Drug Monitor

ONLINE EDITION

Epoprostenol's Effect on Acute Pulmonary Embolism

Adding the pulmonary vasodilator epoprostenol to standard treatment of acute pulmonary embolism (PE) in patients with right ventricular overload does not significantly improve right ventricular dilation, say researchers from VU University Medical Center, Amsterdam, the Netherlands. The results of their single-blind study contrast with findings from several other case reports and animal studies.

In this study, 14 patients with acute PE received epoprostenol (at least 4 ng/kg/min) or placebo infusion for 24 hours in addition to conventional treatment. Using serial echocardiography, the researchers assessed the effects of epoprostenol on right ventricular end-diastolic diameter, systolic pulmonary artery pressure, right ventricle fractional area change, and tricuspid annular plane systolic excursion.

Results showed that treatment with epoprostenol did not improve right ventricular dilation, or any other measured variables of right ventricular overload, in patients with acute PE. In right ventricular end-diastolic diameter, epoprostenol was associated with a relative increase of 2% from baseline after 2.5 hours and a relative decrease of 8% after 24 hours when compared with placebo. No significant effect was observed between epoprostenol administration and systolic pulmonary artery pressure, right ventricular fractional area change, or tricuspid annular plane systolic excursion.

The researchers say that this was the first randomized controlled trial of the effect of a pulmonary vasodilator for treatment of acute PE. They note that the small study size prevented detection of minor treatment effects of epoprostenol, but emphasize that the point estimate of any treatment effect on right ventricular diameter and function is very small and unlikely to be clinically relevant.

The authors suggest that one possible explanation for epoprostenol's ineffectiveness in this study may be that patients were already past the acute pulmonary vasoconstriction phase. Because getting to the hospital and undergoing diagnosis and echocardiography take time, earlier treatment may be difficult in normal practice, the authors say, noting that for inpatients with acute PE—whose circumstances may be different—pulmonary vasodilatory therapy may be effective.

Source: *BMC Pulm Med.* 2010;10:18.

Estrogen Plus Progestin Therapy—Increased Risk for CAD?

For the first few years after starting estrogen plus progestin therapy, postmenopausal women are at greater risk of developing coronary artery disease (CAD). Researchers from the Harvard School of Public Health, Boston, MA; the Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA; and the National Heart, Lung, and Blood Institute, Bethesda, MD sought to determine whether this increased risk disappears over time.

The Women's Health Initiative (WHI) estrogen plus progestin trial is a randomized, double-blinded, placebo-controlled trial of 16,608 postmenopausal women who were randomly assigned to receive conjugated equine estrogens plus medroxyprogesterone acetate (0.625 mg/day and 2.5 mg/day, respectively) or matching placebo from 1993 to 1998. Data on each patient's demographic characteristics; medical, reproductive, and family history; hormone use; and dietary intake also were collected. Physical examinations of the participants were administered at baseline and during follow-up. Safety and adherence data also were periodically collected after randomization.

Trial results showed no reduced risk for CAD within the first two years of continuous estrogen plus progestin use, including women who began hormone therapy (HT) within 10 years after menopause. Compared with no HT, the hazard ratio for continuous use of estrogen plus progestin therapy was 2.36 for the first two years and 1.69 for the first eight years. Among women starting the HT regimen within 10 years after menopause, the hazard ratios were 1.29 for the first two years and 0.64 for the first eight years. A possible cardioprotective effect in women who began therapy closer to menopause became evident only after six years of use.

These study results are similar to those of the Nurses' Health Study (NHS), an observational study that found no protective effect in the first three years of HT started within 10 years after menopause. The researchers comment that the combined findings from the WHI and the NHS suggest a 29% increase in CAD risk during the first two years of HT in women within 10 years of menopause. Although the researchers warn that this result does not attain statistical significance, they say "our pooled WHI and NHS estimates are, and will probably be for a long time, the most precise estimates on this topic."

Source: *Ann Intern Med.* 2010;152(4):211–217.