Simple Regimen Reins In Resistant Hypertension

Adding angiotensin II receptor blocker to diuretic brought hard-to-treat hypertensives below target BP.

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — A simple, aggressive hypertension treatment regimen controlled systolic hypertension in 77% of 1,005 hard-to-treat patients after 18 weeks, Elijah Saunders, M.D., reported.

The initial treatment consisted of a diuretic alone. If blood pressure control was not achieved, patients were switched to a combination pill containing the same diuretic and an angiotensin II receptor blocker.

The study included at least 100 patients from each of several populations in which high blood pressure often is difficult to control: patients aged 65 years or older, African Americans and Hispanic patients, patients with type 2 diabetes, and patients with metabolic syndrome.

The study, known as the Irbesartan/Hydrochlorothiazide Blood Pressure Reductions In Diverse Patient Populations (INCLUSIVE) trial, is the first large-scale hypertension study to include such a broad range of patient groups, Dr. Saunders said at the annual meeting of the American Society of Hypertension. Women comprised 52% of the cohort.

Some of the study participants had risk factors for cardiovascular disease including obesity, abnormal glucose tolerance, high triglyceride levels, or low HDL cholesterol. A large proportion of hypertensive people have these risk factors, and they often need two or more medications to control hypertension.

Systolic blood pressures dropped an average of 21 mm Hg, from 154 to 133 mm Hg. Diastolic pressures fell 10 mm Hg, from 91 to 81 mm Hg.

Patients entered the trial with high blood pressure that was not controlled adequately with one medication. After a 4-week washout period in which patients received placebo, treatment began with the diuretic hydrochlorothiazide at 12.5 mg/day. After 2 weeks, blood pressures were under control in 27% of patients.

The remaining patients were switched to combination treatment with 12.5 mg of hydrochlorothiazide and 150 mg of the angiotensin II receptor blocker irbesartan in a single daily pill (Avalide) for 8 weeks. During this second phase of treatment, a majority of patients reached blood pressure control: Systolic pressure was under control in 56% of patients, and diastolic was controlled in 72%.

Patients who still had high blood pressures 12 weeks into the study were switched to a double dose of Avalide: 25 mg of hydrochlorothiazide with 300 mg of irbesartan per day.

At the end of the 18-week study, the study regimen had controlled 77% of systolic blood pressures and 83% of diastolic pressures, said Dr. Saunders, professor of medicine at the University of Maryland, Baltimore. The other principal investigator in the study was Joel Neutel, M.D., of the Orange County Research Center, Tustin, Calif., and the University of California, Irvine.

No particular efforts were made by the study patients to alter diet or exercise habits, suggesting that the benefits could be attributed to the medications.

Study patients were seen in 119 clinics, showing that high rates of blood pressure control can be achieved in general clinic settings, Dr. Neutel said.

The study was funded by the two companies that distribute Avalide in partnership, Bristol-Myers Squibb Co. and Sanofi-Synthelabo. Dr. Saunders is a consultant to both companies. Dr. Neutel is a speaker for Bristol-Myers Squibb.

The treatment was well tolerated. Dizziness was the most common side effect, occurring in 3% of patients. The incidence of hypokalemia did not increase with the higher thiazide dose.

In the United States, 53% of patients treated for hypertension reach recommended blood pressure goals of less than 140/90 mm Hg for the general population or 130/80 mm Hg for people with diabetes or chronic kidney disease, a 2000 study found. The magnitude of success in the current study surprised investigators, Dr. Saunders said.

Systolic blood pressures in the study dropped an average of 21 mm Hg, from 154 to 133 mm Hg. Diastolic pressures fell 10 mm Hg, from 91 to 81 mm Hg.

Improvements in blood pressure were similar between the subgroups studied, with systolic pressures dropping 15-23 mm Hg on average. The subgroup of diabetic patients had the lowest rates of control, with systolic pressure controlled in 56% and diastolic pressure controlled in 63% of patients. In the other subgroups, 72%-82% achieved systolic pressure control and 77%-96% achieved diastolic pressure control. ■

Lower BP, Lower Event Risk

CAD Patients *from page 1*

both alone (Norvasc) and in combination with atorvastatin (Caduet).

He reported results of the CAMELOT trial (Comparison of Amlodipine vs. Enalapril to Limit Ischemic Occurrences of Thrombosis) and a substudy prospectively embedded in it that assessed plaque progression by intravascular ultrasound—the NORMALISE study (Norvasc for Regression of Manifest Atherosclerotic Lesions by Intravascular Sonographic Evaluation).

Findings from both the main study and the substudy make a strong case for antihypertensive therapy in the setting of normal blood pressure and coronary artery disease, he said. "I think it is further evidence supporting the suggestion that we have to be more aggressive" in lowering blood pressures in patients with established coronary artery disease, Dr. Nicholls said.

High rates of concomitant use of statins, β-blockers, and aspirin by the study patients made it an ideal setting to examine potential benefits of further antihypertensive therapy, he said.

Average baseline blood pressures of 129/77 mm Hg decreased 5/2.5 mm Hg on average in both the amlodipine and enalapril groups. The study's primary end point was a combination of clinical events that included death from coronary heart disease, resuscitation after cardiac arrest, MI, stroke, coronary revascularization, hospitalization for angina, or heart failure.

These cardiovascular events occurred in 23% of the placebo group, 20% of the enalapril group, and 17% of the amlodipine group. The difference between the amlodipine and enalapril groups was not significant.

The significantly lower rate of events in the amlodipine group compared with placebo was driven by a decrease in angina-related events with amlodipine. Eight percent of patients on amlodipine were hospitalized for angina, compared with 13% of patients on either enalapril or placebo, for example.

The NORMALISE substudy followed 274 patients for an average of 20 months using intravascular ultrasound to calculate plaque area. Atheroma volume increased in patients on placebo, consistent with progression of plaque. Atheroma volume did not increase significantly in either the amlodipine or enalapril group, but showed a trend for increase with enalapril, he said.

In a subset of 136 patients with blood pressures above the mean, however, amlodipine significantly slowed plaque progression compared with placebo.

The study's findings were limited by its small size, wide confidence intervals for some of the results, and the difference in the duration of action between the two drugs, he said.

The results build on similar findings from smaller studies, such as PREVENT (Prospective Evaluation of Vascular Effects of Norvasc Trial) (Circulation 2000;102:1503-10), Dr. Nicholls said. ■

In-Office Detection of White Coat Hypertension Is Possible

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — You may not need to send patients with suspected "white coat hypertension" home with an ambulatory blood pressure monitor. Automated repeat measurements in the office work just as well for ruling out this type of hypertension, Giuseppe Crippa, M.D., said at the annual meeting of the American Society of Hypertension.

In a study of 122 patients, measurements from an automated, in-office oscillometric device that obtained 10 valid BP readings matched ambulatory BP measurements closely enough that the in-office readings identified 40 out of 41 patients with white coat hypertension, said Dr. Crippa of Guglielmo da Saliceto Hospital, Piacenza, Italy.

The study included consecutive patients referred to the hospital's hypertension unit to confirm or rule out suspected hypertension. All patients had clinic readings above 140/90 mm Hg, but reported measurements at home that were consistently below 140/90 mm Hg.

For each patient, in-office BPs were taken by a physician, a nurse, and the automated device (in random order) and compared with ambulatory BP measurements. The doctor and nurse each took three readings after the patient had rested for 20 minutes. The automated repeat measurements were taken at 2.5-minute intervals with the patient sitting alone in a clinic room. Investigators compared the average of the last two measurements taken by the doctor and nurse with the average of the last five measurements by the automated device and the mean daytime ambulatory BP.

Blood pressures taken by doctors and nurses were significantly higher than daytime ambulatory measurements. The automated and ambulatory measurements closely overlapped, however, with no significant differences between them, he said.

Doctor's measurements averaged 15/11 mm Hg higher, and nurses' measurements averaged 11/9 mm Hg higher, than daytime ambulatory BPs. Only 1 of 41 patients who were normotensive on daytime ambulatory monitoring had hypertension on automated in-office testing.

Automated repeat office BP measurements "could be a substitute for home blood pressure monitoring," he said.

Hypertension was defined as BPs above 132/85 mm Hg. Conventional measurements by physicians in the office can be inaccurate because of variable reactions by the patients and errors in technique. This can lead to an overestimate of hypertension, incorrect diagnoses, and inappropriate treatment, Dr. Crippa said.

Average diastolic blood pressure readings in patients with white coat hypertension were 86 mm Hg when taken by doctors, 83 mm Hg by nurses, 75 mm Hg by the automated device, and 73 mm Hg by ambulatory monitoring. ■