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Taking BP Meds at Bedtime May Thwart Diabetes Onset

Marlene Busko | September 28, 2015

Blood pressure that does not drop as expected at nighttime (nondipping) seems to precede the development of diabetes, according to a new study. Moreover, the same researchers showed, in a second study, that popping a blood-pressure pill at bedtime instead of first thing in the morning appears to lower the risk of getting type 2 diabetes.

Ramón C Hermida, PhD, and colleagues from the bioengineering and chronobiology laboratories at the University of Vigo, in Spain, report these latest findings from the Monitorización Ambulatoria para Predicción de Eventos Cardiovasculares (Ambulatory Blood-Pressure Monitoring for Prediction of Cardiovascular Events [MAPEC]) trial in two papers published online September 23 in *Diabetologia*.

Most hypertensive patients still take their prescribed medications in the morning, although no prospective, randomized study has ever reported any advantages of such a treatment regimen, Dr Hermida told *Medscape Medical News* in an email. "On the contrary, there is growing evidence that ingesting hypertension medication at bedtime significantly reduces cardiovascular and cerebrovascular events."

In fact, the researchers have previously reported that in the same cohort, taking antihypertensives at bedtime lowered the risk of cardiovascular disease. "Our studies now add into this body of evidence, showing that, in addition [to cardiovascular benefits], bedtime treatment also markedly reduces the risk of developing diabetes."

Together, this suggests that "all hypertensive patients, after confirmation of the condition by ambulatory BP monitoring, might benefit from bedtime treatment," according to Dr Hermida.

Faulty Nighttime BP Lowering and Subsequent Diabetes

Many patients with diabetes have a nighttime blood pressure that falls by less than 10% of daytime blood pressure (that is, they are "nondippers"), and this has been consistently associated with increased CVD risk, Dr Hermida and colleagues write.

They aimed to investigate whether 24-hour ambulatory blood-pressure readings over time might predict the development of type 2 diabetes and whether reducing daytime (awake) or nighttime (sleeping) blood pressure might lower a person's risk of developing diabetes.

They evaluated 2012 hypertensive patients and 644 patients with normal blood pressure — 1292 men and 1364 women with a mean age of 50.6 and no diabetes — who were enrolled in the MAPEC study.

The patients with hypertension were randomized to either take their blood-pressure medications upon awakening or take one or more pill at bedtime and any remaining dose upon awakening.

Patients wore an activity sensor on their wrist (that distinguished between activity and sleep time) and they also wore an ambulatory blood-pressure monitor for 48 hours at baseline and at least once a year during a median follow-up of 5.9 years.

The researchers examined the patients' systolic and diastolic clinic blood pressure and mean awake, asleep, and 48-hour blood pressure, as well as sleep-time relative decline, morning surge, preawakening surge, and nighttime fall in blood pressure.

A total of 190 patients developed type 2 diabetes. Compared with the other patients, those who developed diabetes were more likely to be nondippers (62% vs 43%; $P < .0001$).

The mean asleep systolic blood pressure was the most significant predictor of new-onset diabetes, after adjustment for age, glucose, waist circumference, chronic kidney disease, and hypertension treatment.

The results suggest that treatment with antihypertensives in the evening to target abnormalities in the mean asleep systolic blood pressure might lower the risk of new-onset diabetes.

Bedtime vs Morning BP Meds and Future Diabetes Risk

In the second study, Dr Hermida and colleagues looked at only the 2012 hypertensive patients in the MAPEC study — 976 men and 1036 women with a mean age of 52.7 — to see if bedtime antihypertensive therapy offered protection against the development of diabetes. They also aimed to see if renin-angiotensin-aldosterone-system (RAAS) inhibitors were the best therapies for this.

In this study, 1029 of the patients received morning antihypertensive treatment and 983 received their medication at bedtime, and during the median follow-up of 5.9 years, 171 participants developed type 2 diabetes.

Nondipping occurred less often among patients who took antihypertensives at bedtime as opposed to morning (32% vs 52%; $P < .0001$).

The risk of developing diabetes was 57% lower in patients who took their antihypertensive medications at bedtime as opposed to early morning (hazard ratio, 0.43), after adjustment for fasting glucose, waist circumference, mean nighttime systolic blood pressure, dipping category, and chronic kidney disease.

Patients had a much lower risk of developing diabetes with bedtime as opposed to morning treatment with angiotensin receptor blockers (ARBs, a 61% lower risk), ACE inhibitors (a 69% lower risk), or β-blockers (primarily nebivolol, a 65% lower risk).

But the risk was not significantly lower with bedtime as opposed to morning dosing of calcium-channel blockers, alpha-blockers, or diuretics.

Nebivolol, a third-generation, long-acting β-blocker, induces vasodilation through activation of the L-arginine/nitric oxide pathway and has a regulatory effect on the RAAS, the authors note.

"Since the RAAS activates during nighttime sleep, the results [suggest] that RAAS inhibition or blockade and the corresponding potential improved control of impaired glucose and insulin tolerance might be among the factors associated with reduced risk of new-onset diabetes," the authors say.

Some practice guidelines already recommend taking antihypertensives at bedtime, Dr Hermida noted.

"After we first reported about 4 years ago that bedtime treatment markedly reduces cardiovascular risk, bedtime therapy has already been recommended as the treatment of choice by…the American Diabetes Association, the European Society of Cardiology in conjunction with the European Association for the Study of Diabetes, the Japanese Society of Hypertension, the International Society for Chronobiology, and the Spanish Society of Atherosclerosis," he said.

The group is coordinating the HYGIA project at 40 clinical sites in Galicia (Northwest Spain) with 292 investigators, which has already recruited more than 18,000 patients who are undergoing periodic evaluation by ambulatory BP monitoring.

"Data from this huge trial, now entering its ninth year, will eventually allow [us] to corroborate the findings described in the two manuscripts published [in] *Diabetologia*." Dr Hermida concluded.

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