Study answers question of timing in use of eptifibatide

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An international study to resolve a decade of debate over the best timing for administering an anti-clotting drug for certain heart patients has come up with an answer: It doesn't matter.

Patients with coronary artery disease who are at high risk for complications after a heart attack often need procedures to check their arteries for blockages. During those procedures, physicians use an anti-clotting agent called eptifibatide (marketed as Integrilin) to prevent potentially life-threatening complications. But practice guidelines are not clear on when the drug should be used. Is it better to administer eptifibatide in the emergency room, when patients come in with chest pain and are first diagnosed with acute coronary disease? Or is it better to give it later, if needed, during procedures to open blocked arteries?

According to findings from The Early Glycoprotein IIb/IIIa Inhibition in Non-ST-Segment Elevation Acute Coronary Syndrome (EARLY-ACS) trial, the answer is - it's a draw. The timing of the drug doesn't appear to make much difference at all.

The findings were released today at the American College of Cardiology's 58th Annual Scientific Session and simultaneously published online in the New England Journal of Medicine.

"This study answers a question we have debated for nearly ten years," says L. Kristin Newby, M.D., a member of the Duke Heart Center and senior author of the study. "World-wide, there is quite a bit of variability

in how eptifibatide is used. Interpretation of current guidelines differs by region, and one could successfully argue that the guidelines support both approaches. We thought it was important to clarify if one strategy were better than the other."

Eptifibatide blocks a key platelet receptor that triggers a clotting reaction whenever there is injury to the body. Patients with non-ST-segment elevation acute coronary syndromes often have problematic plaque build-up that results in chest pain and increased susceptibility to platelet-driven events that could block blood flow to the heart.

Newby and colleague Robert Giugliano, M.D., Senior Investigator, TIMI Study Group, Brigham and Women's Hospital, Harvard Medical School and lead author on the paper, led a team of investigators to determine if early use of eptifibatide among high-risk patients with coronary artery disease was superior to later use of the drug. Enrollment in the double-blinded, placebo-controlled trial began in 2004. By 2008, the study had enlisted 9,492 patients at 440 sites in 29 countries.

The study was open to patients with non-ST-segment elevation acute coronary disease who experienced symptoms within 24 hours before randomization and who had at least two of three additional risk factors, including specific electrocardiogram changes (ST-segment depression or transient elevation), elevated levels of troponin or
creatine kinase MB (blood markers of a heart attack) or being over age 60.

After randomization, all patients received an infusion, with half getting eptifibatide and half receiving a placebo. Physicians performing invasive procedures had the option of requesting a kit which would allow them to ensure that any patients randomized to the placebo treatment could receive eptifibatide if needed.

Researchers followed the patients for four days following enrollment. They focused on the primary endpoint - the combined rate of death, heart attack, any event requiring immediate revascularization or the need to administer eptifibatide for a complication during a procedure. A key secondary endpoint was the combined rate of death and heart attack over 30 days.

They found that early use of eptifibatide was not associated with any significant reduction in either the primary or the secondary endpoints. They did find, however, that earlier use of eptifibatide was associated with more non-life-threatening bleeding.

"This study gives physicians important new information they can readily use, but it is not the end of the story," says Giugliano. "We will be working on additional analyses and one-year follow-up that could potentially yield important differentiating information for particular subgroups of patients."

Source: Duke University Medical Center