

The Impact of Proton Pump Inhibitors on Clopidogrel Effectiveness

Presented by Ronald E. Aubert, Ph.D., of Medco Health Solutions, Inc., at the American Heart Association 2008 Scientific Sessions

PPI therapy with clopidogrel increased the risk of major cardiovascular events by 50%.

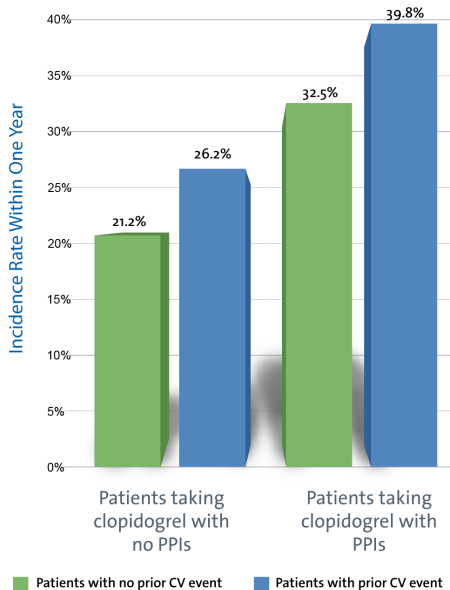
Background

Patients taking the antiplatelet medication clopidogrel, also known by the brand name *Plavix*®, are commonly prescribed proton pump inhibitors (PPIs) to prevent bleeding complications. This study examines the impact of PPIs on the effectiveness of clopidogrel in preventing adverse coronary events. The antiplatelet properties of clopidogrel are activated when the drug is converted to its active form by cytochrome P450 2C19, but this activation step can be inhibited by PPIs, and therefore PPIs may reduce the antiplatelet effects of clopidogrel.

Data and Population

This retrospective cohort study used the National Medco Integrated Database, which contains claims data on approximately 19 million people. Patients selected for inclusion in the study when they had undergone a percutaneous coronary intervention (PCI), such as a stent placement or balloon angioplasty, began taking clopidogrel within one month of the PCI. They were at least 80% compliant during the one-year study time frame and were continuously eligible for their drug benefit for six months prior to PCI and 12 months following (n=14,383). Patients were segregated into two cohorts: The Concurrent PPI Therapy cohort consisted of patients concomitantly taking a PPI and clopidogrel at any time during the 12-month follow-up period (n=4,521); the Non-PPI Therapy cohort included patients who had no prescription for a PPI during the study period (n=9,862).

Incidence of major cardiac events in patients taking clopidogrel



Methods

The pharmacy and medical claims data of patients in the two cohorts were tracked over a one-year period from 2005 to 2006 for the incidence of major cardiovascular events, including cerebrovascular events (stroke or TIA), acute coronary syndrome (myocardial infarction or unstable angina), cardiovascular death, and coronary revascularization (CABG and PCI). The incidence rates of adverse cardiac events for patients in the two cohorts were calculated and compared, controlling for baseline differences in age, gender, and comorbidity.

Results

Concomitant PPI therapy for patients taking clopidogrel significantly increased the relative risk of a major adverse cardiovascular event by 50%. Patients with no prior cardiovascular events taking PPIs with clopidogrel showed a 32.5% incidence of a major CV event within one year compared with 21.2% of patients using clopidogrel but not taking PPIs (adjusted OR 1.79, CI 1.62-1.97). A more pronounced effect was seen among patients with a preceding CV event: a 39.8% incidence rate was seen in the Concurrent PPI Therapy cohort versus 26.2% for the Non-PPI Therapy patients (adjusted OR of 1.86, CI 1.63-2.12). For patients taking both PPIs and clopidogrel, increased risk was driven primarily by hospitalizations for recurrent MI, PCI, and unstable angina.

Discussion

This large-scale comprehensive analysis assessing multiple cardiovascular outcomes confirms findings from several previous studies. These results add to the growing body of evidence suggesting the presence of a clinically significant adverse interaction between clopidogrel and PPIs. While this study raises important concerns about the concurrent use of these drugs, methodological and clinical considerations need to be weighed and further investigation is required before broad recommendations affecting patient care can be made.

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