

In Blacks With Hypertensive Kidney Disease:

Ramipril Reduced Diabetes Risk

In the AASK, three different drug classes were compared.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

The African American Study of Kidney Disease and Hypertension (AASK) was a multicenter trial of nondiabetic black patients with chronic kidney disease due to hypertension. Patients were randomized to an angiotensin-converting enzyme (ACE) inhibitor (ramipril), a beta-blocker (metoprolol) or a calcium antagonist (amlodipine). Denyse Thornley-Brown, MD, and the AASK Study Group compared the incidence of type 2 diabetes and the composite outcome of impaired fasting glucose (IFG) or diabetes for these interventions.

The incidence of type 2 diabetes and its complications are higher among blacks, American Indians and Latinos than among white Americans, Dr. Thornley-Brown and colleagues wrote in the *Archives of Internal Medicine*. Dr. Thornley-Brown is in the division of nephrology, University of Alabama at Birmingham. Recent clinical trials of hypertension treatment have reported a lower incidence of diabetes among patients treated with an ACE inhibitor or an angiotensin II receptor antagonist compared with other classes of drugs. Only one previous trial enrolled a population made up of >20% blacks, and the association of the drug interventions and diabetes risk were not stratified by race.

Therefore, the authors wrote, it is unknown if the lower associated risk of diabetes with ACE inhibitors occurs in black patients. Because only one trial had more than two randomized drug groups, it is difficult to assess whether the net benefit of ACE inhibitor treatment results from the drug or from an adverse effect of the comparison treatment.

In AASK, Cox regression models were used to evaluate (post hoc) the association of the randomized interventions and the relative risk (RR) of diabetes and IFG/diabetes as well as to assess the RR of diabetes and IFG/diabetes by several prerandomization characteristics, they wrote.

Of 1,017 patients, 14.5% developed diabetes; 42.9% of 776 participants developed IFG/diabetes. Respective diabetes event rates were 2.8%, 4.4% and 4.5% per patient-year in the

ramipril, amlodipine and metoprolol groups.

The RRs of diabetes with ramipril were 0.53 ($P=.001$) compared with metoprolol and 0.49 ($P=.003$) compared with amlodipine. Respective IFG/diabetes event rates were 11.3%, 13.3% and 15.8% per patient-year in the ramipril-, amlodipine- and metoprolol-assigned patients. The RRs of IFG/diabetes with ramipril were 0.64 ($P<.001$) compared with metoprolol and 0.76 ($P=.09$) compared with amlodipine treatment. The RRs of diabetes and IFG/diabetes with amlodipine compared with metoprolol were 1.07 ($P=.76$) and 0.84 ($P=.26$), respectively.

Dr. Thornley-Brown and the AASK investigators found that fasting serum glucose levels increased over time in black patients with hypertensive kidney disease, and these patients were at high risk of developing diabetes and IFG/diabetes. Ramipril was associated with a smaller rise in fasting serum glucose compared with amlodipine and metoprolol.

“The AASK is distinctive because it compared multiple classes of drugs,” they wrote. “The results of this analysis are the first to demonstrate the superiority of an ACE inhibitor over a metabolically neutral agent ... suggesting that the metabolic effects of blockade of the renin angiotensin system are more than simple neutralization of the adverse effects of beta-blockers or thiazide diuretics.”

The racial make up of the trial was also unique, the authors said. AASK underscores the beneficial effects of ACE inhibitors in black patients with renal disease and demonstrates that these drugs have additional benefits that are independent of their blood pressure effects. ■

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Thornley-Brown D, Wang X, Wright JT, et al for the AASK Study Group. Differing effects of antihypertensive drugs on the incidence of diabetes mellitus among patients with hypertensive kidney disease. *Arch Intern Med*. 2006;166:797-805.