Benazepril was effective and safe for advanced chronic kidney disease without diabetes


Clinical impact ratings: GM/FP/GP ★★★★★★☆ Nephrology ★★★★★☆☆☆☆

Question
In patients with advanced chronic kidney disease (CKD) without diabetes, does benazepril delay the progression of renal dysfunction?

Methods
Design: Randomized placebo-controlled trial.
Allocation: [Concealed]†.*
Blinding: Blinded (patients, outcome assessors, monitoring committee, [data collectors, and data analysts]†).*
Follow-up period: Mean 3.4 years.
Setting: A hospital in Guangzhou, China.
Patients: 224 patients 18 to 70 years of age (mean age 45 y, 50% men) who had a serum creatinine level 3.1 to 5.0 mg/dL (274 to 442 μmol/L) with < 30% change in the previous 3 months, nondiabetic renal disease, and persistent proteinuria and had not received angiotensin-converting enzyme (ACE) inhibitors in the past 6 weeks. Exclusion criteria included immediate need for dialysis; current treatment with corticosteroids, nonsteroidal antiinflammatory drugs, or immunosuppressive drugs; renovascular disease; myocardial infarction or cerebrovascular events within the previous year; connective tissue disease; and obstructive uropathy.
Intervention: Benazepril, 10 mg twice daily (n = 112), or placebo (n = 112). All patients had an 8-week run-in phase (benazepril, 10 mg/d for 4 wk; then 10 mg twice daily for 4 wk) and a 3-week treatment wash-out period before the trial started. All patients received open-label antihypertensive drugs to maintain systolic blood pressure < 130 mm Hg and diastolic blood pressure < 80 mm Hg and were advised to restrict intake of sodium chloride (5 to 7 g/d), protein (0.5 to 0.7 g/kg per d), and foods rich in potassium.

Outcomes: A composite endpoint of doubling of serum creatinine level from baseline, end-stage renal disease, or death. Secondary outcomes included urinary protein excretion, renal function, glomerular filtration rate (GFR), and adverse events.

Patient follow-up: 96% (intention-to-treat analysis).

Main results
Fewer patients in the benazepril group had the primary composite endpoint than did those in the placebo group (Table). Benazepril led to a greater reduction in proteinuria (52% vs 20%, P < 0.001) and delayed rates of decline in renal function (median slope −0.09 vs −0.11 dL/mg per y, P = 0.02) and GFR (6.8 vs 8.8 mL/min per 1.73 m², P = 0.006) more than placebo.

Groups did not differ for adverse events (death, nonfatal cardiovascular events, hyperkalemia, acute decline in renal function, dry cough, and hypotension).

Conclusion
In patients with advanced chronic kidney disease without diabetes, benazepril delayed the progression of renal dysfunction.

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*See Glossary.
†Information provided by author.

The trial by Hou and colleagues was done in China. Most patients with CKD do not live in North America or Europe (3), and provision of renal replacement therapy would be expensive in many developing countries. Hence, appropriate application of proven effective therapies to retard progression of CKD will be critical and literally life-saving.

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References