Drug helps maintain platelet inhibition and anti-clotting levels prior to cardiac surgery

January 17 2012

Patients who discontinued use of an antiplatelet agent such as clopidogrel prior to undergoing cardiac surgery to lower their bleeding risk and received intravenously the platelet inhibitor cangrelor achieved a higher rate of maintenance of platelet inhibition, compared to patients who received placebo, according to a study in the January 18 issue of *JAMA*.

"Thienopyridines [antiplatelet agents] are among the most widely prescribed medications, but their use can be complicated by the unanticipated need for surgery. Despite increased risk of thrombosis, guidelines recommend discontinuing thienopyridines 5 to 7 days prior to surgery to minimize bleeding," according to background information in the article. However, premature discontinuation of antiplatelet therapy prior to surgical procedures such as coronary artery bypass grafting (CABG) has been associated with an increase in ischemic complications. The authors write that there is a need to define strategies of platelet inhibition that allow to safely "bridge" patients to their surgical procedure with minimum risk of ischemic events or bleeding complications. Cangrelor is characterized by rapid, potent, predictable, and reversible platelet inhibition with rapid offset of effect, desirable pharmacodynamic properties for these types of patients.

Dominick J. Angiolillo, M.D., Ph.D., of the University of Florida, Jacksonville, and colleagues conducted a study to examine whether cangrelor would be an effective and safe drug for bridging thienopyridine-treated patients to CABG surgery. The randomized,

multicenter trial included 210 patients with an acute coronary syndrome (ACS) or treated with a coronary stent and receiving a thienopyridine awaiting CABG surgery. Thienopyridines were stopped (a recommended 5-7 days before surgery) and patients were administered cangrelor or placebo for at least 48 hours, which was discontinued 1 to 6 hours before surgery. The median (midpoint) duration of infusion was 2.8 days for cangrelor vs. 3.4 days for placebo. The primary measure of effectiveness was platelet reactivity of less than 240 P2Y12 Reaction Units (PRUs), which was assessed daily. Excessive CABG surgery-related bleeding was the main safety end point.

The percentage of patients with platelet reactivity less than 240 PRU throughout the entire infusion of the study drug was significantly higher in the cangrelor group (98.8 percent [83 of 84]) than in the placebo group (19.0 percent [16 of 84]). "The percentage of overall samples displaying platelet reactivity less than 240 PRU, patients with all samples with baseline PRU value, total patient samples that maintained higher than 60 percent platelet inhibition during study drug infusion were all greater with cangrelor than with placebo," the authors write.

Study-defined excessive CABG surgery-related bleeding occurred in a total of 22 patients and was not significantly different between patients randomly assigned to receive cangrelor (11.8 percent [12 of 102]) or placebo (10.4 percent [10 of 96]). Pre-CABG-surgery major-bleeding events were rare and not different between treatment groups; minor bleeding events were numerically more frequent with cangrelor.

"In this trial, cangrelor achieved and maintained target levels of platelet inhibition known to be associated with a low risk of thrombotic events compared with placebo, without a significant excess in bleeding complications. Our data support the hypothesis that intravenous cangrelor is a feasible management strategy in patients waiting for cardiac surgery who require prolonged platelet P2Y12 inhibition after

thienopyridine discontinuation," researchers conclude.

More information: *JAMA*. 2012;307[3]:265-274.

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