Importance of Achieving Lower Blood Pressure in Hypertensive Patients With Diabetes

Charles S. Brooks, James R. Sowers

T
he The International Verapamil SR-trandolapril Study (INVEST), a prospective open trial with blinded end point design, included 6400 participants with diabetes, coronary artery disease, and hypertension among a total of 22,576 participants. The trial was designed to compare a nondihydropyridine calcium antagonist verapamil SR-based and atenolol-based antihypertensives regimen. The protocol provided for an option of adding an angiotensin-converting enzyme (ACE) inhibitor, trandolapril or hydrochlorothiazide, to achieve blood pressure targets from the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI), less than 130/85 mm Hg in the cohort with diabetes. Diabetes was defined as anyone with a history of diabetes mellitus or use of an oral hypoglycemic agent or insulin at baseline. Mean follow-up was 2.7 years in the diabetic group. The diabetic group had almost twice the risk for cardiovascular disease (CVD) events compared with those without diabetes in INVEST.

The primary outcome (composite of first occurrence of all-cause death, nonfatal myocardial infarction, or nonfatal stroke) was not different between treatment strategies. Thus, this is the first outcome study to demonstrate a similar CVD outcome benefit between β-blocker and nondihydropyridine-based blood pressure treatment strategies in diabetic patients with coronary artery disease. Further, on-treatment analysis showed a trend for reduced primary outcomes with the addition of trandolapril to verapamil or hydrochlorothiazide to atenolol (combination therapy). These results are similar to those observed in the Controlled ONset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE) trial, where the primary outcome of the diabetes subgroup was similar between verapamil and a β-blocker–based treatment. Further, the Losartan Intervention For Endpoint reduction (LIFE) study showed that an angiotensin receptor blocker was more effective than a β-blocker in reducing the primary outcome of CVD mortality in diabetic patients with hypertension and a high risk for CVD. In addition, in the Captopril Prevention Project (CAPP), ACE inhibitor–based therapy was more effective than a diuretic, β-blocker combination in diabetic patients with hypertension. Collectively, these data suggest that antihypertensive therapy with calcium antagonists and ACE inhibitors are at least comparable to β-blockers in reducing CVD events in diabetic patients with hypertension and a high risk for CVD.

Blood pressure control was laudatory in diabetic patients in INVEST, as almost half of the participants achieved the JNC VI goal of less than 130/85 mm Hg. This control rate is considerably better than in other trials and in practice-based settings (26.7% and 22%, respectively). On treatment analysis in the current study indicated a trend for reduced CVD with the addition of trandolapril to verapamil or hydrochlorothiazide to atenolol. Further, use of combination therapy likely accounted, in part, for the relatively high percentage of diabetic patients achieving goal blood pressure. Because both treatment strategies achieved very similar blood pressure goals and CVD risk reduction, these data provide additional evidence for achieving a lower blood pressure goal regardless of the specific agents used in combination. Consistent with this notion, achievement of systolic BP of <140 mm Hg and diastolic blood pressures of <90 mm Hg was associated with reduced risks of the primary outcome in both treatment strategies. Indeed, there was a decrease in CVD event risks down to a blood pressure of 110/60 mm Hg. Further, because most of the blood pressure reduction was accomplished in the first 6 months, this early blood pressure control appears to be an important determinant of final outcomes in trials of several years duration, such as the Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT), and the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trials as well as INVEST. Collectively, the results of INVEST and other recent trials underscore the importance of achieving the lower blood pressure goal of 130/80 mm Hg in patients with diabetes and hypertension that is currently recommended by a number of guideline committees in North America and Europe.

References


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