Circadian BP Patterns May Predict Vascular Events

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Treated hypertensive patients who have either extreme or very slight dips in nighttime blood pressure are at greater cardiovascular risk than are those with moderate dips, according to a study in 1,472 patients.

Prior research has shown that people whose blood pressure fails to dip at night ("nondippers") are at much higher risk for cardiovascular events than are patients whose BP follows the normal diurnal pattern and falls by 10%-20% during sleep. The new data extend these findings to include "extreme dippers," or those whose nighttime systolic and/or diastolic BP dips by at least 20%.

The evidence supports 24-hour blood pressure monitoring at least in patients at very high risk of being nondippers.

DR. BAKRIS

"Circadian blood pressure pattern influences cardiovascular outcome in treated hypertension and its evaluation allows a better prognostic stratification and may suggest a more appropriate pharmacological management," lead investigator Dr. Sante D. Pierdomenico and associates reported in a poster at the annual meeting of the American Society of Hypertension.

The investigators studied 388 patients with a dipper BP pattern (systolic and diastolic nighttime BP reduction of at least 10% and less than 20%), 745 with a nondipper BP pattern (systolic and/or diastolic reduction of less than 10%), and 339 with an extreme-dipper BP pattern. Blood pressure measurements were taken with a 24-hour ambulatory blood pressure monitoring system.

Nondippers (mean age 61 years) were significantly older than dippers (58 years) or extreme dippers (55 years), and were more likely to have diabetes (8%) than were dippers (4.4%) or extreme dippers (4%). But nondippers were significantly less likely to be smokers (17%) than were dippers (25%) or extreme dippers (22%).

During an average of 5 years of follow-up, there were 116 cardiovascular events. The event rate per 100 patient-years was 0.91, 1.93, and 1.73 in dipper, nondipper, and extreme-dipper patients, respectively. Event-free survival was significantly different among the groups, reported Dr. Pierdomenico, professor of medicine and aging science at G. d'Annunzio University in Chieti, Italy.

A Cox regression analysis that adjusted for various covariates, including 24-hour BP and drug therapy, showed that cardiovascular risk was significantly higher in nondipper patients (relative risk 1.7) and in extreme-dipper patients (RR 2.2), compared with dipper patients.

"This and many other studies would argue for 24-hour blood pressure monitoring at least in the subgroup of people at very high risk of being nondippers," said Dr. George Bakris, director of the hypertension center at the University of Chicago, in a statement, "for example, those with kidney disease [glomerular filtration rate less than 60 mL/min per 1.73 m^2]; those who are obese, with or without sleep apnea; blacks with hypertension; and those with insulin resistance." ■

Nighttime Is the Right Time For Patients to Take ARBs

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Bedtime dosing of valsartan is more efficient than morning dosing in controlling blood pressure and improving renal function in hypertensive patients with or without diabetes, Ramon Hermida, Ph.D., said at the annual meeting of the American Society of Hypertension.

Dr. Hermida suggests this time-dependent effect is not unique to valsartan, but may be class related for angiotensin II receptor blockers (ARBs) and should be taken into account when treating hypertensive patients.

Dr. Hermida and his colleagues randomized 204 untreated hypertensive patients to receive valsartan 160 mg/day either upon awakening or at bedtime. Blood pressure was measured at 20-minute intervals from 7:00 a.m. to 11:00 p.m., and at 30-minute intervals at night for 48 hours before and after 12 weeks of therapy. Urine was collected by the patients during the first 24 hours of BP monitoring. The patients' mean age was 52 years, and 97 had type 2 diabetes mellitus.

Bedtime dosing with valsartan was significantly more effective than morning dosing in reducing nocturnal BP in patients with or without diabetes, said Dr. Hermida, of the University of Vigo (Spain). The diurnal/nocturnal BP ratio was unchanged after taking valsartan on awakening, but significantly increased by 5.3% when taken before bedtime.

Urinary albumin excretion was significantly reduced by 23% from baseline in patients without diabetes and by 31% in those with diabetes only after bedtime administration.

This reduction was independent of the significant decrease in 24-hour or diurnal mean BP after treatment. It was highly correlated with the decrease in nocturnal BP, and mainly correlated with the increase in diurnal/nocturnal BP ratio, said Dr. Hermida, who disclosed no potential conflicts of interest.

When analyzed separately, the decrease in urinary albumin excretion associated with the increase in diurnal/nocturnal BP ratio was statistically significant for patients both with and without diabetes.

Bedtime administration of valsartan is preferred to morning dosing because it seems to improve the diurnal/nocturnal BP ratio, Dr. Hermida said.

When asked by an audience member if the time-dependent effects observed in the trial are specific to valsartan's duration of action, Dr. Hermida responded with a definitive "no." Data from two similarly designed independent randomized trials presented at the same meeting show "the results are exactly the same" with nighttime administration of two other ARBs with completely different half-lives—telmisartan and olmesartan, he said.

"This could be a class effect that would be potentially applicable to all ARBs," Dr. Hermida said. ■

Hyperuricemia Linked to Hypertension

BY MITCHEL L. ZOLER
Philadelphia Bureau

ORLANDO — Hyperuricemia was an independent risk factor for the development of hypertension in a post hoc analysis of data collected on more than 3,000 men.

Future studies will need to address whether reducing a high serum level of uric acid is a safe and effective way to reduce a person's risk of developing hypertension, Dr. Eswar Krishnan said while presenting a poster at a conference on cardiovascular disease epidemiology and prevention sponsored by the American Heart Association.

The standard agent used to reduce hyperuricemia is allopurinol, a drug that's commonly used to treat patients with gout and a high uric acid level. If treatment of people with hyperuricemia with allopurinol could prevent the onset of hypertension, it would be an attractive option because allopurinol is cheap and is usually well tolerated except in a small percentage of people who are allergic to the drug, Dr. Krishnan said in an interview.

If a link between hyperuricemia and subsequent hypertension is confirmed, another way to apply the finding would be to advise people with hyperuricemia to take lifestyle steps to reduce their risk for hypertension, such as increased activity and weight loss, he said.

The study used data collected in the Multiple Risk Factor Intervention Trial (MRFIT), a study that enrolled nearly 13,000 men in the mid-1970s. The primary goal of MRFIT was to test the efficacy of a program of interventions aimed at cutting the risk of coronary heart disease in men who were at high risk for adverse coronary events (JAMA 1982;248:1465-77).

The analysis focused on the 3,073 men who were free from hypertension, metabolic syndrome, and diabetes at baseline, and for whom usable, baseline serum uric-acid levels were available. Men were followed for an average of 6 years, during which they had annual examinations. The probability that a man with a normal serum level of uric acid developed hyperuricemia at the next annual visit was 14%. The probability that a man with hyperuricemia would remain at an elevated level of serum uric acid at the next annual visit was 68%. For this analysis, hyperuricemia was defined as a serum uric acid level of more than 7.0 mg/dL; about a third of the men in the study had hyperuricemia at baseline.

During follow-up, 51% of the studied men (1,569) developed hypertension, defined as a systolic pressure of 140 mm Hg or greater or a diastolic pressure of 90 mm Hg or greater.

In a multivariate analysis that controlled for baseline differences in age, blood pressure, serum creatinine, total cholesterol, smoking, alcohol use, body mass index, proteinuria, and other potential confounders, men with hyperuricemia at baseline had an 81% increased risk of developing hypertension, a statistically significant difference, reported Dr. Krishnan, a rheumatologist at the University of Pittsburgh. For every 1 mg/dL increase in the serum level of uric acid at baseline, the risk of developing hypertension during follow-up increased by 9%, also a statistically significant difference. ■

Benefit of BP Treatment Leads to Large Trial's Halt

A large, randomized international trial assessing the benefits of giving blood pressure–lowering medications to hypertensive patients aged 80 and older has been halted early because treatment significantly reduced the incidence of stroke and mortality, compared with those who did not receive treatment.

Launched in 2001, the double-blind, placebo-controlled study, known as the Hypertension in the Very Elderly Trial (HYVET), enrolled 3,845 patients with high blood pressure aged 80 and older. Patients took either the placebo or indapamide 1.5 mg and perindopril once a day.

"It was not clear prior to our study whether the over-80s would benefit from blood pressure–lowering medication in the same way as younger people," the study's primary investigator, Dr. Chris Bulpitt, professor of geriatric medicine at Imperial College London, said in a prepared statement. "Our results are great news for people in this age group because they suggest … such treatment can cut their chances of dying as well as stroke."

Specific data from the trial have not been released but are expected to appear in the peer-reviewed medical literature. In the meantime, study participants who were on the trial medication will have the option to switch to active indapamide 1.5 mg SR at their final visit.

The British Heart Foundation and the Institut de Recherches Internationales Servier funded the study, which is the largest of its kind.

—Doug Brunk