Certain combined medications following heart attack may increase risk of death

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Following an acute coronary syndrome such as a heart attack or unstable angina, patients who receive a medication to reduce the risk of gastrointestinal bleeding that may be associated with the use of the antiplatelet drug clopidogrel and aspirin have an increased risk of subsequent hospitalization for acute coronary syndrome or death, according to a study in the March 4 issue of *JAMA*.

Treatment with clopidogrel in addition to aspirin reduces recurrent cardiovascular events following hospitalization for acute coronary syndrome (ACS) for patients treated either medically or with angioplasty or stent placement. Proton pump inhibitor (PPI) medications are often prescribed at the start of treatment with clopidogrel, with the goal of reducing the risk of gastrointestinal tract bleeding while patients are taking dual-antiplatelet therapy. Recent studies, however, suggest that PPIs may reduce the effectiveness of clopidogrel, but the clinical significance of these findings to patients is not clear, according to background information in the article.

P. Michael Ho, M.D., Ph.D., of the Denver VA Medical Center, and colleagues evaluated the use of clopidogrel plus PPI following hospital discharge for ACS and compared rates of all-cause death and rehospitalization for ACS, between patients taking clopidogrel plus PPI vs. clopidogrel without PPI. The study included patients from 127 Veterans Affairs hospitals. Vital status information was available for all patients through September 30, 2006.

Of 8,205 patients with ACS taking clopidogrel after hospital discharge, 63.9 percent (n = 5,244) were prescribed PPI at discharge or during follow-up. Death or rehospitalization for ACS occurred in 29.8 percent of patients prescribed clopidogrel plus PPI and 20.8 percent of patients prescribed clopidogrel without PPI . Use of clopidogrel plus PPI at any point in time was associated with a 25 percent increased odds of death or rehospitalization for ACS compared with use of clopidogrel without PPI.

For the individual outcomes, the rates of recurrent hospitalization for ACS (14.6 percent vs. 6.9 percent) and revascularization procedures (15.5 percent vs. 11.9 percent) were higher among patients taking clopidogrel plus PPI compared with those taking clopidogrel without PPI. However, the risk of death was similar between the two groups.

"When patients were not taking clopidogrel after hospital discharge, a prescription for PPI was not associated with death or rehospitalization for ACS, supporting the hypothesis that the interaction of PPI and clopidogrel, rather than PPI itself, was associated with increased adverse outcomes," the authors write.

"… this study raises some concern about concomitant [accompanying] use of PPI medications and clopidogrel following hospitalization for ACS. While the risk estimates associated with clopidogrel plus PPI vs. clopidogrel without PPI were modest, the absolute number of adverse events attributable to this potential drug interaction is considerable when extrapolated to a population level, given how frequently PPI medications are prescribed to patients receiving dual-antiplatelet therapy," the researchers write. "Pending additional evidence, however, the results of this study may suggest that PPIs should be used for patients with a clear indication for the medication, such as history of gastrointestinal tract bleeding, consistent with current guideline recommendations, rather than routine prophylactic prescription. Alternative gastrointestinal tract medication regimens also may be considered until additional data

regarding concomitant use of PPI and clopidogrel becomes available."

More information: JAMA. 2009;301[9]:937-944.

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