No increase in bleeding complications with rivaroxaban post-ACS

20 March 2017

Patients with acute coronary syndrome who were treated with the blood-thinning drug rivaroxaban in addition to an antiplatelet medication (clopidogrel or ticagrelor) experienced no increase in bleeding complications compared with patients who received the standard treatment of aspirin plus an antiplatelet drug, according to research presented at the American College of Cardiology's 66th Annual Scientific Session.

Acute coronary syndrome, or ACS, occurs when blood flow to the heart is suddenly blocked. It may take the form of a heart attack or unstable angina, chest pain that may signal a possible heart attack. Aspirin has been a mainstay of treatment for more than 30 years.

"The current standard of care for acute coronary syndrome is for patients to take lifelong aspirin, even though there is little evidence that this is effective in preventing a recurrent heart attack after the early phase in ACS," said E. Magnus Ohman, MD, professor of medicine at Duke University Medical Center and lead author of the study. "This study is important because it is the first to show that replacing aspirin with a newer, more targeted drug—low-dose rivaroxaban, an anticoagulant—presents no additional risk of bleeding complications when given as dual therapy with an antiplatelet drug."

Current guidelines published by the American College of Cardiology and the American Heart Association recommend treatment with aspirin plus clopidogrel or a similar drug such as ticagrelor—a regimen known as dual antiplatelet therapy—after a heart attack. Other studies, however, show that even when patients receive optimal dual antiplatelet therapy, nearly 10 percent will experience an adverse event such as a heart attack or stroke. Earlier trials exploring the effect of adding an anticoagulant agent such as rivaroxaban to dual antiplatelet therapy showed that this three-drug approach increased the risk of bleeding complications twofold or more.

In the current study, however, clinically significant bleeding—the study's primary endpoint—occurred equally, in 5.3 percent of patients who received rivaroxaban compared with 4.9 percent of those who received aspirin, a non-statistically significant difference, Ohman said. The most common type of bleeding was minor bleeding, such as a nosebleed for which the patient needed to see a doctor. Bleeding rates did not significantly differ between patients on clopidogrel and those on ticagrelor.

A total of 3,037 patients in 21 countries (average age 63, 75 percent male) participated in the study, known as the GEMINI-ACS-1 trial. Patients were enrolled in the study within 10 days of being hospitalized with a heart attack (89 percent) or unstable angina (11 percent). Patients were excluded if they had a history of impaired kidney function, active bleeding, or bleeding in the brain or gastrointestinal tract within the previous year. Also excluded were patients receiving long-term anticoagulant therapy.

After patients had been on a stable dose of clopidogrel or ticagrelor for more than 48 hours, they were randomly assigned to receive either low-dose rivaroxaban (2.5 mg, twice a day) or aspirin (100 mg a day). The study was double blinded, meaning that neither the patients nor their doctors knew who was receiving which drug. Patients were treated for a median of 291 days; the median follow-up period was 326 days. The number of patients who discontinued the study treatment prematurely was similar in both the rivaroxaban and aspirin groups (11.3 percent of those treated with rivaroxaban and 12.7 percent treated with aspirin).

In addition to collecting data on the study's primary endpoint of clinically significant bleeding, the research team also looked at the rate of death due to a heart attack, stroke, other heart or vascular disease, or a blood clot in a coronary artery in

which a stent had been placed. Here the rate was 5 percent among patients treated with rivaroxaban and 4.7 percent among those who received aspirin, again a non-statistically significant difference.

Although the findings of this Phase 2 trial show that treatment with rivaroxaban and an antiplatelet drug is safe, Ohman said, they do not demonstrate that this drug regimen is effective in preventing recurrent heart attacks. A larger, Phase 3 trial would be required to definitively establish that this treatment approach is both safe and effective. Another limitation is that because 93 percent of those participating in the study were white, the findings may not apply to more racially and ethnically diverse groups of patients, Ohman said.

Provided by American College of Cardiology