Class of Antihypertensive Unimportant if It Works

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SNOWMASS, COLO. — Oft-heard claims that some antihypertensive agents possess blood pressure–independent cardioprotective effects don't hold up to scrutiny, Dr. Robert A. Vogel said at a conference sponsored by the Society for Cardiovascular Angiography and Interventions.

Indeed, the major lesson to be gleaned from examining the seven big, published, randomized, class-to-class treatment trials is that in hypertensive patients without heart failure, the key consideration in preventing cardiovascular events is to just lower the blood pressure. Which classes of drugs are employed to reach this goal is not of great importance, according to Dr. Vogel, professor of medicine and director of clinical vascular biology at the University of Maryland, Baltimore.

"The point I want to make, and it's critical and yet it's something we often forget, is that treating hypertension is one of the most rewarding things we can do. For every 1–mm Hg increase in systolic blood pressure, we get a 4% increase in ischemic heart disease events; conversely, we get the same benefit as we drop blood pressure," he said.

"When you look at these seven trials, it doesn't make much sense. I can't look at them and say, 'This is the agent I want for my patients with cardiovascular disease,'" he added. For one thing, only three of the seven trials even achieved a level playing field by producing equal blood pressure reductions in both study arms.

In one of the three trials—the Comparison of Amlodipine vs. Enalapril to Limit Occurrence of Thrombosis (CAMELOT) study—the calcium channel blocker proved more effective than the angiotensin-converting enzyme inhibitor for prevention of cardiovascular events.

In the International Verapamil SR/Trandolapril Study (INVEST), the calcium channel blocker–based treatment strategy and β-blocker–based approach proved equally effective for cardiovascular risk reduction. And in the Second Australian National Blood Pressure Study, the ACE inhibitor came out ahead of diuretic therapy. So no clear winning strategy emerged from the studies featuring equal lowering of blood pressure.

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DR. VOGEL

In contrast, in the four trials in which the blood pressures achieved were unequal, the conclusion in every case was that lower blood pressure provided protection against cardiovascular events.

The blood pressure differences between study arms were small, typically only 1-3 mm Hg, but in these large studies ranging in size from 9,000 to 33,000 patients, the resultant spread in event rates became statistically significant.

For example, in the 33,257-patient Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), the rates of stroke, heart failure, and combined cardiovascular events were significantly lower in patients on diuretics than in those on ACE inhibitors—findings opposite those of the Australian study. The explanation appears to be that in ALLHAT, the achieved systolic blood pressure in the ACE inhibitor group was 2 mm Hg higher than in the diuretic group.

The story was similar in the other three trials with unequal blood pressure. In the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study, and Valsartan Antihypertensive Long-Term Use Evaluation (VALUE) trial, the "winning" strategy for cardiovascular protection was the one backed by the trial's commercial sponsors—and also the one that resulted in significantly lower blood pressure than the comparator, he said.

According to Dr. Vogel, what physicians could really use now is a tool to help them know if they've lowered a patient's blood pressure sufficiently, much as C-reactive protein levels help gauge cardiovascular risk. Brachial artery flow-mediated dilation—a reflection of nitric oxide availability and endothelial function—shows considerable promise in this regard, but it's not yet ready for routine use, he said. ■

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