Losartan Cut Blood Pressures In Obese Hypertensive Patients

BY PATRICE WENDLING
Chicago Bureau

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.

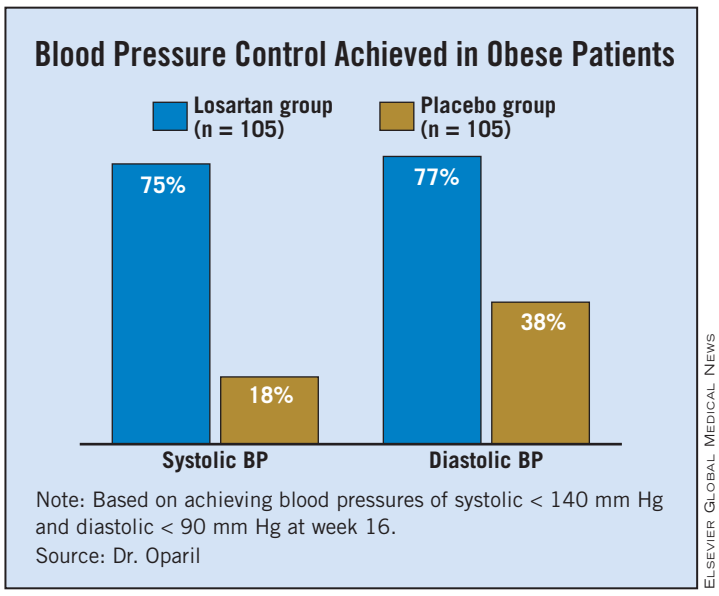
In all, 105 patients in each group completed the study, which was sponsored by Merck & Co. Inc., which has provided research support to Dr. Oparil.

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 those on losartan achieved systolic BP control to less than 140 mm Hg, and 77% achieved diastolic control to less than 90 mm Hg. In comparison, control rates on placebo were 18% for systolic BP and 38% for diastolic.

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



Hyperuricemia Linked to Rise in Hypertension Risk

BY MITCHEL L. ZOLER
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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 at a conference on cardiovascular disease epidemiology and prevention sponsored by the American Heart Association.

The standard agent used to reduce hyperuricemia is allopurinol. 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 for 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.

The study used data collected in the Multiple Risk Factor Intervention Trial (MRFIT), which enrolled nearly 13,000 men in the mid-1970s. Its primary goal 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.

The analysis focused on the 3,073 men who were free from hypertension, metabolic syndrome, and diabetes at baseline, and for whom usable baseline uric-acid levels were available. Men were followed in the MRFIT for an average of 6 years, during which they had annual examinations. The probability that a man with a normal level of uric acid developed hyperuricemia (serum uric acid level > 7.0 mg/dL) at the next annual visit was 14%. The probability that a man with hyperuricemia would remain at an elevated level of uric acid at the next annual visit was 68%. 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 at least 140 mm Hg or a diastolic pressure of at least 90 mm Hg.

In a multivariate analysis that controlled for baseline differences in age, blood pressure, serum creatinine, total cholesterol, smoking, alcohol use, BMI, 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 level of uric acid at baseline, the risk of developing hypertension during follow-up increased by 9%, also a significant difference. ■

Valsartan Shown Effective in Young Hypertensive Children

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Valsartan significantly reduced both systolic and diastolic blood pressure without significant adverse events in the first trial of an angiotensin II receptor blocker in children younger than 6 years.

Valsartan is indicated for the treatment of hypertension and heart failure in adults, but had never been studied in children. In November 2006, the Food and Drug Administration approved safety labeling revisions for valsartan tablets to advise of the risk of fetal and neonatal morbidity when used by pregnant women.

Dr. Joseph Flynn and associates presented preliminary results at the annual meeting of the American Society of Hypertension from a multicenter, placebo-controlled study evaluating three doses of valsartan in 90 children with a mean seated systolic BP of at least the 95th percentile of the National High Blood Pressure Education Program normative BP values for children.

After a 1-week placebo washout screening phase, the children were randomized to low, medium, and high doses of valsartan for 2 weeks (phase 1), and then rerandomized to placebo or valsartan for 2 more weeks (phase 2).

In phase 1, the doses were 5, 20, or 40 mg/day for those children weighing less than 18 kg, and 10, 40, or 80 mg/day for those weighing more than 18 kg. Half of the children stayed on the same dose in phase 2, and half were withdrawn to placebo.

At admission, the children's mean age was 3 years; 60% were boys, and 30% were black. Most children (79%) had hypertension related to renal disease; some (3%) were hypertensive because of heart disease, and 18% because of other causes.

In phase 1, valsartan significantly reduced both systolic and diastolic BP at all three doses, reported Dr. Flynn, who conducted the study while at Children's Hospital at Montefiore, New York, and is now a professor of pediatrics at Children's Hospital and Regional Medical Center, in Seattle. (See box.)

In phase 2, systolic and diastolic BP was significantly lower in children receiving valsartan, compared with those receiving placebo. The mean difference between valsartan and placebo was –4.1 mm Hg for systolic BP and –3.7 mm Hg for diastolic.

"Since many of these children have hypertension due to underlying renal disease, valsartan may be well suited for treatment of hypertension in this age group," Dr. Flynn said in an interview.

Adverse events, such as cold symptoms, were minor and were similar between the different dose groups, he said. No participants discontinued treatment because of an adverse event. ■