MedicalXpress

Gene variations associated with effectiveness of blood pressure medications

January 22 2008

Patients with hypertension and certain gene variations experienced varying results with some blood pressure medications, suggesting matching a patient's genotype with certain hypertension medications could result in more favorable outcomes, according to a study in the January 23 issue of JAMA.

Approximately 71 million individuals in the United States have one or more types of cardiovascular disease (CVD), of whom at least 65 million have hypertension. Although control of hypertension has been improving in recent years, among those treated, only about two-thirds have their hypertension controlled, according to background information in the article. Seeking ways to reduce CVD illness and death by tailoring treatment to a patient's particular genotype has been an area of research, but results have yet to yield therapeutic choices for the clinical setting.

Amy I. Lynch, Ph.D., of the University of Minnesota, Minneapolis, and colleagues conducted a study to examine whether patients with hypertension with minor NPPA (atrial natriuretic precursor A) genotypes (NPPA G664A and NPPA T2238C) randomized to the diuretic chlorthalidone had different outcomes for CVD measures than patients who were randomized to other classes of antihypertensive medication. Previous research has suggested that the NPPA gene may influence the effectiveness of some antihypertensive drugs.

The study included 38,462 participants with hypertension from ALLHAT (Antihypertensive and Lipid Lowering Treatment to Prevent

Heart Attack Trial), a multicenter randomized clinical trial conducted in the United States and Canada. Genotyping was performed from February 2004 to January 2005. Participants were randomly assigned to receive a diuretic (chlorthalidone; n = 13,860), a calcium channel blocker (amlodipine; n = 8,174), an angiotensin-converting enzyme (ACE) inhibitor (lisinopril; n = 8,233), or an alpha-blocker (doxazosin; n = 8,195). Follow-up averaged 4.9 years.

The researchers found evidence of a pharmacogenetic association of the NPPA T2238C variant with coronary heart disease (CHD), stroke, all-cause death, combined CHD, and combined CVD when comparing the chlorthalidone (diuretic) group with the amlodipine (calcium channel blocker) group, and for stroke when comparing the chlorthalidone group with those receiving amlodipine or lisinopril (ACE inhibitor). The association was consistent for all outcomes: those with at least one copy of the minor C allele (alternative form of a gene) had lower risk of disease and/or death when assigned to chlorthalidone compared with those assigned to amlodipine (and the amlodipine group plus the lisinopril group for stroke), while those in the chlorthalidone group with the TT genotype had higher risk of disease and/or death than those assigned to amlodipine.

“We also observed a pharmacogenetic association of NPPA T2238 on change in systolic and diastolic blood pressure 6 months after treatment randomization in a similar direction: generally, minor C allele carriers had greater reductions in blood pressure when randomized to chlorthalidone vs. either lisinopril or doxazosin relative to those with the common TT genotype,” the authors write.

“This study demonstrates the importance (and sometimes paradoxical findings) of pharmacogenetic research; for example, while minor NPPA T2238C allele carriers (as well as the entire study population viewed as a whole) may have had more favorable outcomes when randomized to a

diuretic (chlorthalidone), participants with the most common genotype (TT) responded better when assigned to a calcium channel blocker (amlodipine) for some clinical outcomes."

"Further research is needed to determine the optimal approach for personalizing antihypertensive medication treatment regiments according to genotype information and for achieving the best possible clinical outcomes," the researchers conclude.

Source: JAMA and Archives Journals