

APPENDIX

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NHLBI Stops Part Of Study- High Blood Pressure Drug Performs No Better Than Standard Treatment

The National Heart, Lung, and Blood Institute (NHLBI) has stopped one part of a large high blood pressure study early because one of the tested drugs, an alpha-adrenergic blocker, was found less effective than the more traditional diuretic in reducing some forms of cardiovascular disease.

Called ALLHAT-for Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial-the main portion of the study is comparing newer drug treatments for high blood pressure with a more conventional and less costly treatment. Another portion is comparing treatments for elevated cholesterol.

The NHLBI acted after an independent data review by an advisory committee. Patients were informed as soon as possible thereafter. Those on the alpha-adrenergic blocker were being offered an alternate medication, in consultation with their ALLHAT or personal physician.

The alpha-adrenergic blocker is doxazosin; the diuretic is chlorthalidone. Users of doxazosin had 25 percent more cardiovascular events and were twice as likely to be hospitalized for congestive heart failure as users of chlorthalidone. The drugs were similarly effective in preventing heart attacks and in reducing the risk of death from all causes.

Of the approximately 24 million Americans who take medication to treat their hypertension, about 1 million use an alpha blocker. Doxazosin, the alpha blocker used in ALLHAT, is sold under the brand name CarduraR. (Other alpha blockers used for hypertension are terazosin, sold under the brand name Hytrin, and prazosin, sold under the brand name Minipres).

"This finding adds important information to our understanding of antihypertensive drugs," said NHLBI Director Dr. Claude Lenfant. "No large-scale blood pressure treatment study had ever compared these two classes of drugs. Earlier studies were small and could not, for example, detect an increase in patients' risk of congestive heart failure."

The rest of the ALLHAT study, which began in 1994, will continue as scheduled and is expected to end in 2002.

ALLHAT involves 42,448 patients, enrolled through 623 clinics and centers across the United States, Canada, Puerto Rico, and the US Virgin Islands. About 7,000 U.S. veterans are participating through 69 Department of Veterans

Affairs clinics.

ALLHAT participants are aged 55 or older. Forty-seven percent are women, 47 percent are white, 35 percent are African American, and 16 percent are Hispanic, while 36 percent have diabetes.

On enrollment in the study, participants had been diagnosed with systolic and/or diastolic hypertension (140 mm Hg or higher and 90 mm Hg or higher, respectively), and had at least one added risk factor for coronary heart disease, such as diabetes, cigarette smoking, and a low level of high-density lipoprotein (HDL cholesterol), or had a history of (but no recent) heart attack or stroke.

ALLHAT participants receive periodic checkups and currently have between 2 and 6 years of followup.

ALLHAT also is comparing chlorthalidone with two other high blood pressure drugs—a calcium antagonist, called amlodipine, and an angiotensin-converting enzyme (ACE) inhibitor, called lisinopril.

About a quarter of ALLHAT's hypertensive patients also are participating in the cholesterol-lowering portion of the study. This includes a fourth of the patients on doxazosin, who will be able to continue their involvement in this aspect of the study.

The cholesterol-lowering study involves older patients with slightly to moderately elevated cholesterol. It is testing whether treatment with dietary changes and an HMG CoA reductase inhibitor, called pravastatin, reduces deaths from all causes better than dietary changes alone.

Other findings about doxazosin in comparison to chlorthalidone are:

Those in the doxazosin group had slightly higher systolic blood pressures than the chlorthalidone group, although the diastolic pressures were the same.

The doxazosin group also had poorer compliance with treatment—only 75 percent were still on the drug or another alpha blocker after 4 years, compared with 86 percent still taking chlorthalidone or another diuretic.

Due to the finding, NHLBI advises high blood pressure patients who now take an alpha-adrenergic blocker drug to consult with their doctors about a possible alternative. If a patient is just starting drug treatment, an alpha-adrenergic blocker may not be the best choice for initial therapy.

“Patients on an alpha blocker for high blood pressure should see their doctor and not just stop taking it,” emphasized Dr. Jeffrey Cutler, director of the NHLBI Clinical Applications and Prevention Program and ALLHAT project officer. “We cannot conclude that the drug was harmful. Rather it didn't work as well as the diuretic in reducing cardiovascular disease.”

About 50 million Americans have high blood pressure and about 52 million have high blood cholesterol. Both conditions are major risk factors for coronary heart disease and both strike particularly hard at older adults. High blood pressure

also is the chief risk factor for both congestive heart failure and stroke.

Treatment for both high blood pressure and high blood cholesterol typically starts with lifestyle changes, including increased physical activity and weight loss for the overweight. A healthy, low-saturated fat, low-cholesterol eating plan is advised and, for high blood pressure, avoiding excess salt, sodium, and alcohol.

When those changes do not lower elevated blood pressure or cholesterol enough, then drug therapy is needed.

For an interview about ALLHAT, contact the NHLBI Communications Office at (301) 496-4236.

NHLBI press releases, fact sheets, and other materials are available online at www.nhlbi.nih.gov

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