Intensified blood pressure (BP) control was not better than conventional BP control in non-diabetic chronic renal disease


Clinical impact ratings Nephrology ******

Q In patients with non-diabetic nephropathy and persistent proteinuria, is an intensified blood pressure (BP) control programme more effective than conventional BP control for slowing progression to end stage renal disease (ESRD)?

METHODS

Design: randomised controlled trial (Ramipril Efficacy In Nephropathy [REIN] 2 trial).

Allocation: concealed.*

Blinding: unblinded.*

Follow up period: median 19 months (total follow up period 36 mo).

Setting: 29 centres in Bulgaria, Italy, Spain, and Switzerland.

Patients: 338 patients (age range 18–70 years) with non-diabetic nephropathy and persistent proteinuria (ie, a proteinuria of 1–3 g/d and creatinine clearance <45 ml/min per 1.73 m² or proteinuria ≥3 g/d and creatinine clearance <70 ml/min per 1.73 m²) who had not received angiotensin converting enzyme (ACE) inhibition treatment for >6 weeks. Exclusion criteria included use of corticosteroids, non-steroidal anti-inflammatory drugs, or immunosuppressive drugs; and acute myocardial infarction or cerebrovascular accident in previous 6 months.

Intervention: intensified BP control (<130 mm Hg systolic and <80 mm Hg diastolic) (n = 169) or conventional BP control (<90 mm Hg diastolic irrespective of systolic BP) (n = 169). Patients in the intensified BP control group received felodipine (5–10 mg/d). All patients received ramipril (2.5–5 mg/d) plus any needed concomitant antihypertensive drugs.

Outcomes: time to ESRD over 36 months’ follow up. The study had 90% power to detect a 50% difference in the cumulative incidence of ESRD between the 2 treatment groups.

Patient follow up: 99% (mean age 54 y, 75% men) (intention to treat analysis).

*See glossary.

MAIN RESULTS

Throughout follow up, mean BP was 129.6/79.5 mm Hg in the intensified group and 133.7/82.3 mm Hg in the conventional group. Groups did not differ for progression to ESRD (table).

CONCLUSION

In non-diabetic nephropathy and persistent proteinuria, intensified blood pressure (BP) control was not more effective than conventional BP control for slowing progression to end stage renal disease.

Commentary

To slow kidney function decline, guideline committees have recommended BP levels <125–130 / 75–80 mm Hg for patients with kidney disease.

Results from the MDRD study are often cited as evidence for the lower targets. In the MDRD study, patients were randomised to a mean arterial pressure (MAP) of 92 or 107 mm Hg. Although the overall results were inconclusive, patients with proteinuria >1 g/day had a slower decline in glomerular filtration rate if they were assigned to a MAP of 92 compared with 107 mm Hg.* A recent 10 year follow up from this study showed a 32% reduction in ESRD risk for patients randomised to the low BP arm.† Lack of BP measurements for the final 7 years of the trial and differential use of angiotensin converting enzyme (ACE) inhibitors (16–20% higher ACE inhibitor use in the low BP arm) are clear limitations of this study.

Two other clinical trials have addressed the issue of target BP in non-diabetic kidney disease. The AASK trial randomised patients to a MAP of 92 mm Hg compared with 102–107 mm Hg. No difference in GFR decline or clinical events was seen over 4 years despite mean achieved BP of 128/78 mm Hg compared with 141/85 mm Hg. Results from the REIN-2 trial by Ruggenenti et al support these findings, although the difference in achieved BP was only 1.4 mm Hg systolic and 2.8 mm Hg diastolic.

How do we interpret these trials in patients with non-diabetic nephropathies? Given the MDRD study limitations, more credence should be given to the AASK and REIN-2 results. Intensive BP control does not appear to be warranted in patients with non-diabetic kidney disease. Higher thresholds may be more practical and evidence-based, recognising that not all share this opinion.‡

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<table>
<thead>
<tr>
<th>Outcomes at median 19 months</th>
<th>Intensified BPC</th>
<th>Conventional BPC</th>
<th>RRI (95% CI)†</th>
<th>NNH</th>
</tr>
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<tbody>
<tr>
<td>End stage renal disease</td>
<td>23%</td>
<td>20%</td>
<td>0% (−0.36 to 0.53)</td>
<td>Not significant</td>
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</tbody>
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*Abbreviations defined in glossary; RRI and CI calculated from hazard ratio in the article. †Adjusted for sex, age, mean arterial pressure, concentration in serum of creatinine, and log transformed 24 hour proteinuria.

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