Angiotensin-Converting Enzyme Inhibitors vs. Angiotensin Receptor Blockers

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Clinical Question

In which clinical situations are angiotensin receptor blockers (ARBs) preferred over angiotensin-converting enzyme (ACE) inhibitors?

Evidence-Based Answer

ACE inhibitors should be used in patients with hypertension because they reduce all-cause mortality, whereas ARBs do not. (Strength of Recommendation [SOR]: A, based on a meta-analysis.) ARBs are preferred for patients who have adverse reactions to ACE inhibitors. (SOR: A, based on a meta-analysis.) ARBs cause less cough than ACE inhibitors, and patients are less likely to discontinue ARBs because of adverse effects. ACE inhibitors and ARBs may be used in patients with vascular disease or diabetes mellitus with end-organ damage because they produce equal reductions in mortality and hospital admissions. (SOR: B, based on a randomized controlled trial [RCT].)

Evidence Summary

A 2012 meta-analysis of 20 clinical trials involving 158,998 patients examined the effect of ACE inhibitors and ARBs in patients with hypertension.[1] ACE inhibitors reduced all-cause mortality (hazard ratio [HR] = 0.90; 95% confidence interval [CI], 0.84 to 0.97; $P = .004$), whereas ARBs did not (HR = 0.99; 95% CI, 0.94 to 1.04; $P = .683$).

A 2012 meta-analysis of 12 RCTs evaluated the tolerability of ARBs in patients with previous ACE inhibitor intolerance due to cough, angioedema/anaphylaxis, hypotension, renal dysfunction, and hyperkalemia.[2] Patients receiving ARBs were less likely to have cough (relative risk [RR] = 0.37; 95% CI, 0.28 to 0.48) compared with those receiving ACE inhibitors. The risks of hypotension (RR = 2.63; 95% CI, 1.77 to 3.92), renal dysfunction (RR = 2.07; 95% CI, 1.45 to 2.95), and hyperkalemia (RR = 3.37; 95% CI, 1.60 to 7.11) were higher among those receiving ARBs compared with placebo, but were not reported for those receiving ACE inhibitors.

Two RCTs and a meta-analysis assessed the safety of ARBs in patients with ACE inhibitor–induced angioedema.[3-5] The first RCT included 75 patients who discontinued ACE inhibitors because of angioedema or anaphylaxis.[3] Patients were randomized to 80 mg of telmisartan (Micardis) or placebo. One patient who was receiving placebo developed recurrence of angioedema. The second RCT included 39 patients who had heart failure and angioedema with ACE inhibitor use; they were randomized to 32 mg of candesartan (Atacand) per day or placebo.[4] Three patients receiving candesartan (7.7%) developed angioedema. The meta-analysis included three studies that evaluated the risk of angioedema recurrence with the use of ARBs in 71 patients with prior ACE inhibitor–induced angioedema.[5] Eight patients receiving ARBs (11.2%) developed recurrence of angioedema.

A double-blind RCT involving 25,620 patients with vascular disease or diabetes with end-organ damage compared three groups: patients receiving ramipril (Altace) alone, telmisartan alone, or a combination of both.[6] The composite primary outcomes were equivalent in the telmisartan and the ramipril groups (RR = 1.01; 95% CI, 0.94 to 1.09), but the combination therapy resulted in higher mortality rates. Outcomes included ▶

death from cardiovascular disease, myocardial infarction, or stroke, and hospitalization for congestive heart failure. Patients receiving telmisartan had less cough (1.1% vs. 4.2%; $P < .001$) and angioedema (0.1% vs. 0.3%; $P = .01$), but more hypotension (2.6% vs. 1.7%; $P < .001$) compared with those receiving ramipril. Rates of renal impairment (RR = 1.04; 95% CI, 0.96 to 1.14) and syncope (RR = 1.27; $P = .49$) were equivalent in those treated with telmisartan or ramipril.

Recommendations from Others

The Eighth Joint National Committee recommends ACE inhibitors as an option for initial management of hypertension in patients who are not black, and recommends either an ACE inhibitor or an ARB in patients with chronic kidney disease.[7] The National Institute for Health and Care Excellence recommends ACE inhibitors as first-line therapy for reducing blood pressure in patients with type 2 diabetes, but clinicians may substitute an ARB if the patient cannot tolerate ACE inhibitors (except if there is hyperkalemia or renal dysfunction).[8]

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