end of the sleep duration continuum is an excess of cardiovascular deaths, while in long sleepers the increase in mortality is due to noncardiovascular causes, according to the results of the Whitehall II study, said Dr. Cappuccio of Warwick Medical School, Coventry, England.

Whitehall II is a prospective cohort study of 10,308 white-collar British civil servants who were 35-55 years old when enrolled in the study in 1985-1988. The Whitehall II analysis of the impact of changes in sleep duration included data on baseline sleep patterns in 7,729 participants and changes in those patterns over the next 5 years. Participants then were followed for mortality through 2004.

Cardiovascular mortality was 2.4-fold higher among subjects who slept an average of 6-8 hr/night at baseline but cut their sleep duration to 5 hr/night or less over the next 5 years' follow-up, compared with those who held fast to the 6- to 8-hour pattern. The findings held after adjustment for potential confounding factors including age, gender, employment grade, marital status, blood pressure, body mass index, alcohol intake, smoking status, comorbid illnesses, and physical activity.

In subjects who increased their sleep duration from 7 to 8 hr/night at baseline to 9 or more, there was an adjusted 2.1-fold increase in noncardiovascular mortality.

Short sleep duration is known to be associated with hypertension, weight gain, and diabetes, all of which increase cardiovascular risk. In contrast, the mechanism for the relationship between long sleep and increased mortality is unclear, Dr. Cappuccio added. ■

EVIDENCE-BASED PSYCHIATRIC MEDICINE

Hypnotics and Sleep Apnea

The Problem
You have a patient with obstructive sleep apnea who requests a hypnotic. Knowing that benzodiazepines can worsen the condition, you consider prescribing one of the common hypnotics.

The Question
Which of the commonly prescribed hypnotics are safe to use in patients who have obstructive sleep apnea?

The Analysis
We performed a Medline search that combined "sleep apnea" and "zolpidem (Ambien), eszopiclone (Lunesta), ramelteon (Rozerem), zaleplon (Sonata), or zopiclone (Imovane)."


BY JAN LEARD-HANSSON, M.D.


BY LAURENCE GUTTMACHER, M.D.

The Evidence
Most patients with obstructive sleep apnea (OSA) experience daytime sleepiness. Many, however, also experience initial or midcycle insomnia. Benzodiazepines should be used with caution in OSA patients because of the muscle-relaxant properties of benzodiazepines (particularly on the upper airway muscles), and because of their central depressant action. But how risky is a nonbenzodiazepine receptor agonist, or a melatonin receptor agonist, in an OSA patient?

Zolpidem is a nonbenzodiazepine receptor agonist that was approved by the Food and Drug Administration in 1992 for treatment of insomnia characterized by difficulty initiating sleep. The effect of a single oral dose of zolpidem 20 mg (twice the recommended dosage) was compared with placebo in this randomized, crossover, double-blind trial involving 12 participants (average age, 49 years) with mild OSA (Pharmacol. Biochem. Behav. 1988;29:807-9). The participants received 1 night of polysomnographic recording for diagnosis and adaptation with 6 days of drug-free washout. Zolpidem reduced arterial oxygen percent saturation (SaO_2) during snoring, but statistical significance was not reached. Zolpidem also increased the apnea index, although not significantly. That increase, however, provoked greater O_2 desaturation than was seen with placebo.

Zaleplon is a nonbenzodiazepine receptor agonist approved by the FDA in 1999 for insomnia characterized by difficulty falling asleep. Investigators conducted a crossover study, involving 15 patients who had mild to moderate OSA while on continuous positive airway pressure, in which zaleplon 10 mg (half of the maximum daily dosage) was compared with placebo (J. Clin. Sleep Med. 2005;1:97). Study medication was administered over a period of 5 nights, and patients were examined using a home-monitoring device. (Blinding and washout periods were not noted.) No differences in apnea-hypopnea index or in SaO_2 between the zaleplon and placebo groups were noted.

Eszopiclone is a nonbenzodiazepine receptor agonist approved by the FDA in 2004 for sleep-onset and sleep-maintenance insomnia. In a double-blind, randomized, crossover study of 21 patients (aged 35-64 years) that compared eszopiclone 3 mg with placebo (Sleep Med. 2007;8:464-70), patients had mild to moderate OSA as defined by an apnea-hypopnea index of 10-40. As expected for an OSA population, the relative body mass index was high.

Patients underwent 2 nights of polysomnographic recording to establish eligibility and baseline reading with 5- to 7-day washout periods between drug administrations. Each treatment was administered over 2 consecutive nights. (Prior researchers have noted a 50% false-negative rate for the first polysomnograph in diagnosing OSA.) The eszopiclone group did not experience an increase in the apnea-hypopnea index when compared with placebo. The average or longest duration of apnea and hypopnea episodes also were similar between the eszopiclone and placebo groups, as was the degree of oxygen saturation.

Ramelteon is a selective MT1/MT2 (melatonin)-receptor agonist that was approved in 2005 for insomnia characterized by difficulty initiating sleep. Researchers conducted a double-blind crossover study on 26 adults (aged 21-64 years) with mild to moderate OSA in which ramelteon 16 mg (twice the recommended daily dosage) was compared with placebo (Sleep Breath. 2007;11:159-64). Mild OSA was defined as an apnea-hypopnea index of 5-9, and moderate OSA was defined as an apnea-hypopnea index of 10-20.) Again, as expected, the study population's BMI (kg/m^2) was high (mean, 30). After a screening polysomnograph, two treatment periods were administered, with a 5- to 12-day washout between treatments. Ramelteon had no statistically significant effects on the apnea-hypopnea index or on SaO_2.

The Conclusion
These small, nonreplicated, but well-designed studies indicate that the nonbenzodiazepine agonists and the melatonin receptor agonist approved for use in insomnia do not worsen mild to moderate obstructive sleep apnea, as long as they are prescribed within guidelines. We could not locate any studies examining these medications' effects on severe obstructive sleep apnea, nor could we locate any studies examining the safety of zopiclone.

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