Aspirin Doesn't Weaken Effects of ACE Inhibitors

ARTICLES BY
SHERRY BOSCHERT
San Francisco Bureau

SEATTLE — Low-dose aspirin did not reduce the beneficial effects of ACE inhibitors in patients with atrial fibrillation and a history of heart failure, a subset analysis of 2,031 patients found.

The analysis addressed recurring concerns that aspirin use attenuates the effects of ACE inhibitors in heart failure patients and supported the use of both low-dose aspirin and an ACE inhibitor when indications for both treatments exist, Dr. Akshay S. Desai said at the annual meeting of the Heart Failure Society of America.

Dr. Desai and associates studied data from the Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE-W). The prospective, open-label study randomized patients with atrial fibrillation to combination antiplatelet therapy with clopidogrel and 75-100 mg/day of aspirin or to oral anticoagulation with warfarin. ACTIVE-W was discontinued early because warfarin clearly reduced the risk of MI, vascular events, or death.

Compared with all ACTIVE-W patients, the 2,031 patients with prior heart failure were more likely to be hypertensive or diabetic; have left ventricular dysfunction, a prior MI, or coronary disease; and be on an ACE inhibitor or angiotensin receptor blocker at baseline. Patients with prior heart failure in ACTIVE-W were twice as likely to develop MI, vascular events, or death, as those with no such history.

Notably, however, the relative benefits of antiplatelet or anticoagulant therapy to prevent thromboembolic events did not differ significantly either in ACTIVE-W patients as a whole or in the subset of patients with heart failure, said Dr. Desai of Brigham and Women's Hospital, Boston. The risk of bleeding complications also did not differ between treatment groups.

Looking at the composite end point of death or hospitalization for heart failure, patients with a history of heart failure carried triple the risk, compared with non–heart failure patients, but again there was no significant difference between the antiplatelet and anticoagulant treatment groups.

The investigators stratified patients with heart failure based on whether they did or did not use an ACE inhibitor at baseline, expecting to see a greater relative benefit in the warfarin group if aspirin attenuated the effects of ACE inhibitors. They found no statistically significant differences between the antiplatelet and anticoagulation groups, suggesting no interaction between aspirin and ACE inhibitors.

Some heart failure patients in the warfarin group also were on ACE inhibitors at baseline, which might have limited the power to detect an aspirin-ACE inhibitor interaction, so they repeated the analyses after excluding patients on an ACE inhibitor at baseline who were randomized to warfarin. Again, they found no significant aspirin-ACE inhibitor interaction.

Concerns about such an interaction began with a 1992 hemodynamic study, later confirmed by others, that showed that coadministration of enalapril and aspirin in 18 patients with severe heart failure attenuated some of the hemodynamic effects of ACE inhibitors on vascular resistance. A retrospective analysis of the SOLVD trial suggested that patients on enalapril were more likely to die if they also took aspirin. A similar finding came from a retrospective analysis of the Scandinavian CONSENSUS II study. A large meta-analysis of ACE inhibitor trials, however, found no significant increase in death or hospitalization for heart failure with concurrent use of aspirin, said Dr. Desai, who has no relationships with the companies that make the drugs he discussed. ■

Heart Failure Society Issues Comprehensive Guidelines

SEATTLE — The Heart Failure Society of America introduced at its annual meeting its 2006 Comprehensive Heart Failure Practice Guidelines, which updates its original 1999 guidelines.

"There wasn't much data available then. It was a good start, but this is a completely different document," said Dr. JoAnn Lindenfeld, current chair of the heart failure practice guideline committee and director of heart transplantation at the University of Colorado Health Sciences Center, Denver.

The Heart Failure Society of America (HFSA) guidelines are more comprehensive than two other sets of heart failure guidelines put out separately in 2005 by the European Society of Cardiology (ESC) and jointly by the American Heart Association and American College of Cardiology (AHA/ACC), she said.

The AHA/ACC recommendations don't address acute heart failure, and the ESC created separate sets of guidelines for acute and chronic heart failure. The HFSA guidelines include both.

"I think the ESC guidelines go further in [discussion of] subpopulations," Dr. Kirkwood F. Adams Jr. commented in a discussion session on the HFSA guidelines. "Heart failure [encompasses] about 18 different populations. I think as people look back 100 years from now, they'll be perhaps laughing that we had something called heart failure guidelines when really there are so many different patient varieties."

One of the values of the HFSA's comprehensive approach is that the guidelines focus attention on the enormous public health problem that heart failure presents, causing more than 1 million U.S. hospitalizations per year, added Dr. Adams, who cochaired the guidelines committee with Dr. Lindenfeld and is director of the heart failure program at the University of North Carolina, Chapel Hill. "It's good to push recognition" of the problem among both specialists and primary care physicians, who manage 80% of patients with heart failure.

The HFSA guidelines comprise 16 sections that include acute or chronic heart failure, disease management, heart failure in special populations, hypertension in heart failure, heart failure with preserved ejection fraction, and more. The recommendations come in four strengths:

- ► Is recommended—part of routine care, with very few exceptions.
- ► Should be considered—the majority of patients should receive the intervention.
- ► May be considered—individualize the therapy to the patient.
- ► Is not recommended—don't use the intervention.

The guidelines also present the level of evidence for recommendations, following routine models for rating evidence with one exception: One randomized trial could constitute the highest level of evidence (A). "That's controversial," Dr. Adams said.

In some categories, recommendations of the highest level are not based on the highest level of evidence. Although the guidelines on acute decompensated heart failure include many interventions that are "recommended," none of these are based on level A evidence, for example, Dr. Lindenfeld said.

"This points out how far we have to go in the data and studies of acute decompensated heart failure," she said.

The HFSA committee elected not to present majority and minority opinions on its recommendations, as some other guidelines do. "I think majority/minority opinions are useless. You go to the guidelines to get a recommendation," Dr. Adams said.

The HFSA committee plans to update the guidelines yearly. Topics not covered in the current guidelines that may be included in future versions include genetic screening and testing of patients with heart failure, the timing of altering diuretic therapy, and more guidance on implantable devices.

Clinicians can request a free copy of the pocket guidelines or request pricing for multiple copies by contacting info@hfsa.org. The full guidelines can be found at www.heartfailureguideline.com along with an executive summary and educational materials in the form of PowerPoint slides for each section, site navigation tools, and ways to give feedback on the guidelines or their presentation on the Web. ■

Aspirin Resistance More Prevalent in Heart Failure Patients

SEATTLE — Blood tests on 507 patients seen in emergency departments for chest pain found resistance to aspirin in 20% of those with a history of heart failure and 12% of patients without heart failure, Dr. Lori B. Daniels reported in a poster presentation at the annual meeting of the Heart Failure Society of America.

"Physicians should be aware of the high rate of aspirin nonresponsiveness in patients with heart failure, since they may be susceptible to thrombotic events" even if treated with aspirin, and may need other antithrombotic therapy, said Dr. Daniels of the University of California, San Diego, and her associates.

Aspirin prevents MI, stroke, or other vascular events by causing platelet dysfunction so that platelets do not aggregate. It irreversibly inhibits platelet cyclooxygenase, a key enzyme in prostaglandin synthesis, so that platelets lose the capacity to synthesize thromboxane A2, an inducer of platelet aggregation with vasoconstrictive properties.

Between 8% and 18% of patients treated with aspirin, however, develop recurrent vascular events within 2 years, a phenomenon described as aspirin resistance "or perhaps more accurately as aspirin nonresponsiveness," the investigators wrote.

They took blood samples from patients with suspected acute coronary syndromes seen at five medical centers. All were on outpatient aspirin therapy or were given an aspirin when they arrived at the emergency department. The 25% of patients with a history of heart failure were older than those without heart failure (62 vs. 58 years) and were more likely to be taking aspirin as an outpatient (81% vs. 60%), but the two groups did not differ by sex or body mass index.

The high rate of aspirin nonresponsiveness in heart failure patients may make them susceptible to thrombotic events.

DR. DANIELS

Blood samples were tested using the Ultegra Rapid Platelet Function Assay on a VerifyNow testing device. The Ultegra assay is a turbidimetric-based optical detection system that measures platelet-induced aggregation as an increase in light transmittance. Aspirin nonresponsiveness was defined as an "aspirin reaction unit" value of at least 550. Results showed a mean of 479 aspirin reaction units in patients with a history of heart failure, compared with 458 units in patients without heart failure.

None of the investigators are associated with Accumetrix, the company that makes the VerifyNow device.

Heart failure patients were more likely to have a history of hypertension, coronary artery disease, MI, diabetes, chronic renal insufficiency, and tobacco use than were non–heart failure patients. Those with heart failure had averaged 4 years of aspirin use, compared with 2 years in patients without prior heart failure, she said. ■