Cardiovascular and Renal Outcomes of Renin-Angiotensin System Blockade in Adult Patients with Diabetes Mellitus: A Systematic Review with Network Meta-Analyses.

Abstract

BACKGROUND:
Medications aimed at inhibiting the renin-angiotensin system (RAS) have been used extensively for preventing cardiovascular and renal complications in patients with diabetes, but data that compare their clinical effectiveness are limited. We aimed to compare the effects of classes of RAS blockers on cardiovascular and renal outcomes in adults with diabetes.

METHODS AND FINDINGS:
Eligible trials were identified by electronic searches in PubMed/MEDLINE and the Cochrane Database of Systematic Reviews (1 January 2004 to 17 July 2014). Interventions of interest were angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and direct renin (DR) inhibitors. The primary endpoints were cardiovascular mortality, myocardial infarction, and stroke-singly and as a composite endpoint, major cardiovascular outcome-and end-stage renal disease [ESRD], doubling of serum creatinine, and all-cause mortality-singly and as a composite endpoint, progression of renal disease. Secondary endpoints were angina pectoris and hospitalization for heart failure. In all, 71 trials (103,120 participants), with a total of 14 different regimens, were pooled using network meta-analyses. When compared with ACE inhibitor, no other RAS blocker used in monotherapy and/or combination was associated with a significant reduction in major cardiovascular outcomes: ARB (odds ratio [OR] 1.02; 95% credible interval [CrI] 0.90-1.18), ACE inhibitor plus ARB (0.97; 95% CrI 0.79-1.19), DR inhibitor plus ACE inhibitor (1.32; 95% CrI 0.96-1.81), and DR inhibitor plus ARB (1.00; 95% CrI 0.73-1.38). For the risk of progression of renal disease, no significant differences were detected between ACE inhibitor and each of the remaining therapies: ARB (OR 1.10; 95% CrI 0.90-1.40), ACE inhibitor plus ARB (0.97; 95% CrI 0.72-1.29), DR inhibitor plus ACE inhibitor (0.99; 95% CrI 0.65-1.57), and DR inhibitor plus ARB (1.18; 95% CrI 0.78-1.84). No significant differences were showed between ACE inhibitors and ARBs with respect to all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, angina pectoris, hospitalization for heart failure, ESRD, or doubling serum creatinine. Findings were limited by the clinical and methodological heterogeneity of the included studies. Potential inconsistency was identified in network meta-analyses of stroke and angina pectoris, limiting the conclusiveness of findings for these single endpoints.

CONCLUSIONS:
In adults with diabetes, comparisons of different RAS blockers showed similar effects of ACE inhibitors and ARBs on major cardiovascular and renal outcomes.
Compared with monotherapies, the combination of an ACE inhibitor and an ARB failed to provide significant benefits on major outcomes. Clinicians should discuss the balance between benefits, costs, and potential harms with individual diabetes patients before starting treatment.

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--Lilian Hoffecker and Dana Abbey, Health Sciences Library, University of Colorado.