# Investigational drug reduces heart damage during angioplasty

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A single dose of an investigational anti-inflammatory drug, inclacumab, reduced damage to heart tissue during angioplasty in a study presented today at the American College of Cardiology's 62nd Annual Scientific Session.

More than 1 million coronary angioplasty procedures are performed in the United States each year, at a cost of more than $10 billion. Heart tissue can be damaged during angioplasty, often leading to additional procedures, poor outcomes and higher health care costs.

In this trial, researchers compared a single dose of inclacumab administered one hour before angioplasty with a placebo.

Inclacumab is a human monoclonal antibody that blocks p-selectin, a molecule found in platelets and the cells that line blood vessels. P-selectin is activated in response to inflammation, which can ultimately lead to tissue damage. The study met its primary endpoint: decrease in levels of troponin I, a protein found in the bloodstream when heart damage has occurred, after angioplasty.

"Our hypothesis was that by using the p-selectin antagonist inclacumab, we'd be able to demonstrate vascular benefit," said Jean-Claude Tardif, MD, director of the Research Centre at the Montreal Heart Institute, professor of medicine at the University of Montreal and the study's lead investigator.

The SELECT-acute coronary syndrome phase II trial involved 530 patients with a median age of 61 experiencing a type of heart attack called non-ST-elevation myocardial infarction or NSTEMI. Patients were randomized to receive an infusion of inclacumab at 20 mg/kg, inclacumab at 5 mg/kg or placebo one hour before angioplasty.

Researchers measured heart damage using two standard molecular markers: troponin I and CK-MB. These markers are used clinically to diagnose heart attacks. They were measured at baseline and at eight, 16 and 24 hours after PCI. The co-primary endpoints were the change in troponin I at 16 hours and 24 hours.

In patients receiving 20 mg/kg of inclacumab, troponin I levels dropped 22.4 percent more at 16 hours (p=0.066) and 24.4 percent more at 24 hours (p=0.05), compared with patients on placebo. CK-MB levels dropped 16.3 percent more at 16 hours (p=0.088) and 17.4 percent more at 24 hours (p=0.055), compared with patients on placebo.

Also, at 24 hours after angioplasty, 18.3 percent of patients on placebo had CK-MB increases of more than three times the upper limit of normal, a threshold that many clinical trials use to define a post-angioplasty heart attack. This compared with 8.9 percent of patients who received the higher dose of inclacumab (p=0.051).

The 5 mg/kg dose of inclacumab had no significant effects on the cardiac markers. Researchers also measured p-selectin levels to see if they correlated with changes in CK-MB and troponin I. Levels did not drop significantly in the group that received 5 mg/kg inclacumab. However, levels dropped 19.2 percent with the 20 mg/kg inclacumab dose, compared with placebo (p=0.0002).

"It was exciting to see that a single administration of inclacumab would yield clinical benefit," Dr. Tardif said.

The researchers analyzed a subgroup of patients who were not taking antiplatelet drugs called glycoprotein 2b3a inhibitors. These are given to some patients to prevent blood clots but can increase the risk of bleeding. In patients not taking 2b3a inhibitors, those who received the 20 mg/kg dose of inclacumab experienced a 36 percent decrease in troponin I at 24 hours (p=0.008 compared with placebo).

"If we're able to confirm these results in potential future studies, this drug could become part of the therapeutic armamentarium in modern cardiology," Dr. Tardif said. "You could use this drug more widely, in all patients coming in with heart attacks, although that would require additional large studies."

**More information:** Dr. Tardif will present the study "Effects of the P-Selectin Antagonist Inclacumab in the Select-Acute Coronary Syndromes Trial" on Sunday, March 10 at 11:21 a.m., in Moscone Center, South, Esplanade Ballroom.

Provided by American College of Cardiology