

Losartan was more effective than atenolol for isolated systolic hypertension and left ventricular hypertrophy

Kjeldsen SE, Dahlöf B, Devereux RB, et al. Effects of losartan on cardiovascular morbidity and mortality in patients with isolated systolic hypertension and left ventricular hypertrophy: a Losartan Intervention for Endpoint Reduction (LIFE) substudy. *JAMA*. 2002;288:1491-8.

QUESTION

In patients with isolated systolic hypertension (ISH) and left ventricular hypertrophy (LVH), is losartan-based therapy more effective than atenolol-based therapy?

DESIGN

Randomized {allocation concealed*}†, blinded {patients, clinicians, data collectors, outcome assessors, data analysts, and manuscript writers}†,* controlled trial with mean 4.7-year follow-up.

SETTING

945 outpatient settings in Europe and the United States.

PATIENTS

1326 patients between 55 and 80 years of age (mean age 70 y, 60% women) with ISH (sitting blood pressure [BP] 160 to 200 mm Hg systolic and < 90 mm Hg diastolic after 1 to 2 wk of placebo) and electrocardiographic signs of LVH. Follow-up was 99.8%.

INTERVENTION

Patients were allocated to once-daily losartan-based therapy ($n = 660$) or atenolol-based therapy ($n = 666$) with hydrochlorothiazide as the second agent in both groups to reach a target systolic BP < 140 mm Hg.

MAIN OUTCOME MEASURES

A composite endpoint of cardiovascular mortality, myocardial infarction (MI), and stroke. Secondary outcomes included all-cause mortality and new-onset diabetes mellitus.

MAIN RESULTS

Analysis was by intention to treat. After adjustment for degree of LVH and Framingham risk score (sex, cholesterol, high-density lipoprotein cholesterol, smoking, presence of diabetes and LVH, systolic BP, and body mass index) at baseline, groups did not differ for the composite endpoint (Table) or MI. Cardiovascular mortality, stroke, all-cause mortality, and new-onset diabetes occurred less frequently in patients

who received losartan than in those who received atenolol (Table).

CONCLUSION

In patients with isolated systolic hypertension and left ventricular hypertrophy, losartan reduced cardiovascular mortality, stroke, all-cause mortality, and new-onset diabetes more than atenolol.

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For correspondence: Dr. S.E. Kjeldsen, Ullevaal Hospital, Oslo, Norway. E-mail sverre.kjeldsen@ioks.uio.no. ■

*See Glossary.

†Information provided by author.

Losartan vs atenolol in isolated systolic hypertension and left ventricular hypertrophy (LVH) at mean 4.7 years†

Outcomes	Losartan	Atenolol	Adjusted RRR (95% CI)§	Adjusted NNT
Composite endpoint	11%	16%	25% (-1 to 44)	Not significant
				Unadjusted NNT (CI)
Cardiovascular mortality	4%	8%	46% (13 to 66)	27 (16 to 84)
Stroke	5%	8%	40% (8 to 62)	28 (16 to 112)
All-cause mortality	10%	14%	28% (0 to 47)	25 (13 to 213)
New-onset diabetes	6%	9%	38% (3 to 60)	31 (16 to 735)

‡Abbreviations defined in Glossary; unadjusted NNT and CI calculated from data in article.

§Adjusted for degree of LVH and Framingham risk score at baseline.

||Cardiovascular mortality, stroke, and myocardial infarction.

COMMENTARY

In the study by Kjeldsen and colleagues of patients with ISH and electrocardiographic evidence of LVH, blockade of the renin angiotensin system with the angiotensin-receptor blocker losartan reduced cardiovascular events more than did the β -blocker atenolol, despite similar BP lowering. Given that the goal of antihypertensive therapy is to prevent cardiovascular events, this shows that the choice of antihypertensive agent is just as important as lowering BP in ISH.

Although losartan reduced the rate of stroke and cardiovascular mortality more than did atenolol, noticeably absent in these results was any treatment benefit in MI. Kjeldsen and colleagues propose that "cardioprotective" actions of β -blockers may also extend to hypertension. However, the Medical Research Council (MRC) trial in older adults (1) found that the diuretic combination of hydrochlorothiazide and

amiloride reduced MI by 24%, but the β -blocker atenolol showed no substantial reduction despite similar levels of BP lowering. Importantly, 43% of the participants in the MRC trial had ISH. Because the MRC trial suggests that atenolol was not as "cardioprotective" as hydrochlorothiazide combined with amiloride, further study is probably required. In the meantime, we no longer have to treat hypertension with β -blockers as if it was "pre-" coronary disease.

Christopher M. Rembold, MD
University of Virginia
Charlottesville, Virginia, USA

Reference

1. Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. *BMJ*. 1992;304:405-12.