Simvastatin, Pravastatin Lower Blood Pressure

BY MITCHEL L. ZOLER
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NEW ORLEANS — Statins produce a small but significant blood pressure reduction that might explain some of the benefits that these drugs provide.

Treatment with either simvastatin or pravastatin led to significant reductions of both systolic and diastolic BP that averaged about 2.5 mm Hg in a controlled study with 1,016 patients, Beatrice A. Golomb, M.D., reported at the annual scientific sessions of the American Heart Association.

"Some patients who are on the cusp of having hypertension and are not on antihypertensive therapy may benefit from the statin effect," which may help them continue to avoid needing a blood pressure–lowering drug, said Dr. Golomb, a cardiologist at the University of California, San Diego. This modest degree of BP reduction may explain the ability of statin therapy to cut the risk of stroke, a finding that has been hard to attribute to lipid-lowering effects.

The study enrolled men and postmenopausal women who did not have heart disease, diabetes, or hypertension, and whose LDL-cholesterol level was 115-190 mg/dL. These patients were randomized to treatment with 20 mg/day simvastatin, 40 mg/day pravastatin, or placebo, and the treatment continued for 6 months.

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After 6 months of treatment, systolic BP had fallen by an average of 2.8 mm Hg in the simvastatin group and by 2.5 mm Hg in the pravastatin group, compared with baseline. Diastolic pressures had dropped by an average of 2. 7 mm Hg and 2.5 mm Hg, compared with baseline in the simvastatin and pravastatin groups, respectively. Once patients were off statin treatment for 2 months, these BP reductions largely disappeared.

The results of a second study presented at the meeting suggested that the blood pressure–lowering effect of a statin is independent of the drug's lipid-lowering effect. This analysis used data collected from the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). This study enrolled more than 19,000 patients with hypertension but without known coronary artery disease to an intervention trial that was primarily designed to compare the effects of different antihypertensive regimens. The study also randomized a 10,305-patient subgroup to treatment with either 10 mg of atorvastatin daily or placebo. The blood pressures recorded in this subset were evaluated in a posthoc analysis to explore whether atorvastatin had any effect on blood pressure.

Although all patients in the study were on combined regimens of antihypertensive drugs, those who also received atorvastatin had small but consistently lower systolic and diastolic BPs than the patients who did not receive statin therapy, reported Bjorn Dahlof, M.D., professor of medicine at the University of Göteborg (Sweden). The 5,168 patients treated with atorvastatin had an average systolic pressure that was about 1 mm Hg lower than that among 5,137 patients treated with placebo at several times during 3 years of follow-up. Diastolic BP averaged about 0.6 mm Hg lower in the atorvastatin group, compared with those on placebo.

Although these differences in pressure were very small, they were statistically significant because the study involved so many people, Dr. Dahlof said.

A further analysis was then done to see if there was a correlation between the blood pressure–lowering effect of atorvastatin and patients' levels of total or LDL cholesterol.

This assessment showed virtually no link between the two effects. Lipid lowering "explained perhaps 1%" of the effect of atorvastatin on blood pressure, Dr. Dahlof reported.

Statins probably have other effects that lower blood pressure, such as activating nitric oxide synthetase, down-regulating angiotensin II, and enhancing flow-mediated vasodilation, Dr. Golomb said. ■

High Folate Linked to Lower Risk Of Hypertension in Young Women

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — High folate intake may lower the risk of hypertension, particularly in young women, according to data presented at a conference of the Council for High Blood Pressure Research.

Young women who consumed at least 800 mcg/day of folate reduced their risk of developing high blood pressure by almost a third, compared with those who consumed less than 200 mcg/day. Folate also reduced the risk in older women to a lesser degree, reported John P. Forman, M.D., a research and clinical fellow at Brigham and Women's Hospital in Boston.

The most striking effects of folate intake were seen among women aged 35 years or younger, he said. Supplemental folic acid also contributed to this decrease in risk, as most of the women in the higher range of folate intake obtained much of their intake from supplements.

Dr. Forman and colleagues based their findings on data from the Nurses' Health Study (NHS) I, comprising 62,260 women aged 43-70 years, and the NHS II, comprising 93,034 women aged 26-46 years. None of the women had high blood pressure at baseline.

Semiquantitative food-frequency questionnaires were used to gather information about dietary and supplemental folate intake at baseline, and were followed up with additional questionnaires every 4 years. Information about physician-diagnosed high blood pressure was self-reported every 2 years.

Cox regression analysis was used to estimate relative risk after the investigators controlled for age, body mass index, smoking, exercise, family history of hypertension, and intake of alcohol, caffeine, salt, calcium, magnesium, potassium, fiber, methionine, and vitamins B_6, B_{12}, and D.

One hypothesis for why the effect of folate varies by age is that the pathogenesis of hypertension may be different in older versus younger women.

Over 8 years of follow-up, there were 12,347 incident cases of hypertension in NHS I and 7,373 incident cases in NHS II.

Young women who consumed at least 800 mcg/day of folate had a 29% lower risk of high blood pressure than did those who consumed less than 200 mcg/day. Older women who consumed at least 800 mcg/day had a 13% lower risk than did those who consumed less than 200 mcg/day.

There was no significant interaction between age and reduced risk among women in the older cohort when divided into three additional subgroups.

One hypothesis for why the effect of folate varies by age is that the pathogenesis of hypertension may be different in older versus younger women, Dr. Forman said at the meeting, sponsored by the American Heart Association.

The Food and Drug Administration began requiring folate supplementation of several foods, including bread and cereals in 1998. But fortification had begun in 1996, spanning the last 2 years of the NHS I and the last 3 years of the NHS II.

The researchers did not directly measure serum folate, which was a limitation of the study, Dr. Forman said. However, the food-frequency questionnaires used in the cohort have been previously validated and are highly correlated with both dietary records and serum folate levels. Additionally, all of the study participants were registered nurses, and self-reported hypertension was thought to be reliable. ■

Body Mass Index Affects CV Event Rate in Hypertensives

NEW ORLEANS — Hypertensive patients at the extremes of body build have a markedly greater cardiovascular event rate than those who are of normal weight, Giovanni de Simoni, M.D., reported at the annual scientific sessions of the American Heart Association.

Dr. de Simoni of Federico II University, Naples, Italy, presented a secondary analysis of the double-blind multinational Losartan Intervention for Endpoint reduction in hypertension (LIFE) trial, in which 9,079 hypertensive individuals were randomized to losartan- or atenolol-based antihypertensive therapy and followed for 4-6 years.

The primary LIFE end point—a composite of cardiovascular (CV) death and nonfatal MI and stroke—occurred in 1,081 patients. The adjusted risk was 25% greater in the 2.2% of study participants who were thin—that is, with a body mass index of less than 20 kg/m^2—than in the 24% of LIFE participants who were of normal weight.

Similarly, after adjusting for age, gender, race, smoking status, diabetes, left ventricular hypertrophy, and other pertinent variables, the rate of the primary study end point was 17% greater in the 45% of LIFE participants who were overweight—that is, having a BMI of at least 25 and less than 30 kg/m^2—than in the normal-weight patients. Among the 8% of LIFE participants with class II or III obesity (defined by a BMI of 35-39.9 kg/m^2 or at least 40 kg/m^2, respectively), the adjusted risk of the primary end point was 35% greater than in normal-weight individuals, he continued.

The differences in outcome based on BMI category were even more striking with respect to cardiovascular mortality, which occurred in 432 LIFE participants. The adjusted risk was 71% greater in thin patients and 80% greater in those with class II-III obesity than in normal-weight hypertensive patients.

Losartan-based therapy was associated with a highly significant 15% reduction in the primary composite end point relative to atenolol-based treatment, regardless of BMI category.

Results of this analysis underscore the necessity of particularly aggressive control of blood pressure and other cardiovascular risk factors in hypertensive patients at the extremes of body build distribution, Dr. de Simoni said.

—Bruce Jancin