

Administration of clopidogrel prior to PCI associated with reduction in major cardiac events

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Among patients scheduled for a percutaneous coronary intervention (PCI; procedures such as balloon angioplasty or stent placement used to open narrowed coronary arteries), pretreatment with the antiplatelet agent clopidogrel was not associated with a lower risk of overall mortality but was associated with a significantly lower risk of major coronary events, according to a review and meta-analysis of previous studies published in the December 19 issue of *JAMA*.

"In addition to aspirin, clopidogrel has been shown to improve ischemic outcomes of patients with stable <u>coronary artery disease</u> following PCI and of patients with <u>acute coronary syndromes</u> (ACS; such as heart attack or <u>unstable angina</u>) who were either medically treated or who had undergone either revascularization by fibrinolysis or PCI," according to background information on the article. "Clopidogrel pretreatment is recommended for patients with ACS and stable coronary artery disease who are scheduled for PCI, but whether using clopidogrel as a pretreatment for PCI is associated with positive clinical outcomes has not been established."

Anne Bellemain-Appaix, M.D., of the Service de Cardiologie-La Fontonne Hospital, Antibes, France, and colleagues conducted a review and meta-analysis of data from randomized trials and registries involving patients with <u>coronary artery</u> disease (stable or with ACS) undergoing catheterization for potential revascularization to evaluate the association



between clopidogrel pretreatment with mortality and major bleeding after PCI. After a search of the medical literature, the researchers identified 15 articles published between August 2001 and September 2012 that met the study inclusion criteria: 6 randomized controlled trials (RCTs), 2 observational analyses of RCTs, and 7 observational studies. Pretreatment was defined as the administration of clopidogrel before PCI or catheterization. The primary efficacy and safety end points were all-cause mortality and major bleeding. Secondary end points included major cardiac events.

Of the 37,814 patients included in the meta-analysis, 8,608 patients had participated in RCTs; 10,945 in observational analyses of RCTs; and 18,261 in observational studies. In the RCT cohort of patients, clopidogrel pretreatment was not significantly associated with a reduction of all-cause mortality (absolute risk, 1.54 percent vs. 1.97 percent). These results were consistent across the observational analyses of RCTs and the observational studies analyses. Clopidogrel pretreatment was also not associated with a significantly increased risk of major bleeding in the main analysis of RCTs (absolute risk, 3.57 percent vs. 3.08 percent).

In the main analysis, clopidogrel pretreatment was significantly associated with a reduction of major coronary events (absolute risk, 9.83 percent vs. 12.35 percent) and heart attack (absolute risk, 4.53 percent vs. 5.90 percent).

The authors note that although no significant heterogeneity existed for clinical presentation, the higher-risk ST-segment elevation myocardial infarction (STEMI; a certain pattern on an electrocardiogram following a heart attack) population appeared to gain the most benefit from pretreatment. "In contrast, patients undergoing elective PCI had no apparent benefit from <u>clopidogrel</u> pretreatment, questioning the need of such a systematic strategy at least in low-risk patients."



"Although a pretreatment strategy has been recommended for years in patients undergoing PCI, this study shows the limits of the available evidence, with no significant benefit on hard outcomes. The value of pretreatment, including with new antiplatelet agents, needs to be assessed in large prospective studies."

More information: *JAMA*. 2012;308(23):2507-2517

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