Drug Monitor

Warfarin and Ethnicity

Does a patient's ethnicity matter when it comes to warfarin dosing? Recent evidence suggests that it does, so researchers from the University of California at San Francisco conducted a retrospective cohort study of patients treated at a university anticoagulation clinic between January 2000 and September 2001 to learn more.

Of the 345 adults who had at least five clinic visits over the course of three months or more, 185 (54%) were white, 94 (27%) were Asian-American, 47 (14%) were black, and 19 (6%) were Hispanic. Although age, weight, indication for anticoagulation, and comorbidities differed significantly between the ethnic groups, the researchers adjusted for any factors believed to affect warfarin dosing in the multivariate regression analysis.

This analysis showed ethnicity to be an independent predictor of warfarin requirements. The mean adjusted weekly warfarin dose needed to achieve the target international normalized ratio (2 to 3) was lowest in Asian-Americans (24 mg), followed by Hispanics (31 mg), whites (36 mg), and blacks (43 mg). Dose differences were significant for all between-group comparisons, except for those between Asian-Americans and Hispanics and between Hispanics and whites.

Because of warfarin's narrow therapeutic index, accurate initial warfarin dosing is important to avoid hemorrhagic and thrombotic complications. The researchers say that their results may be related to genetic variations affecting warfarin metabolism. Until genetic research reveals more about the underlying mechanisms, they suggest giving Asian-American patients about 50% of the starting warfarin dose given to white or black patients.

Source: *Ann Pharmacother*. 2005;39:1008–1012.

Comparing COPD Combination Treatments

Two inhaled combination treatments for chronic obstructive pulmonary disease (COPD)—fluticasone propionate/salmeterol (FSC) and ipratropium bromide/albuterol sulfate (IB/ALB)—are used widely due to their multiple mechanisms of action. Thus far, however, little is known about how the two stack up against each other.

Researchers from National Jewish Medical and Research Center, Denver, CO; Baylor College of Medicine, Houston, TX; St. Francis Hospital and Medical Center, Hartford, CT; and GlaxoSmithKline, Research Triangle Park, NC conducted an eight-week, randomized, double-blind, double-dummy, parallel group study involving 361 patients with moderate to severe COPD at 46 U.S. research centers. Of these patients, 180 were assigned to treatment with FSC 250/50 µg twice daily, and 181 were assigned to treatment with IB/ALB 36/206 µg four times daily.

While both treatments improved lung function and symptoms, FSC was more effective in improving dyspnea and daytime and nighttime symptoms, as well as reducing the need for rescue albuterol. The two treatments were similar with respect to COPD exacerbations and other adverse events.

These results are consistent with those found in the one previous published study comparing the two combination drugs, which had a very similar design and patient sample. The researchers suggest several possible reasons for the advantages seen with FSC. For example, since FSC pairs a corticosteroid (fluticasone) with a beta-agonist (salmeterol), it has an anti-inflammatory effect that IB/ALB, composed of an anticholinergic bronchodilator (ipratropium) and a beta-agonist (albuterol), lacks. FSC also has a longer duration of action. Because this trial had a short follow-up period, the researchers call for longer studies to evaluate more thoroughly the occurrence of adverse effects and COPD exacerbations.

Source: *Clin Ther*. 2005; 27:531–542.

Fibrates for MI Risk in Metabolic Syndrome

Patients with metabolic syndrome have a high risk of myocardial infarction (MI). Could bezafibrate retard, a derivative of fibric acid, help?

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To find out, researchers from Neufeld Cardiac Rehabilitation Institute at Chaim Sheba Medical Center, Tel-Hashomer, Israel performed a post hoc analysis of a subgroup of patients from the long-term, placebo-controlled Bezafibrate Infarction Prevention (BIP) study. This subgroup of 1,470 patients all had three or more of the following features of metabolic syndrome: fasting glucose level of at least 110 mg/dL; triglyceride level of at least 150 mg/dL; high-density lipoprotein (HDL) cholesterol level less than 40 mg/dL in men or 50 mg/dL in women; systolic blood pressure of at least 130 mm Hg or diastolic blood pressure of at least 85 mm Hg; and a body mass index (BMI) of at least 28 kg/m^2. Most of them had experienced a previous MI.

Follow-up data on changes in cholesterol levels, glucose levels, and BMI and occurrence of MI (fatal or nonfatal), sudden death, or other cardiac events were collected for a mean of six years. Mortality data were collected for an additional two years.

During the follow-up period, 193 patients had a new MI: 82 (11.1%) of the 740 taking bezafibrate and 111 (15.2%) of the 730 taking placebo. Overall, bezafibrate treatment was associated with a reduced risk of any MI, nonfatal MI, and cardiac mortality.

Among the 575 patients with four to five metabolic syndrome features, those taking bezafibrate had an especially pronounced reduction in cardiac mortality (hazard ratio, 0.44). Furthermore, the drug markedly improved HDL and triglyceride levels, whereas placebo had no significant effects on these parameters.

Fibrates have not yet been compared head-to-head with statins in a clinical endpoint trial, the researchers note. Nevertheless, with their glucose-lowering properties, fibrates "appear to more selectively target the therapeutic goals" in obese patients with features of insulin resistance and metabolic syndrome, they say. The drugs also may be useful, the researchers suggest, as an adjunctive therapy in patients whose low-density lipoprotein levels are well controlled by statins but whose HDL and triglyceride levels are persistently abnormal. ●

Source: *Arch Intern Med.* 2005;165:1154–1160.

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