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FPIN's Clinical Inquiries

Angiotensin Blockade in Patients with Diabetic Nephropathy

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Clinical Question

What type of angiotensin blockade is preferred in patients with diabetic nephropathy?

Evidence-Based Answer

When used to delay the progression of early nephropathy in patients with type 2 diabetes mellitus, angiotensin receptor blockers (ARBs) are not superior to angiotensin-converting enzyme (ACE) inhibitors. (Strength of Recommendation: C, multiple randomized controlled trials [RCTs]).

Evidence Summary

A multicenter, double-blind trial called the Diabetics Exposed to Telmisartan and Enalapril (DETAIL) study randomized 250 patients with type 2 diabetes and early nephropathy to receive telmisartan (Micardis; 120 persons) or enalapril (Vasotec; 130 persons). The study followed the patients for five years. The primary outcome, which was change in glomerular filtration rate (GFR) from the baseline value to the last available value during the study period, was not significantly different between the two groups. The mean GFR declined by 17.5 mL per min per 1.73 m² in the telmisartan group compared with 15.0 mL per min per 1.73 m² in the enalapril group (treatment difference: -2.6 mL per min per 1.73 m²; 95% confidence interval [CI], -7.1 to 2.0 mL per min per 1.73 m²).¹

An earlier multicenter, double-blind, one-year trial comparing the effects of losartan (Cozaar) and enalapril on kidney function randomized 103 patients with type 2 diabetes and early nephropathy to receive losartan (52 persons) or enalapril (51 persons). The primary outcome was change of urine albumin excretion (UAE) from baseline to week 52. Although UAE decreased in both groups, the reduction was not significantly different between the two groups.²

Most recently, a study on stabilization and regression of albuminuria in Chinese patients with type 2 diabetes randomized 42 patients with normal renal function or early nephropathy to valsartan (Diovan; 22 persons) or enalapril (20 persons) for one year. The primary outcome was the change of UAE from baseline to week 52. The absolute difference in decrease of UAE between the two treatment groups was 1 percent, which was not statistically or clinically significant. The sample size required for clinical relevance was calculated at 20 patients in each group.³

These are the only trials that have directly compared an angiotensin-II receptor blocker with an ACE inhibitor in persons with type 2 diabetes and early nephropathy. In all three studies, the patients had an age range of 30 to 80 years, mild to moderate hypertension, and were allowed to be on additional antihypertensive agents with the exception of ACE inhibitors, ARBs, and dihydropyridine calcium channel blockers. All three studies had sufficient numbers of persons to achieve a power of at least 80 percent.

Adverse events in the ACE inhibitor and ARB groups were similar; however, one study found that the ACE inhibitor group was associated with a significantly higher incidence of cough (number needed to harm = 7, P = .006). In the DETAIL study, telmisartan and enalapril were associated with similar incidence of end-stage renal disease, myocardial infarction, stroke, congestive heart failure, and all-cause mortality¹; these events were not studied in the other two trials.^{2,3} In other RCTs and systematic reviews, the survival benefit (mainly from cardiovascular events) is better substantiated in ACE inhibitors than ARBs.⁴⁻⁸

Recommendations from Others

The American Diabetes Association recommends using ACE inhibitors or ARBs for the treatment of early nephropathy in patients with type 2 diabetes mellitus, regardless of the presence of hypertension, to delay the progression of microalbuminuria.⁹

Clinical Commentary

From an effectiveness standpoint, ARBs have not been shown to be superior to ACE inhibitors for prevention of diabetic nephropathy. Because of the availability of generic versions, ACE inhibitors have a lower cost and, therefore, should be favored for this indication. In addition to managing diabetes, other compelling indications for ACE inhibitors include managing chronic kidney disease and congestive heart failure.

The side effect profile for ACE inhibitors is similar to that of ARBs. However, for reasons that are not entirely clear, some patients will develop a cough when taking an ACE inhibitor. In general, ARBs should be reserved for use when ACE inhibitors cannot be tolerated because of cough.

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resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/levels_of_evidence.asp).

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