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


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

Design
Randomised [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 US.

Patients
1326 patients between 55 and 80 years of age (mean age 70 y, 60% women) with ISH (sitting blood pressure [BP] 160–200 mm Hg systolic and <90 mm Hg diastolic after 1–2 wk of placebo) and electrocardiographic signs of LVH. Follow up was 90.8%.

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 more than atenolol.

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.

COMMENTARY
In the study by Kjeldsen et al 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 on MI. Kjeldsen et al propose that “cardioprotective” actions of β blockers may also extend to hypertension. However, the Medical Research Council (MRC) trial in older adults 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 and the fact that 43% of the patients 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.

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

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Losartan</th>
<th>Atenolol</th>
<th>Adjusted RRR (95% CI)§</th>
<th>Adjusted NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite endpoint†</td>
<td>11%</td>
<td>16%</td>
<td>25% (−1 to 44)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>4%</td>
<td>8%</td>
<td>46% (13 to 66)</td>
<td>27 (16 to 84)</td>
</tr>
<tr>
<td>Stroke</td>
<td>5%</td>
<td>8%</td>
<td>40% (8 to 62)</td>
<td>28 (16 to 112)</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>10%</td>
<td>14%</td>
<td>28% (0 to 47)</td>
<td>25 (13 to 213)</td>
</tr>
<tr>
<td>New onset diabetes</td>
<td>6%</td>
<td>9%</td>
<td>38% (3 to 60)</td>
<td>31 (16 to 735)</td>
</tr>
</tbody>
</table>

*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.