Bedtime Dosing Curbs Nondipper BP Patterns

BY SHERRY BOSCHERT

SAN FRANCISCO — Patients on three or more medications for resistant hypertension were more likely to have blood pressure under control and less likely to have a nondipper blood pressure pattern at night if they took at least one of the drugs at bedtime, according to ambulatory blood pressure monitoring study involving 1,306 patients.

For 48 consecutive hours, a device automatically measured blood pressure and heart rate every 20 minutes from 7 a.m. to 11 p.m. and every 30 minutes during the night. Simultaneous wrist actigraphy was used to monitor physical activity every minute. A comparison of data from the two devices allowed investigators to determine blood pressure means during waking and sleep time according to each individual's rest-activity cycle.

Among 573 patients who took at least one of their antihypertensives at bedtime and the remainder in the morning, 32% had blood pressure under control, which was significantly better compared with 23% of the 733 patients who took no antihypertensive medications at bedtime and all of them on awakening, Dr. Ramon C. Hermida and his associates reported at the annual meeting of the American Society of Hypertension.

The bedtime-dose group also had significantly lower blood pressures at nighttime and morning, and lower ambulatory pulse pressure compared with the morning-only group. The bedtime group patients had a higher awake/asleep blood pressure ratio, and thus were significantly less likely to have a nighttime nondipper blood pressure pattern that has been associated with a higher risk of cardiovascular and cerebrovascular events. A nondipper blood pressure pattern is defined as less than a 10% decline in mean blood pressure during sleep compared with awake blood pressure.

In the bedtime-dose group, 40% had a nondipper pattern, compared with 83% in the morning-only group.

DR. HERMIDA

In the bedtime group, 40% had a nondipper pattern, compared with 83% in the morning-only group, said Dr. Hermida of the University of Vigo, Spain.

In addition, the bedtime group had significantly lower mean levels of glucose, total cholesterol, LDL cholesterol, fibrinogen, and urinary albumin excretion.

In general, patients with resistant hypertension have a high prevalence of the nondipper blood pressure pattern. Conventional strategies for managing resistant hypertension focus on adding another drug or changing a drug to see if that improves the combination therapy.

Research findings suggest that up to 89% of patients who take antihypertensives ingest them all in the morning, including patients with resistant hypertension.

With better timing of medication administration, blood pressure control could be improved and the number of patients with the nondipper pattern reduced, Dr. Hermida proposed.

The investigators are studying whether this normalization of the blood pressure pattern might reduce cardiovascular risk beyond the benefits conferred by reducing mean blood pressure values.

In the current study, the cohort had a mean age of 61 years; 52% of the participants were male.

Mean morning blood pressures were 136/79 mm Hg in the bedtime group and 142/82 mm Hg in the morning group.

Mean glucose values were 116 mg/dL in the bedtime group and 121 mg/dL in the morning group. Mean values for total cholesterol and LDL cholesterol were 201 mg/dL and 129 mg/dL in the bedtime group, respectively, and 206 mg/dL and 134 mg/dL in the morning group, respectively.

Fibrinogen levels were 339 mg/dL in the bedtime group and 351 mg/dL in the morning group. In the bedtime group, the urinary albumin excretion rate was 29 mg/day, compared with 39 mg/day in the morning group.

There were no significant differences in heart rates between the groups.

An audience member pointed out that the researchers did not indicate which antihypertensives were being taken in the a.m. or the p.m., an observation that was relevant since not all medications are effective for a 24-hour period.

The investigators reported having no relevant conflicts of interest. ■

Isradipine Effective for Acute Hypertension in Children

BY SHERRY BOSCHERT

SAN FRANCISCO — The first pediatric study of isradipine therapy for acute hypertension suggests that it effectively lowers blood pressure and that a lower starting dose may be appropriate for children younger than 2 years.

The retrospective, single-center, observational study looked at the effects of a first-time dose of isradipine in the hospital or emergency department to treat acute hypertension in 391 children over a 2-year period. Mean blood pressures fell significantly from 147/92 mm Hg before treatment to 122/69 mm Hg, reaching a nadir 2.7 hours after treatment, Dr. Yosuke Miyashita and associates reported in a poster presentation at the annual meeting of the American Society of Hypertension.

Treatment also decreased mean arterial pressure significantly from 110 mm Hg to 86 mm Hg, said Dr. Miyashita of the University of Washington, Seattle.

Mean arterial pressure decreased by a median 24% in the 34 patients (9%) aged younger than 2 years, by 22% in 127 patients (32%) aged 2-11 years, by 18% in 167 patients (43%) aged 12-16 years, and by 20% in 63 patients (16%) aged 17 years or older.

Greater than 25% declines in mean arterial pressure—and adverse effects—were significantly more likely with dosages of 0.09 mg/kg compared with dosages of 0.08 mg/kg or lower. By age groups, a greater than 25% decrease in mean arterial pressure was seen in 47% of patients younger than 2 years of age, 43% of those aged 2-11 years, 29% of patients aged 12-16 years, and 27% of those 17 years or older.

A lower starting dose of 0.05 mg/kg may be needed for the youngest patients, the investigators suggested.

Fourteen percent of patients received dosages up to 0.05 mg/kg, 60% received 0.05-0.1 mg/kg, and 26% got more than 0.1 mg/kg. Most patients (63%) received isradipine capsules; the rest got a suspension formulation.

Among the diagnoses that contributed to the acute hypertension, four were predictive of significant decreases in blood pressure with isradipine therapy: renal disease, nonrenal transplant, oncologic disease, and neurologic disease.

Treatment produced another adverse effect—a significant pulse increase of seven pulses per minute among the whole cohort. By dosage category, however, the changes in pulse were not significant with dosages of 0.05 mg/kg or less (an extra three pulses per minute), but were significant at higher doses (an extra seven or eight pulses per minute).

Forty adverse events in 33 patients included emesis, headache, nausea, hypotension, flushing, feeling hot, dizziness, and lightheadedness. Adverse events were not necessarily dose dependent, Dr. Miyashita said.

The investigators did not disclose relevant conflicts of interest.

Study limitations include its retrospective, uncontrolled design, incomplete documentation of adverse events, and misclassification of diagnoses. ■

Nebivolol Improves BP in Obese African Americans

BY PATRICE WENDLING

CHICAGO — Monotherapy with the cardioselective beta-1 blocker nebivolol improved vascular function and significantly reduced blood pressure in high-risk, obese African Americans with recently diagnosed stage 1 hypertension, in an open-label study of 43 patients.

The findings are encouraging because the observed vasodilatory effects may be protective against cardiovascular and renal disease in African Americans, a group at high risk of these diseases and in whom hypertension treatment with conventional beta blockers is often suboptimal, Nadya Merchant, Ph.D., and associates reported at a meeting sponsored by the International Society on Hypertension in Blacks.

Mean systolic blood pressure decreased from 143.8 mm Hg at baseline to 133.0 mm Hg in 33 patients who completed 8 weeks of treatment with nebivolol (Bystolic). Diastolic blood pressure decreased from 90.4 mm Hg to 83.6 mm Hg. Significant improvements were seen in aortic augmentation index, from 16.6% to 11.1% post treatment, and in time to wave reflection, from 164 milliseconds to 137 milliseconds. These findings suggest nebivolol improves arterial compliance, said Dr. Merchant, a research fellow in the cardiology department at Emory University in Atlanta.

She noted there was also a significant jump in flow mediated dilation, from 3.4% before treatment to 11% post treatment. Finally, levels of erythrocyte extracellular superoxide dismutase increased with nebivolol treatment from 465.2 units/mL to 537.4 units/mL, suggesting increased bioavailability of nitric oxide.

"These findings imply that nebivolol, if used by obese hypertensive African Americans, can … decrease blood pressure significantly," she said, adding that "there may be some positive vascular changes and therefore protection against the development of cardiovascular and renal disease." In the current trial, patients received nebivolol 5 mg per day and were titrated to 10 mg/day if at week 2 there was no change in blood pressure. Their average body mass index was 36.5 kg/m^2, and their baseline blood pressure ranged from 140 to 159 mm Hg (systolic) and 90 to 99 mm Hg (diastolic) in the seated position. None of the study patients withdrew because of adverse events, but there was a 25% dropout rate, Dr. Merchant said.

Forest Pharmaceuticals Inc., which markets nebivolol, provided an unrestricted grant and the study drug. Dr. Merchant is director of investor relationships for InVasc Therapeutics Inc., a company in Tucker, Ga., that develops drugs for diabetes and cardiovascular diseases. ■