Angioedema Risk Up in Blacks on ACE Inhibitors

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ORLANDO, FLA. — About 2% of African Americans treated with an ACE inhibitor develop angioedema within the first 6 months on the drug, according to results from a prospective study of enalapril with more than 12,000 patients.

Although angioedema is a known potential adverse effect of treatment with an ACE inhibitor, prior findings never established the risk patients face in a prospective, controlled study, John B. Kostis, M.D., said while presenting a poster at the annual meeting of the American College of Cardiology. Among whites in the study, about 0.5% developed angioedema during the first 6 months of treatment with enalapril.

Patients who developed angioedema most commonly had it soon after starting enalapril, but the results also showed that the adverse effect could occur at any time, especially in African Americans. A time plot of the appearance of angioedema in African Americans showed an increasing cumulative incidence throughout the 6 months of treatment. For example, about 1% of these patients developed angioedema within the first 40 days on enalapril, and another 0.5% had the effect during the next 30 days. During the final 110 days of the study, another 0.5% were affected. In contrast, virtually all white patients who developed angioedema had their reaction within the first 70 days of treatment.

This analysis used data collected in a 25,000-patient study that compared the drugs omapatrilat and enalapril in patients with hypertension. Randomization assigned 12,634 patients to treatment with enalapril, of whom about 10% were African American. Patients were allowed to have a history of treatment with an ACE inhibitor, and 35% of enrolled patients had this background.

Dosages of both drugs were titrated during the first 8 weeks so that blood pressures were below 140/90 mm Hg. During the subsequent 16 weeks, adjunctive antihypertensive therapy could be added to help patients reach or maintain the target blood pressure.

African Americans had a 2.9-fold increase in risk, compared with whites. A history of seasonal allergies and age over 65 years also raised risk.

Overall, angioedema developed in 86 (0.7%) of the patients treated with enalapril, reported Dr. Kostis, chairman of the department of medicine at the Robert Wood Johnson University Hospital in New Brunswick, N.J.

Most patients' first symptom of angioedema is lip swelling. All patients had been instructed at the start of treatment to immediately stop their medication and contact their physician if this or other symptoms of angioedema occurred.

Among the 86 patients with angioedema in the study, 65 (75%) had the mildest form, class I, which required no special treatment aside from stopping enalapril. A class II reaction occurred in 19 (22%) patients, requiring treatment with catecholamines or steroids. Two patients (2%) had a class IIIa reaction that required hospitalization but without airway compromise. No patients had the most severe form of angioedema, class IV, which means that either airway protection is needed or that the patient dies.

A step-wise logistic regression analysis was done using several candidate demographic and clinical variables to calculate the risk contributed by individual factors. The strongest risk factor was a history of rash in response to drugs, which boosted the risk of angioedema 3.8-fold.

African Americans had a 2.9-fold increased risk, compared with white patients. The other significant risk factors were a history of seasonal allergies, which raised risk by 79%, and age greater than 65 years, which boosted risk by 60%.

It's unclear why ACE inhibitors cause angioedema. The most commonly proposed hypothesis is that the effect stems from their inhibition of the breakdown of bradykinin, which then accumulates. The swelling seen in angioedema resembles what happens in patients with a C1 inhibitor deficiency, which is known to be caused by excess bradykinin production, said Harold J. Kim, M.D., a cardiologist at Robert Wood Johnson University Hospital and a collaborator on this study. ■