Amlodipine or lisinopril was not better than chlorthalidone for reducing CVD risk in hypertensive black or nonblack patients

Wright JT Jr., Dunn JK, Cutler JA, et al. **Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril.** JAMA. 2005;293:1595-608.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Cardiology ★★★★★★☆

QUESTION

In black or nonblack patients with hypertension, is amlodipine or lisinopril better than chlorthalidone for reducing cardiovascular disease (CVD)?

METHODS

Design: Randomized controlled trial (Antihypertensive and Lipid-lowering Treatment to Prevent Heart Attack Trial [ALLHAT]).

Allocation: Concealed.*

Blinding: Blinded {clinicians, patients, data collectors, outcome assessors, and steering committee}†.*

Follow-up period: Mean 4.9 years.

Setting: 623 centers in the United States, Canada, Puerto Rico, and the U.S. Virgin Islands.

Patients: 33 357 black and nonblack patients ≥ 55 years of age (mean age 67 y, 35% black, 53% men overall, 54% women among blacks) who had untreated or treated hypertension with ≥ 1 additional risk factor for coronary heart disease (CHD), including left ventricular (LV) hypertrophy, type 2 diabetes mellitus, current smoker, high-density lipoprotein cholesterol level < 0.9 mmol/L (35 mg/dL), and myocardial infarction (MI) or stroke in the previous 6 months. Patients with treated symptomatic heart failure (HF) or LV ejection fraction < 35% were excluded.

Intervention: Chlorthalidone, 12.5 to 25 mg/d (n = 15 255); amlodipine, 2.5 to 10 mg/d (n = 9048); or lisinopril, 10 to 40 mg/d (n = 9054).

Outcomes: Composite endpoint of fatal CHD and nonfatal MI. Secondary outcomes included all-cause mortality, fatal and nonfatal stroke, combined CHD, and combined CVD.

Patient follow-up: 97% (intention-to-treat analysis).

MAIN RESULTS

Overall, fewer blacks than nonblacks had the composite endpoint (9.7% vs 12.3%), combined CHD (15.9% vs 22.5%), and combined CVD (28.4% vs 33.7%) (P for all interactions < 0.001). Blacks had higher rates of stroke (6.5% vs 5.3%, P < 0.001), end-stage renal disease (2.6% vs 1.5%, P < 0.001), and overall mortality (17.7% vs 16.8%, P = 0.003) than nonblacks. The 3 treatment groups did not differ for the composite endpoint in either racial subgroup (Table). In blacks or nonblacks, no difference was found between amlodipine and chlorthalidone for any secondary outcomes except for HF (relative risk [RR] for blacks 1.46, 95% CI 1.24 to 1.73; nonblacks 1.32, CI 1.17 to 1.49; overall 1.37, CI 1.24 to 1.51). In blacks, lisinopril was associated with more combined CHD or CVD, stroke, and HF than chlorthalidone (RR range 1.15 to 1.40, lower CI range 1.02 to 1.17, upper CI range 1.30 to 1.68).

CONCLUSIONS

In black or nonblack patients with hypertension, amlodipine or lisinopril was not better than chlorthalidone for reducing cardiovascular disease. Chlorthalidone was associated with a lower risk for heart failure than amlodipine or linisopril in either racial subgroup.

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For correspondence: Dr. J.T. Wright Jr., Case Western Reserve University, Cleveland, OH, USA. E-mail jackson.wright@case.edu. ■

*See Glossary.

†The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA. 2002;288:2981-97.

Amlodipine (Amlod) or lisinopril (Lis) vs chlorthalidone (Chlor) for combined fatal coronary heart disease and nonfatal myocardial infarction at mean 4.9 years‡

Patients	Comparisons	Event rates	RRI (95% CI)	NNH
Blacks	Amlod vs chlor	7.6% vs 7.4%	1.5% (–13 to 18)	Not significant
	Lis vs chlor	8.1% vs 7.4%	8.7% (–6 to 26)	Not significant
			RRR (CI)	NNT
Nonblacks	Amlod vs chlor	9.5% vs 9.7%	2.2% (–8 to 11)	Not significant
	Lis vs chlor	9.2% vs 9.7%	5.7% (–4 to 15)	Not significant

‡Abbreviations defined in Glossary; event rates, RRI, RRR, NNH, NNT, and CI calculated from data in article.

COMMENTARY

In this planned substudy of the ALLHAT trial (1), Wright and colleagues examined whether CVD outcomes differed between black and nonblack patients who were started on 1 of 3 different classes of antihypertensive agents. Confirming the main trial's results, initial treatment with either amlodipine or lisinopril was not found to be superior to chlorthalidone in either racial group. In blacks, blood pressure (BP) was lowered by all 3 drugs, although less so by lisinopril, as patients on this drug had final systolic BP readings 5 mm Hg higher than in the other groups. This is congruent with other research suggesting reduced responsiveness to angiotensin-converting enzyme (ACE) inhibitors among blacks (2).

In this trial, black patients in the lisinopril group had increased rates of stroke, CHD, and combined CVD. Because lisinopril did not lower BP as much, it is uncertain if lisinopril's worse CVD outcomes were simply caused by ineffective BP control or some ACE inhibitor–related effect.

Despite equivalent BP lowering in patients treated with amlodipine and chlorthalidone, fewer patients of either race developed HF while taking chlorthalidone. Other CV endpoints were equivalent. These data do not support the view that amlodipine is more effective in patients of either race.

These results bolster the recommendation of the Joint National Committee 7, which states that thiazide diuretics be the first-line antihypertensive choice for most patients (3), including blacks and nonblacks.

Mark Rosenberg, MD
Meera Jain, MD
Providence Portland Medical Center
Portland, Oregon, USA

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3. **Chobanian AV, Bakris GL, Black HR, et al.** Hypertension. 2003;42:1206-52.