What first-step antihypertensive drug therapy is optimal for patients with type 2 diabetes mellitus?

Evidence-Based Answer

Angiotensin-converting enzyme inhibitors (ACEIs) are the optimal antihypertensive medication for patients with type 2 diabetes mellitus because of improved renal, cardiovascular (CV), and mortality outcomes compared with placebo and other agents (SOR: A, systematic reviews). Limited evidence also suggests diuretics are helpful because of a decreased risk of heart failure.

A 2012 Cochrane review examined 26 RCTs with more than 61,000 patients, comparing the efficacy of ACEIs, calcium channel blockers (CCBs), angiotensin receptor blockers (ARBs), beta-blockers (BBs), and placebo/no treatment in patients with diabetes with or without hypertension and without kidney disease at baseline. Most patients had type 2 diabetes. Minimum follow-up was 6 months and average follow-up was 3.3 years.

Pooled analysis showed that, compared with placebo/no treatment, ACEIs decreased the risk of new-onset microalbuminuria or macroalbuminuria by 29% (8 trials, N=11,906; RR 0.7; 95% CI, 0.56–0.88) and decreased all-cause mortality by 16% (6 trials, N=11,350; RR 0.84; 95% CI, 0.73–0.97). No difference in these outcomes was found between either ARBs or CCBs and placebo/no treatment. Compared with CCBs, ACEIs decreased the risk of new-onset microalbuminuria or macroalbuminuria by 40% (5 trials, N=1,253; RR 0.6; 95% CI, 0.42–0.85), but there was no difference between ACEIs and either ARBs or BBs for this outcome. There was also no difference in risk of death between ACEIs and either ARBs or CCBs.

A 2009 systematic review examined 8 RCTs with more than 130,000 patients comparing BBs with renin-angiotensin system (RAS) agents (ACEIs and ARBs) and CCBs with respect to CV outcomes in patients with type 2 diabetes and hypertension. Minimum follow-up was 2.7 years and average follow-up was 4.9 years.

BBs were associated with a 39% increase in the risk of CV mortality compared with RAS agents (3 trials, N=2,237; RR 1.4; 95% CI, 1.1–1.8) but no difference compared with CCBs. Other outcomes including myocardial infarction, stroke, and total mortality were not different between BBs and RAS agents or CCBs.

A 2009 Clinical Evidence systematic review searched for systematic reviews of RCTs and RCTs evaluating the effect of antihypertensive agents on CV and renal outcomes in patients with diabetes and hypertension. The author estimated that 95% of the patients in the included studies had type 2 diabetes. ACEIs showed benefits over CCBs, while CCBs and ARBs showed benefits over BBs. Although diuretics were not different from ACEIs and CCBs in most CV outcomes, they did show lower risk of heart failure.