Chronic renal failure

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Drugs to reduce progression

ACE inhibitors

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Summary

Disease progression

Compared with control ACE inhibitors may be more effective at reducing the risk of disease progression and of end-stage renal disease in people with chronic renal failure (low-quality evidence).

Mortality

Compared with control We don't know whether ACE inhibitors are more effective at reducing mortality in people with chronic renal failure (very low-quality evidence).

Cardiovascular effects

Compared with control ACE inhibitors are more effective at lowering blood pressure in people with chronic renal failure (moderate-quality evidence).

For GRADE evaluation of interventions for chronic renal failure, see table.

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Benefits

We found one systematic review [36] and one subsequent RCT. [37] The systematic review (search date 1997) identified 11 RCTs of 1860 people (mean glomerular filtration rate [GFR] not reported, mean serum creatinine 203 µmol/L, standard deviation 106 µmol/L; mean proteinuria 1.8 g/day, standard deviation 2.3 g/day). [36] Fewer people reached end-stage renal disease (ESRD) or died with ACE inhibitors compared with the control group; however, the difference in mortality was not significant

(ESRD: 70/941 [7%] with ACE inhibitors *v* 106/919 [12%] with controls; RR 0.69, 95% CI 0.51 to 0.94; doubling of serum creatinine or ESRD: 124/941 [13%] with ACE inhibitors *v* 187/919 [20%] with controls; RR 0.70, 95% CI 0.55 to 0.88; death: 20/941 [2%] with ACE inhibitors *v* 11/919 [1%] with controls, relative risk not reported, P = 0.12). Follow-up systolic blood pressure was 139 mm Hg with ACE inhibitors and 144 mm Hg with controls; follow-up diastolic blood pressure was 85 mm Hg with ACE inhibitors and 87 mm Hg with controls; decline in systolic blood pressure was 4.5 mm Hg (95% CI 3.0 mm Hg to 6.1 mm Hg) greater in ACE inhibitor compared with controls; decline in diastolic blood pressure was 2.3 mm Hg (95% CI 0.3 mm Hg to 0.6 mm Hg) greater with ACE inhibitor compared with controls (absolute values for decline in blood pressure not reported). We found one subsequent RCT (224 people with serum creatinine 274–442 µmol/L and greater than 0.3 g/day proteinuria for at least 3 months; mean glomerular filtration rate 26.3 mL/minute/1.73m ^{2} , standard deviation 5.3 mL/minute/1.73 m ^{2} ; mean serum creatinine 354 µmol/L, standard deviation 62 µmol/L; mean proteinuria 1.6 g/day, standard deviation 0.7 g/day), which found that benazepril 20 mg/day significantly reduced the composite outcome of doubling of serum creatinine, ESRD, or death compared with placebo over 3.4 years (44/107 [41%] with benazepril *v* 65/108 [60%] with placebo; RR not reported, P = 0.004, analysis was not by intention to treat). [37] This trial was not confounded by blood pressure-lowering effects: open-label drugs other than ACE inhibitors and angiotensin II receptor antagonists were added as needed to maintain the same target blood pressure (systolic blood pressure less than 130 mm Hg, diastolic blood pressure less than 80 mm Hg) in both arms. The decline in blood pressure was similar in the two groups (absolute numbers presented graphically, P = 0.18).

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Harms

The review reported more withdrawals with ACE inhibitors compared with controls (withdrawals: 40/941 [4%] with ACE inhibitors *v* 15/919 [2%] with controls; P = 0.001; withdrawals owing to non-fatal cardiovascular diseases: 18/941 [2%] with ACE inhibitors *v* 18/919 [2%] with controls; P greater than 0.2; withdrawals owing to other non-fatal event: 55/941 [6%] with ACE inhibitors *v* 35/919 [4%] with controls; P = 0.04). [36] In the subsequent RCT, 57/281 (20%) people were excluded while taking benazapril 10 mg daily during an active drug run-in period (for dry cough: 42/281 [15%]; for greater than 30% increase in serum creatinine: 6/281 [2%]; for hyperkalaemia: 4/281 [1%]). During the study, 11/224 (5%) people developed hyperkalaemia, of whom 8/224 (3%) were successfully treated medically, and 3/224 (1%) withdrew (distribution of people between groups not reported). [37] Serum potassium levels were significantly higher among people receiving benazepril compared with placebo (P = 0.001), although the difference never exceeded 0.5 mmol/L (absolute values not reported). The proportion of people receiving erythropoietin, mean dose of erythropoietin, and haemoglobin levels were similar between groups (effect size and significance level not reported).

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Comment

In people at high risk of ESRD (women with serum creatinine greeater than 146 µmol/L, men with serum creatinine greater than 177 µmol/L, people with GFR or creatinine clearance less than 30 mL/minute/1.73 m ^{2}, people in whom proteinuria coexists with abnormal renal function or known renal disease, and people in whom renal disease is progressing [serum creatinine rising or GFR falling]), ACE inhibitors are likely to reduce the risk of progression of disease and ESRD. In other people, risk of ESRD is lower, and the risk of cardiovascular disease dominates the clinical picture. In these people, the overall cardiovascular risk profile should be taken into account in deciding which preventative treatments are most likely to be beneficial.

References

36. Jafar TH, Schmid CH, Landa M, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data. *Ann Intern Med* 2001;135:73–87. [Erratum: *Ann Intern Med* 2002;137:299] Search date 1997; Primary source Medline. [PubMed]

37. Hou FF, Zhang X, Zhang GH, et al. Efficacy and safety of benazepril for advanced chronic renal insufficiency. *New Engl J Med* 2006;354:131–140. [PubMed]