Kidney disorders

Chronic renal failure

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Drugs to reduce progression

Angiotensin II receptor antagonists

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Summary

Disease progression

Compared with placebo We don’t know whether angiotensin II receptor antagonists are more effective at reducing glomerular filtration rate in people with chronic renal failure (very low-quality evidence).

Compared with calcium channel blockers Angiotensin II receptor antagonists and calcium channel blockers seem equally effective at reducing disease progression in people with chronic renal failure (moderate-quality evidence).

Note

We found no clinically important results about ACE inhibitors compared with angiotensin II inhibitors in preventing disease progression or end-stage renal disease in people with chronic renal failure. ACE inhibitors are likely to be beneficial for the prevention of progression of renal disease or end-stage renal disease; however, we don't know if angiotensin II receptor antagonists are beneficial. The intrarenal mechanism of action is similar but not identical, so angiotensin system interruption cannot be considered a class effect.

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

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Benefits

Angiotensin II receptor antagonists versus placebo:

We found one RCT, which compared valsartan versus placebo for 6 months (56 people, mean age 54 years with valsartan *v* 56 years with placebo; proportion of men: 57% with valsartan *v* 62% with placebo; mean glomerular filtration rate [GFR] 19.5 mL/minute/1.73 m^2 with valsartan *v* 22.0 mL/minute/1.73 m^2 with placebo, proteinuria and albuminuria not reported). [45] The RCT found that the GFR reduction (measured by ^{51}Cr ethylenediaminetetra-acetic acid [EDTA]) was similar in both groups (GFR reduction from 19.2 mL/minute/1.73 m^2 (geometric mean; arithmetic mean and standard deviation not reported) to 17.6 mL/minute/1.73 m^2 with valsartan *v* from 21.2 mL/minute/1.73 m^2 to 16.5 mL/minute/1.73 m^2 with placebo; P = 0.577). Analysis was not by intention to treat. This study was not confounded by ACE inhibitor use as ACE inhibitors were prohibited in both groups. Systolic and diastolic blood pressure differed between the two groups (absolute results shown graphically, P less than 0.001 for systolic blood pressure and P less than 0.002 for diastolic blood pressure).

Angiotensin II receptor antagonists versus calcium channel blockers:

We found one systematic review (search date 2001) that searched specifically for RCTs comparing angiotensin II receptor antagonists versus amlodipine, and did not identify any RCTs. [46] We found two additional RCTs comparing angiotensin II receptor antagonists versus amlodipine. [47] [46] The first RCT compared losartan versus amlodipine for 20 weeks (97 people with proteinuria greater than 1.5 g/day, mean age 47–48 years, 73–74% male, serum creatinine 115–124 µmol/L, mean GFR not reported, geometric mean proteinuria 2.5–3.1 g/day). [47] The RCT found that the increase in serum creatinine and the decrease in creatinine clearance measured by 24-hour urine were similar in both groups (serum creatinine: 141 mcmol/L standard deviation 62 mcmol with losartan *v* 123 mcmol/L standard deviation 53 mcmol/L with amlodipine; reported as non-significant, P value not reported; creatinine clearance: 70 mL/minute standard deviation 37 mL/minute with losartan v 81 mL/minute standard deviation 43 mL/minute with amlodipine; significance not assessed). This study was not confounded by ACE inhibitor use as ACE inhibitors were prohibited in both groups. The second RCT compared losartan versus amlodipine for 12 months (117 people with proteinuria at least 0.5 g/day, 14/177 [8%] with diabetes, mean age 56 years; 71% male mean serum creatinine 180–174 µmol/L standard deviation 42–46 mcmol/L; mean GFR not reported; mean proteinuria 2.50–2.89 g/day standard deviation 2.07–2.69 g/day). [46] At 3, 6, and 12 months' follow-up, serum creatinine and creatinine clearance were similar between groups (results presented graphically; P greater than 0.05). However, losartan significantly reduced proteinuria compared with amlodipine (results presented graphically; P = 0.05 at 3 months' follow-up, P = 0.01 at 6 months' follow-up, P = 0.001

at 12 months' follow-up). This RCT was not confounded by ACE inhibitor use as ACE inhibitors were prohibited in both groups.

Angiotensin II receptor antagonists versus ACE inhibitors:

We found no systematic review or RCTs.

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Harms

Angiotensin II receptor antagonists versus placebo:

The RCT reported premature discontinuation of drug for increasing serum creatinine, dizziness, and nausea (increasing serum creatinine: 3/30 [10%] with valsartan *v* 2/26 [8%] with placebo; creatinine elevation persisted in all cases after discontinuation of drug; dizziness: 1/30 [3%] with valsartan *v* 0/26 [0%] with placebo; nausea: 0/30 [0%] with valsartan *v* 1/26 [4%] with placebo). [45] Adverse effects included dizziness, increase in serum creatinine, hypotension, hyperkalaemia, and syncope (dizziness: 4/30 [13%] with valsartan *v* 2/26 [8%] with placebo; increase in serum creatinine: 3/30 [10%] with valsartan *v* 3/26 [12%] with placebo; hypotension: 3/30 [10%] with valsartan *v* 1/26 [4%] with placebo; hyperkalaemia: 2/30 [7%] with valsartan *v* 0/26 [0%] with placebo; syncope: 2/30 [7%] with valsartan *v* 0/26 [0%] with placebo; total events: 14/30 [47%] with valsartan *v* 6/26 [23%] with placebo; significance not reported).

Angiotensin II receptor antagonists versus calcium channel blockers:

In the first RCT, similar rates of minor adverse effects, adverse effects causing withdrawal, and adverse effects unrelated to drug treatment were observed (minor adverse effects experienced in 7/50 [14%] with losartan *v* 12/47 [25%] with amlodipine; P value not reported, reported as not significant; adverse events leading to withdrawal: 3/50 [6%] with losartan *v* 5/47 [12%] with amlodipine; significance not assessed; serious adverse effects unrelated to study treatments: 2/50 [4%] with losartan *v* 1/47 [2%] with amlodipine; significance not reported). [47] The second RCT found increases in aspartate aminotransferase in 2/117 (2%) people, alanine aminotransferase in 1/117 (1%), and gamma glutamyltransferase in 4/117 (3%) (incidence “almost the same” between groups, absolute numbers in each group and statistical significance not reported). [46] Dizziness occurred in 2/117 (2%) people and transient ischaemic attack in 1/117 (1%; absolute numbers in each group not reported). Other adverse effects reported included increase in uric acid, and hyperkalaemia (increase in uric acid: 0/58 [0%] with losartan *v* 2/59 [3%] with amlodipine; hyperkalaemia: 3/58 [5%] with losartan *v* 2/59 [3%] with amlodipine; significance not assessed).

Angiotensin II receptor antagonists versus ACE inhibitors:

We found no RCTs.

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Comment

In people at high risk of end-stage renal disease (ESRD; women with serum creatinine greater 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]), evidence from systematic reviews, specifically of ACE inhibition (see benefits of ACE inhibitors), suggests that ACE inhibition is likely to reduce the risk of progression of disease and ESRD. However, there is no evidence that angiotensin II receptor-blocking drugs prevent progression of disease and ESRD. Because both ACE inhibitors and angiotensin II receptor-blocking drugs act on the renin-angiotensin system, it is reasonable to use angiotensin II receptor-blocking drugs in people unable to tolerate ACE inhibitors because of cough. However, incidence of other adverse effects — such as increase in serum creatinine and hyperkalaemia — is likely to be similar with both drugs. In people at lower risk of ESRD, 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 therapies are most likely to be beneficial.

References

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