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


Clinical impact ratings GP/FP/Primary care ★★★★★☆ IM/Ambulatory care ★★★★★☆

Cardiology ★★★★★☆

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

METHODS

Design: randomised 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 centres in the US, Canada, Puerto Rico, and the US Virgin Islands.

Patients: 33 357 black and non-black patients >55 years of age (mean age 67 y, 35% black, 53% men overall, 54% women among blacks) who had hypertension with >1 additional risk factor for coronary heart disease (CHD), including left ventricular [LV] hypertrophy, type 2 diabetes, current smoker, high density lipoprotein cholesterol concentration <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, 12.5–25 mg/day (n = 15 255); amlodipine, 2.5–10 mg/day (n = 9048); or lisinopril, 10–40 mg/day (n = 9054).

Outcomes: composite end point of fatal CHD and non-fatal MI. Secondary outcomes included all cause mortality, fatal and non-fatal stroke, combined CHD, and combined CVD.

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

^See glossary.

MAIN RESULTS

Overall, fewer blacks than non-blacks had the composite end point (9.7% v 12.3%), combined CHD (15.9% v 22.5%), and combined CVD (28.4% v 33.7%) (p for all interactions <0.001). Blacks had higher rates of stroke (6.5% v 5.3%, p<0.001), end stage renal disease (2.6% v 1.5%, p<0.001), and overall mortality (17.7% v 18.6%, p = 0.003) than non-blacks. The 3 treatment groups did not differ for the composite end point in either racial subgroup (see table on website [www.evidence-basedmedicine.com]). In blacks or non-blacks, 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; non-blacks 1.32, CI 1.17 to 1.49; overall 1.37, CI 1.18 to 1.59).

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

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CONCLUSIONS

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

Abstract and commentary also appear in ACP Journal Club.

Commentary

In this planned substudy of the ALLHAT trial,^ Wright et al examined whether CVD outcomes differed between black and non-black 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 end points 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,^ including blacks and non-blacks.

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

