Refractory Hypertension Dips With Drug Combination

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CHICAGO — Nearly three-fourths of patients with uncontrolled hypertension on monotherapy achieved national blood pressure targets on a fixed-dose combination of amlodipine and valsartan that will soon be available, Dr. Joseph L. Izzo Jr. reported at the annual meeting of the American Society of Hypertension.

Two different formulations of Novartis' single-tablet combination drug, which was approved in June and will be marketed as Exforge, were evaluated in a double-blind, multicenter study that randomized 443 patients to amlodipine 5 mg/valsartan 160 mg and 451 patients to amlodipine 10 mg/valsartan 160 mg. After 8 weeks, hydrochlorothiazide (HCTZ) could be added on, first at 12.5 mg, and then at 25 mg.

The majority of patients, including 145 (16%) of whom had type 2 diabetes, had been previously treated with a β-blocker, angiotensin receptor antagonist, ACE inhibitor, calcium channel blocker, or diuretic.

At admission, their mean age was 58 years, more than 90% were white, and their mean BP was 150/90 mm Hg, said Dr. Izzo, who has received research support and is a consultant for Novartis, which sponsored the study.

The study's primary end point was the proportion of patients after 8 and 16 weeks who had reached a BP of 140/90 mm Hg or 130/80 mm Hg for those with diabetes—the currently recommended dual BP targets in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7).

In an intent-to-treat analysis at week 16, 322 of 440 patients (73%) on the 5-mg/160-mg dose and 338 of 449 patients (75%) on the 10-mg/160-mg dose achieved the dual JNC7 targets, the investigators reported.

Among those with diabetes, 25 of the 61 patients (41%) on the low-dose combination and 27 of the 59 patients (46%) on the high-dose combination reached a BP of less than 130 mm Hg.

Switching patients to the combination therapy resulted in an average additional 20–mm Hg drop in systolic BP, compared with reductions seen with their previous medications. said Dr. Izzo, professor of medicine, State University of New York at Buffalo, said at a press briefing.

BP control rates were similar when stratified by prior medication, age, or ethnicity. There was little increased response after 8 weeks that could be attributed to the addition of HCTZ therapy.

Adverse events were similar between groups, although the incidence of edema was higher with the 10-mg/160-mg dose than with the lower dose (25% vs. 8%).

Exforge was approved by the Food and Drug Administration last month. It is indicated for the treatment of hypertension in patients whose blood pressure has not been adequately controlled with a calcium channel blocker or angiotensin II receptor blocker alone. The pills will be available in four strengths: 5 mg amlodipine/60 mg valsartan, 10 mg/160 mg, 5 mg/320 mg, and 10 mg/320 mg. Exforge has been launched by Novartis in select European countries. The products will be available in the United States no earlier than Sept. 25 of this year, the FDA specified in a December 2006 letter to Novartis, because amlodipine (Norvasc, Pfizer) remains under patent protection until then. ■

Adherence to DASH Diet Slips Among Hypertensive Patients

CHICAGO — Few adults with known hypertension are following the DASH diet plan, even though some evidence suggests that it is roughly the equivalent of being on a single blood pressure medication.

Moreover, accordance with the Dietary Approaches to Stop Hypertension (DASH) plan has deteriorated since it was incorporated into in national guidelines, Dr. Philip Mellen said at the annual meeting of the American Society of Hypertension.

"We appear to be improving somewhat with respect to awareness of hypertension and treatment of hypertension," he said during a press briefing. "But overall, dietary patterns appear to be doing worse."

The landmark 1997 DASH trial showed that a diet rich in fruits, vegetables, grains, and low-fat diary products lowered blood pressure among patients with hypertension by an average of 11.4 mm Hg systolic and 5.5 mm Hg diastolic (N. Engl. J. Med. 1997;336:1117-24).

While hypertension awareness is improving, over time, dietary patterns have gotten worse.

DR. MELLEN

The dietary guidelines were incorporated into the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure reports in 1998 (JNC 6) and 2003 (JNC 7).

Dr. Mellen and his colleagues at Wake Forest University, Winston-Salem, N.C., used 1999-2004 data from the ongoing National Health and Nutrition Examination Survey (NHANES) IV to generate a DASH score for 4,386 adults with hypertension. Scores were based on self-reported 24-hour intake of nine target nutrients identified in the study (fat, saturated fat, protein, cholesterol, fiber, magnesium, calcium, potassium, and sodium). Individuals with a score of 4.5 or more were considered accordant with the DASH diet. These results were compared with scores calculated for 4,556 adults with hypertension in the NHANES III 1988-1994 survey.

DASH accordance fell significantly from 29% in NHANES III to 22% in NHANES IV. The decline was due largely to significantly fewer Americans in the recent survey reaching targets for total fat, fiber, and magnesium, Dr. Mellen said.

The percentage of patients achieving the DASH goal of reducing total fat intake to less than 27% of calories fell from 43% in NHANES III to 36% in NHANES IV.

Similarly, the percentage of participants on a 2,100-kcal diet eating the DASH recommended 31 grams of fiber daily decreased significantly (20% vs. 12%), as did the percentage ingesting the target 500 mg a day of magnesium (14% vs. 6%).

In a multivariate analysis that adjusted for caloric intake and poverty index ratio, participants were significantly more likely to be DASH-accordant if they were aged 40-59 years (odds ratio 2.75, compared with those aged 20-39 years); aged 60 years or older (OR 3.94, compared with those aged 20-39 years); had more than a high school education (OR 1.80); or had diabetes (OR 1.53).

Blacks were significantly less likely than others to follow the DASH diet (OR 0.61), while there was a nonsignificant trend toward higher accordance among Mexican Americans compared with whites, Dr. Mellen said. ■

Losartan Gains Ground Against Hypertension in Obese Patients

CHICAGO — The angiotensin II blocker losartan, alone or in combination with the diuretic hydrochlorothiazide, appears efficacious in the treatment of obesity-associated hypertension, new data suggest.

Current guidelines—based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)—do not specify particular treatments for obesity-related hypertension or for the related metabolic syndrome.

The prominent role of angiotensin II in obesity-induced hypertension, however, suggests the possibility that angiotensin receptor blockade may be useful in its treatment, Dr. Suzanne Oparil said at the annual meeting of the American Society of Hypertension (ASH).

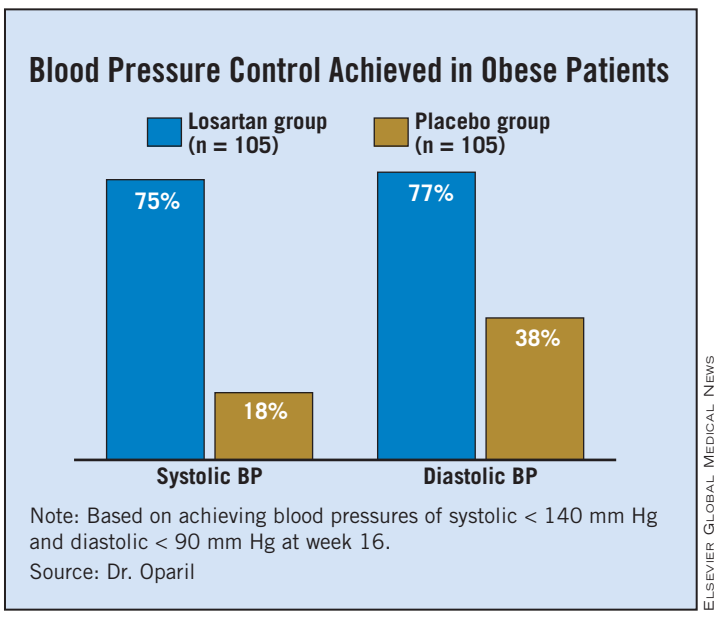
She presented preliminary data from a double-blind trial in which 261 patients from 51 sites were randomized to either placebo or losartan 50 mg/day for 4 weeks, titrated to 100 mg/day. Hydrochlorothiazide 12.5 mg/day was added in the active treatment group at week 8 and titrated to 25 mg/day at week 12.

At admission, the average body mass index was 37 kg/m^2 in the losartan group and 38 kg/m^2 in the placebo group. For both groups, the average waist circumference was 45 inches, and the average BP was 152/99 mm Hg. Entry criteria included use of two or fewer antihypertensive agents, and no diagnosis of diabetes mellitus.

In all, 105 patients in each group completed the study, which was sponsored by Merck & Co. Inc.

Losartan 50 mg reduced the average sitting systolic BP to 140 mm Hg at week 4 and maintained it there through week 8. Adding hydrochlorothiazide to the 100-mg losartan dosage caused significant further reductions to about 133 mm Hg at week 16. Similarly, losartan 50 mg decreased the average sitting diastolic BP to 90 mm Hg at week 4 through week 8. Add-on hydrochlorothiazide decreased the reading to about 85 mm Hg at week 18.

At week 16, 75% of patients on losartan achieved systolic BP control to less than 140 mm Hg, and 77% achieved diastolic BP control to less than 90 mm Hg. In comparison, control rates on placebo were 18% for systolic BP and 38% for diastolic.



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All changes in the losartan group were significantly greater than those in the placebo group for all time points, said Dr. Oparil, president of the ASH and director of the vascular biology and hypertension program at the University of Alabama, Birmingham. Dr. Oparil has received research support from Merck.

The losartan-based treatment regimen had a similar safety and tolerability profile as placebo, she said. ■