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Drug trial results refine treatment during angioplasty operations

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A landmark international study, coordinated by McMaster University, has found that lower doses of a blood thinner called unfractionated heparin (UFH) during angioplasty did not reduce bleeding or vascular complications compared to standard dose UFH in patients initially treated with a blood thinner, fondaparinux.

In a prior study, the OASIS 5 trial, researchers from McMaster University showed that a blood thinner fondaparinux compared to another blood thinner, enoxaparin, reduced serious bleeding and prevented deaths in patients with heart attacks. A limitation of this new agent, fondaparinux, was its higher rates of clot formation in equipment during angioplasty. As a result, an additional blood thinner UFH had been recommended during angioplasty to prevent clotting in those who had received fondaparinux, but there was uncertainty about the optimal dose.

Even though UFH has been used during angioplasty since the procedure was first performed, little is known about the optimal dose of the agent.

An international group of researchers from 18 countries found patients undergoing angioplasty did not benefit from a lower dose of UFH compared to a standard dose in those on fondaparinux.

Importantly, the addition of either low or standard dose UFH to fondaparinux did not increase serious bleeding and prevented clot formation in equipment during angioplasty when compared to patients

treated with fondaparinux alone in OASIS 5. As a result, adding standard dose UFH to fondaparinux maintains the major advantage of fondaparinux (lower bleeding) while preventing clotting during the angioplasty procedure.

"Our data clearly shows that adding UFH to fondaparinux maintains a low rate of major bleeding and prevents catheter thrombosis," said interventional cardiologist Dr. Sanjit Jolly, an assistant professor of medicine in the Michael G. DeGroote School of Medicine at McMaster University.

Dr. Jolly is scheduled to present the results of the FUTURA-OASIS 8 (Fondaparinux with UnfracTionated heparin dUring Revascularisation in Acute coronary syndromes) trial at the annual European Society of Cardiology Congress in Stockholm, Sweden on August 31. The study was also published simultaneously in the Journal of the American Medical Association (JAMA).

FUTURA-OASIS 8 is a Phase III, multicentre, multinational, randomized, parallel-group trial of 2,026 patients undergoing angioplasty within 72 hours of arriving in a hospital with unstable angina or a heart attack. As soon as possible after their arrival, patients were enrolled and received fondaparinux 2.5 mg daily. Patients who required angioplasty were then randomized to low fixed dose heparin or standard dose heparin with activated clotting time (ACT) guidance during angioplasty. The low fixed dose UFH regimen consisted of a dose of 50 U/kg irrespective of use of GP IIb/IIIa inhibitors (another group of drugs used to prevent clots at time of angioplasty). The standard dose UFH regimen consisted of a dose of 85 U/kg or 60 U/kg when GP IIb/IIIa inhibitor used, adjusted by blinded ACT.

The low dose regimen did not reduce the risk of major or minor bleeding or vascular access complications compared to standard dose

regimen. The low dose regimen did not lower the risk of major bleeding but did lower minor bleeding by 60 per cent. There was a trend, however, for higher risk of death, myocardial infarction or target vessel revascularization with low dose vs. standard dose UFH. The rates of catheter thrombosis were very low (0.5 per cent and 0.1 per cent in the low and standard dose UFH groups). In the standard dose arm, only about one in five patients required an additional UFH bolus to reach target ACT.

"There has been a widely believed hypothesis that lowering heparin dose lowers bleeding with similar efficacy during angioplasty but randomized trial data has been lacking," remarked Professor Gabriel Steg, interventional cardiologist at the Université Paris and Hôpital Bichat in France and co-chair of the study. "This study's results challenge this hypothesis and suggest that anticoagulation during PCI (percutaneous coronary intervention, or angioplasty) is important in the stent era."

The rates of peri-PCI major bleeding in FUTURA-OASIS 8 (1.4 per cent low dose and 1.2 per cent standard dose) were not significantly different than the rate observed in the fondaparinux arm of the OASIS 5 trial that underwent PCI (1.5 per cent) but lower than the enoxaparin arm of the OASIS 5 trial that underwent PCI (3.6 per cent).

"What this implies is that the standard dose of UFH may be the optimal treatment strategy in PCI patients on fondaparinux while maintaining the major advantage of fondaparinux which is a low rate of major bleeding," said Dr. Salim Yusuf, chair of the FUTURA-OASIS 8 steering committee, a professor of medicine in the Michael G. DeGroote School of Medicine and director of the Population Health Research Institute at McMaster University and Hamilton Health Sciences in Canada.

Provided by McMaster University