New Hypertension Drugs Not Necessarily the Best

BY JOHN R. BELL
Associate Editor

Newer-generation hypertension drugs were no better than thiazide-type diuretics at preventing heart failure and cardiovascular disease events in hypertensive patients with metabolic syndrome, and in some cases they were worse, according to findings from a subgroup analysis.

These recent findings from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), suggest that results reported earlier for the cohort overall also hold true for the subset of patients with metabolic syndrome:

In particular, in black patients with metabolic syndrome, the ACE inhibitor lisinopril was associated with higher stroke and end-stage renal disease risks.

Despite the fact that the newer agents have a more favorable metabolic profile, the evidence fails to support their use as first-line therapy. In black patients with metabolic syndrome, in particular, the angiotensin-converting enzyme (ACE) inhibitor lisinopril was associated with higher stroke and end-stage renal disease risks and should not be considered as first-line.

Dr. Jackson T. Wright Jr. of Case Western Reserve University, Cleveland, and colleagues compared rates of adverse events among the 37,291 male and female ALLHAT participants with metabolic or cardiometabolic syndrome who were at least aged 55 years and who were randomly assigned to take the calcium-channel blocker amlodipine (Norvasc) (7,945 patients), the α-blocker doxazosin (Cardura) (7,928 patients), the ACE inhibitor lisinopril (Prinivil, Zestril) (7,948 patients), or the thiazide-type diuretic chlorthalidone (13,470 patients).

All of the patients, regardless of race, showed greater risk of heart failure with all three of the newer drugs than with chlorthalidone. For black patients, the relative risks of HF with amlodipine, lisinopril, and doxazosin were 1.5, 1.49, and 1.88, respectively, compared with chlorthalidone; for nonblack patients, the RRs were 1.5, 1.20, and 1.82 (Arch. Intern. Med. 2008;168:207-17).

Regarding combined cardiovascular disease end points (including heart disease, stroke, other treated angina, any heart failure, or peripheral arterial disease), compared with chlorthalidone, lisinopril and doxazosin were both associated with greater risk rates among black patients (RR 1.24 and 1.37, respectively) and nonblack patients (RR 1.10 and 1.18).

A higher risk for stroke was seen only among black patients taking lisinopril (RR 1.37) or doxazosin (RR 1.49). Lisinopril also conferred a higher risk of end-stage renal disease among black patients (RR 1.7).

The investigators used the National Cholesterol Education Program definition of metabolic syndrome but replaced waist circumference with body mass index. Mean follow-up was about 5 years for all comparisons except that of α-blockers with chlorthalidone, which was roughly 3 years.

The authors' strongest statement was regarding the use of ACE inhibitors in black patients: "The magnitude of the excess risk of [end-stage renal disease] (70%), heart failure (49%), and stroke (37%) and the increased risk of combined CVD and combined CHD strongly argue against the preference of ACE inhibitors over diuretics as the initial therapy in black patients with [metabolic syndrome]," Dr. Wright and colleagues wrote.

They acknowledged that a criticism of the previous ALLHAT findings was that the follow-up was too short for the metabolic benefits of the newer drugs to translate into reductions in the risk for the adverse events. However, until long-term data are available, they predicted no change to the outcome of that study or the subanalysis, given the small metabolic changes seen with the drugs in question and that drug-induced increases in blood glucose do not carry the same risk for adverse clinical outcomes as other factors, such as sedentary lifestyle.

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