Ramipril delays progression of hypertensive renal disease more than amlodipine


BACKGROUND

End-stage renal disease resulting from hypertension is increasing, especially among African Americans. The optimal antihypertensive treatment to prevent renal failure is unknown.

OBJECTIVE

To compare effects of the ACE-inhibitor ramipril and the calcium channel blocker amlodipine in African Americans with hypertensive renal disease.

DESIGN

Randomized trial.

SETTING

PARTICIPANTS

Six hundred 18-70 year old African Americans with hypertensive renal disease; glomerular filtration rate 20-65 mL/min per 1.73 m²; 39% women; mean age 54 years. Those with diastolic blood pressure < 95 mm Hg; other identified cause of renal insufficiency; history of diabetes; accelerated or malignant hypertension within 6 months; secondary hypertension; serious systemic disease; congestive heart failure; contraindication to treatments; or urinary protein to creatine ratio > 2.5 were excluded.

INTERVENTION

Amlodipine (5-10 mg per day) or ramipril (2.5-10 mg per day). Median follow-up was 36 months. Other agents added to achieve blood pressure goals.

OUTCOMES

Fall in glomerular filtration rate (defined as 50% reduction from baseline or fall by 25 mL/min per 1.73 m² from baseline); end-stage renal disease; death.

MAIN RESULTS

After adjusting for pre-specified covariates, the ramipril group had 38% reduced risk of the combined end-point of death, fall in glomerular filtration rate or end-stage renal disease (95% CI: 13-56%) and less proteinuria (\( P < 0.001 \)). See Table 1. After 3 months there was no difference between ramipril and amlodipine arms in the mean number of hypertensive drugs prescribed per patient.

<table>
<thead>
<tr>
<th>Event</th>
<th>Events per person year for ramipril group (n = 436)</th>
<th>Events per person year for amlodipine group (n = 217)</th>
<th>Relative risk reduction % (95% confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall in glomerular filtration rate</td>
<td>0.028</td>
<td>0.038</td>
<td>41 (5 to 63)</td>
<td>0.03</td>
</tr>
</tbody>
</table>
**TABLE 1** — Clinical event rates for people with hypertensive renal disease treated with ramipril or amlodipine

<table>
<thead>
<tr>
<th>Event</th>
<th>Events per person year for ramipril group (n = 436)</th>
<th>Events per person year for amlodipine group (n = 217)</th>
<th>Relative risk reduction % (95% confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-stage renal disease</td>
<td>0.03</td>
<td>0.043</td>
<td>44 (13 to 65)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death</td>
<td>0.011</td>
<td>0.016</td>
<td>31 (−41 to 66)</td>
<td>0.31</td>
</tr>
<tr>
<td>End-stage renal disease or death</td>
<td>0.042</td>
<td>0.06</td>
<td>41 (14 to 60)</td>
<td>0.007</td>
</tr>
<tr>
<td>Fall in glomerular filtration rate, end-stage renal disease or death</td>
<td>0.058</td>
<td>0.077</td>
<td>38 (13 to 56)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Note:* ‘Fall in glomerular filtration rate’ defined as 50% reduction from baseline or fall by 25 mL/min per 1.73 m² from baseline.

**AUTHORS’ CONCLUSIONS**

Compared with amlodipine, ramipril more effectively retards renal disease progression in African Americans with hypertensive renal disease.

**NOTES**

The amlodipine arm was terminated early due to safety concerns. Comparative results are therefore derived from short-term data obtained before termination of the amlodipine arm. There is also a metoprolol arm in this study. If and the ramipril arm have continued.
Commentary

Research on renal disease treatment outcomes is important because end-stage renal disease, be it due to hypertensive nephrosclerosis or diabetic nephropathy, has become a major health problem. Furthermore, such studies demonstrate the importance of reducing blood pressure and urinary excretion of protein for preventing end-stage renal disease and cardiovascular events.\(^1\)

The present study suggests that an ACE inhibitor is more effective than a calcium channel blocker for delaying progression of renal disease in people with hypertensive nephrosclerosis, although the blood pressure lowering effect of both drugs is identical. This fact suggests that ACE inhibitors may have a specific additional effect on renal protein excretion in non-diabetic patients with renal disease, a notion which is supported by other research, notably the REIN study.\(^2\) Comparison with previous studies is, however, complicated by the fact that studies use different markers of renal function, such as protein excretion, albumin excretion, urinary protein/creatinine ratio, glomerular filtration rate.

Studies have indicated that in groups at high risk of renal disease, such as normotensive normoalbuminuric diabetics, or normoalbuminuric hypertensive non-diabetics, renal albumin excretion may be decreased.\(^3\) This suggests that the urinary protein/albumin ratio may be important for selecting patients in these groups for early or even prophylactic ACE inhibitor treatment.

Editor’s Note:
The African American ethnic group has previously been found to be less responsive to the antihypertensive action of ACE inhibition\(^1\) and had not been previously studied in sufficient numbers to determine the impact of ACE inhibition on progression of renal disease. The present study demonstrates that the new-protective effect of an ACE inhibitor-based regimen extends to African Americans.

**Literature cited**


**Reference**