Combo Therapy Boosts Blood Pressure Control

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BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Fixed-dose combination therapy increased blood pressure control rates from 37% to 76% over 18 months in patients with high-risk hypertension in an ongoing large, multinational trial reported at the annual meeting of the American Society of Hypertension.

Control rates were even higher in the U.S. cohort, where 80.5% of patients achieved control to less than 140 mm Hg—an unprecedented rate for a U.S. trial, reported Dr. Kenneth Jamerson, who presented interim results from the Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial.

Dr. Jamerson and his associates reported significant reductions in systolic blood pressure were seen across all patient populations, including African Americans.

The investigators randomized 11,463 patients who were aged 55 years or more with a systolic blood pressure of at least 160 mm Hg or currently on antihypertensive therapy to treatment with either Lotrel, which contains the ACE inhibitor benazepril and the calcium-channel blocker amlodipine, or to benazepril plus the diuretic hydrochlorothiazide (HCTZ).

At 18 months, patients achieved an average decline in blood pressure from 145/80 mm Hg to 132/74 mm Hg. Almost one-fifth of patients went on to achieve a systolic BP of less than 120 mm Hg. The study remains blinded, so blood pressure reductions were not stratified based on treatment.

Cardiovascular morbidity and mortality outcomes, which are the study's primary end point, are anticipated after the trial ends in 2008.

Dr. Jamerson believes that the current data will help shift the traditional approach to hypertension management in which providers initiate monotherapy then sequentially use additional medications as needed to achieve target blood pressure goals.

"Too many clinicians have chanted the mantra, 'start low, go slow,' despite having lots of data that multiple drugs are going to be necessary to achieve blood pressure control," said Dr. Jamerson, professor in the department of internal medicine, division of cardiovascular medicine, University of Michigan, Ann Arbor.

"We think we provide substantial evidence to suggest that initial combination therapy is very effective, and think there is substantial evidence to support broadening the use of combination therapy as an initial therapy."

Although 97% of patients in the study were already taking antihypertensive medication, only 37.5% had their blood pressure controlled at baseline to 140/90 mm Hg—the currently recommended target in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).

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DR. JAMERSON

Dosages were titrated at month 2 to a fixed dose of benazepril 40 mg/amlodipine 10 mg or benazepril 40 mg/HCTZ 25 mg, with the option of adding on other antihypertensive agents at month 3. Overall, 35% of patients used add-on medications, said Dr. Jamerson, who has received grant/research support from Novartis, which sponsored the study and markets Lotrel.

At 18 months, the average systolic BP declined from 153 mm Hg to 137 mm Hg among Nordic patients, from 142 mm Hg to 129 among the U.S. cohort, and from 145 mm Hg to 133 mm Hg among African Americans.

A bit more work needs to be done among patients with diabetes and chronic kidney disease, Dr. Jamerson said. Their respective mean systolic BPs decreased from 145 mm Hg to 131.5 mm Hg and from 149 mm Hg to 136 mm Hg—both short of the JNC 7 goal of 130 mm Hg for these difficult-to-treat populations. Overall, 60% of ACCOMPLISH participants have diabetes, and had a BP control rate of 15%.

ASH President Suzanne Oparil said in an interview that these are the highest overall control rates ever achieved, but at roughly 80% are only slightly higher than the 65% reported in previous hypertension trials.

The low systolic BP rates reported in the U.S. cohort may reflect higher values at baseline in the Nordic cohort and a more cautious treatment approach typically used by European physicians.

Dr. Oparil, professor of medicine, physiology, and biophysics at the University of Alabama, Birmingham, took issue with the notion that these results will shift treatment patterns. The VALUE, or Valsartan Antihypertensive Long-term Use Evaluation trial, already provided clinicians with the lesson that controlling blood pressure quickly is important.

"It's not that paradigm shifting because that's what we're preaching anyway," she said. ■

Emotions Drive Angioplasty Rates for Patients With Stable CAD

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WASHINGTON — When it comes to recommending angioplasty for stable coronary artery disease, evidence can take a backseat to worry, guilt, and the fear of legal liability.

"Both cardiologists and primary care physicians [PCPs] have trouble balancing these psychological and emotional factors with scientific evidence in decision making, and this leads to them recommending more tests and procedures," which eventually culminate in a trip to the cardiac catheterization lab, Dr. Grace Lin said at a conference sponsored by the American Heart Association. And once there, if any lesions are identified, "the die is cast" for percutaneous coronary intervention (PCI), she said.

Dr. Lin, of the University of California, San Francisco, drew these conclusions from a series of six focus-group meetings she held with 28 primary care providers and 20 cardiologists (13 interventional and 7 noninterventional). She presented each group with three case scenarios based on actual patients with symptoms of stable coronary artery disease (CAD), and asked them to describe how they would arrive at a treatment recommendation.

All of the physicians lived in California; their mean duration of practice was 17 years. To help identify any regional differences, Dr. Lin drew one-third from San Francisco, one-third from the city's suburbs, and one-third from a rural county. The PCPs and cardiologists were interviewed separately to encourage frank discussion.

The discussions were set around three case scenarios representing minimally symptomatic or asymptomatic patients for whom the current evidence shows no benefit of PCI over optimal medical therapy.

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As the study shows, physicians tend to look for action-based solutions, Dr. Grace Lin said.

One of the cases was that of a 45-year-old man with a family history of myocardial infarction. He worked out three times a week and was asymptomatic. However, his wife was worried about his family history and bought him a coronary calcium scan for his birthday. The scan showed a calcium score of 745. His stress test showed ST-segment depressions of 1-2 mm. A catheterization revealed a tight lesion in the left anterior descending artery.

Dr. Lin asked the group to discuss a range of recommendations, from reassurance and risk reduction interventions to medical therapy, PCI, and coronary artery bypass grafting.

All of the physicians ended up recommending PCI for all three of the case-study patients, even though they acknowledged that no clinical evidence suggested the procedure would be more beneficial than medical therapy.

Several major themes emerged from the physician discussions: They felt guilt over the possibility of missing a lethal lesion, patient expectation of testing and intervention, and liability fears.

The fear of guilt was a particularly strong motivator for more tests and interventions. One PCP summed this when he said: "I had a healthy 42-year-old who dropped dead while jogging. I'm always afraid of missing that widow-maker lesion."

A cardiologist echoed that view: "I don't think you can ignore a lesion, because then, if something happens, it's your fault."

"I think it demonstrates the tendency of physicians to look for solutions based on action," said Dr. Lin.

In addition, the participants stuck to their recommendations despite their intellectual understanding of the clinical evidence. "We know we are not necessarily preventing heart attacks by treating asymptomatic stenosis with PCI. We are going to prevent future heart attacks with lipid-lowering drugs, aspirin, and ACE inhibitors," said one cardiologist. "Nonetheless, when that patient leaves with an open artery, that is the best that my interventional partners can deliver."

Physicians aren't alone in wanting some concrete action in these cases, Dr Lin said. "Patient expectations are a frequent reason for testing. Both PCPs and cardiologists said their patients expected testing regardless of what [the caregivers] thought of it."

Concerns about medicolegal liability also strongly influenced the decision making. "We all would feel more comfortable treating more patients medically if we weren't afraid of being sued," said one PCP.

Again, Dr Lin observed, physicians felt very strongly about this despite evidence to the contrary. "There are no data linking additional testing with fewer lawsuits."

All of these factors "culminate in a cascade effect where screening leads to more testing and eventually to the cath lab," she said. ■