Benazepril-Amlodipine Reduces Cardiovascular Risk in High-Risk Patients

For high-risk patients with hypertension, benazepril plus amlodipine offers greater protection against cardiovascular events than benazepril-hydrochlorothiazide—despite similar effects on blood pressure, according to a report in The New England Journal of Medicine.

The industry-funded ACCOMPLISH trial included 11,506 patients with hypertension and a history of or risk factors for cardiovascular events. One group received the angiotensin-converting enzyme inhibitor benazepril plus the calcium-channel blocker amlodipine. The other group received benazepril plus the thiazide diuretic hydrochlorothiazide. Patients were followed up for a composite end-point of cardiovascular death, nonfatal myocardial infarction or stroke, hospitalization for angina, resuscitation after sudden cardiac arrest, and coronary revascularization.

The study was stopped early after 36 months. There was no more than a 1 mm Hg difference in systolic blood pressure between groups. However, the primary outcome rate was 9.6 percent with benazepril-amlodipine versus 11.8 percent with benazepril-hydrochlorothiazide, with a hazard ratio of 0.80. The benazepril-amlodipine group had a similar reduction in a composite endpoint of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.


Endothelin Antagonist Reduces Albuminuria in Diabetic Nephropathy

Treatment with the endothelin A-selective antagonist avosentan can reduce urinary albumin excretion in diabetic patients with macroalbuminuria, concludes a trial in the Journal of the American Society of Nephrology.

The Endothelin Antagonist Evaluation in Diabetic Nephropathy Study included 286 patients with diabetic nephropathy at 58 European centers. All had macroalbuminuria, with a urinary albumin excretion rate (UAER) of 0.2 to 5.6 mg/min, and blood pressure of less than 180/110 mm Hg. In addition to standard angiotensin-converting enzyme inhibitor and/or angiotensin receptor blocker therapy, patients were randomly assigned to 12 weeks of treatment with avosentan, 5 to 50 mg, or placebo.

All avosentan dosage groups had reductions in UAER: from 16 to 30 percent, compared with a 36 percent increase in the placebo group. Median relative reductions in UAER were 29 to 45 percent with avosentan, compared to a 12 percent increase with placebo. Cretinine clearance and blood pressure were unaffected. Peripheral edema occurred mainly at avosentan doses of 25 mg or higher; the rate of adverse events leading to treatment discontinuation was 7 percent.


Good Outcomes with Sirolimus Combinations in High-Risk Transplant Recipients

Sirolimus, given with either tacrolimus or cyclosporine, provided good one-year efficacy in high-risk renal allograft recipients, reports a trial in Transplantation.

The randomized, open-label, multicenter trial included 448 renal allograft recipients with risk factors for rejection: black race, nonprimary transplant, or high panel-reactive antibodies. They were assigned to sirolimus plus tacrolimus or sirolimus plus cyclosporine.

One-year efficacy failure rates were 22 percent with sirolimus-tacrolimus and 25 percent with sirolimus-cyclosporine. Adverse rejection rates were 14 percent and 17 percent, respectively; graft survival was 90 percent in both groups. In patients receiving their assigned therapy, the glomerular filtration rate tended to be higher with sirolimus-tacrolimus. Other one-year outcomes were similar between groups. Sirolimus-tacrolimus was associated with higher rates of diarrhea and herpes simplex. Other adverse events were more frequent with sirolimus-cyclosporine, including hypertension, calcineurin inhibitor toxicity, and increased creatinine.

It has been difficult to perform randomized trials evaluating outcomes in high-risk renal allograft recipients. This industry-sponsored study shows “equivalent benefit or risk” with the two sirolimus combinations studied, with no clear advantage of one regimen over the other [Gaber AO, Kahan BD, Van Bouwer C, Schulman SL, Scara J, and Neylan JE; for the Sirolimus High-Risk Study Group: Comparison of sirolimus plus tacrolimus versus sirolimus plus cyclosporine in high-risk renal allograft recipients: results from an open-label, randomized trial. Transplantation 2008; 86:1187–1195].

CKD Awareness Is Rising, but Remains Low

Despite efforts to increase awareness, a large majority of Americans with chronic kidney disease (CKD) are still unaware of their disease, reports a study in the Archives of Internal Medicine.

Led by Laura C. Plantinga, ScM, of Johns Hopkins Bloomberg School of Public Health, Baltimore, the study included 2992 patients with stage 1 to 5 CKD from the National Health and Nutrition Examination Survey, 1999–2004. Patients were asked whether they had ever been told they had “weak or failing kidneys.”

Awareness of CKD increased during the study period only in patients with stage 4 and 5 disease, from 4.7 percent in 1999–2000 to 9.2 percent in 2003–04. For patients with stage 1 or 2 CKD, the rate of awareness was about half of that for those in stage 3. Even in stage 4, less than half of respondents were aware of their CKD.

Factors associated with awareness were assessed in 1314 patients with stage 3 CKD. Those with proteinuria or hypertension were about three times more likely to be aware of their disease. Rates of awareness were twice as high for diabetics and for males. Awareness was unrelated to having a regular site for health care, educational attainment, insurance status, or obesity.

Recent guidelines have emphasized the need for early detection and prevention of CKD. The new results suggest that awareness of stage 3 CKD has nearly doubled in recent years, but remains low. The authors urge more aggressive targeting of groups with low awareness of CKD, including older patients, women, and patients without diabetes or hypertension [Plantinga LC, Boulware LE, Coresh J, Stevens LA, Miller ER III, Saran R, Messer KL, Levey AS, and Powe NR: Patient awareness of chronic kidney disease: trends and predictors. Arch Intern Med 2008; 168:2268–2275].