

The Effect of Individual Proton Pump Inhibitors on Cardiovascular Outcomes in Patients Treated with Clopidogrel Following Coronary Stenting: The Clopidogrel Outcomes Study

Based on an abstract by researchers at Medco Health Solutions, Inc., and the Indiana University School of Medicine; presented May 6, 2009, by Eric J. Stanek, PharmD, of Medco Health Solutions, Inc., at the Society for Cardiovascular Angiography and Interventions (SCAI) 2009 Annual Scientific Sessions

Background

Recent evidence from a number of studies including research by Medco investigators shows that proton pump inhibitors (PPIs) decrease the effectiveness of clopidogrel, resulting in a significantly higher risk of cardiovascular (CV) events in patients taking both medications. Clopidogrel, known by its brand name *Plavix*®, is a widely prescribed antiplatelet drug and is used to prevent heart attack and stroke in patients after coronary stenting. PPIs are often prescribed along with clopidogrel to reduce the risk of gastrointestinal bleeding, a possible side effect of the antiplatelet drug. PPIs are known to inhibit the functioning of cytochrome P450 2C19, the enzyme that converts clopidogrel into its active form, thereby decreasing the drug's effectiveness. While there's a considerable body of evidence showing that PPIs as a group are associated with this interaction, there is little information available on whether the spectrum of individual PPIs increases CV event risks. Our study examines the extent to which individual PPIs are associated with the risk of an adverse cardiovascular event in patients taking clopidogrel.

Data and methods

This retrospective analysis was based on medical and pharmacy claims contained in the National Medco Integrated Database System, which draws from over 10 million patients. The study sample included 16,690 patients who were taking clopidogrel for a full year following a stent procedure and were adherent to their medication. The sample was divided into two main cohorts, one in which patients were only taking clopidogrel (n=9,862) and had an average age of 65; the other group of patients was taking a PPI in conjunction with clopidogrel (n=6,828) and had an average age of 68. During a one-year period spanning 2005 and 2006, both cohorts were followed to measure their risk of hospitalization for a major adverse cardiovascular event (MACE), including myocardial infarction, unstable angina, transient ischemic attack/stroke, coronary revascularization, or cardiovascular death. The study examined the overall MACE incidence rates for patients taking any PPI, as well as the incidence rates associated with individual PPIs, and it compared them with those of patients taking only clopidogrel. The PPI agents individually analyzed were pantoprazole (*Protonix*®, N=1,653), esomeprazole (*Nexium*®, N=3,257), omeprazole (*Prilosec*®, N=2,307) and lansoprazole (*Prevacid*®, N=785), which together represented 96% of the PPIs prescribed in the study. There were not enough patients who received rabeprazole (*Aciphex*®, N=298) to yield reliable results, so this agent was not included in the analysis.

Results

Concomitant use of a PPI and clopidogrel increased the overall risk of a major cardiovascular event by 51%. Patients taking clopidogrel and a PPI had a MACE incidence rate of 25.1%, as compared with patients not taking a PPI, whose incidence rate was 17.9%. When PPIs were examined individually the results showed the incidence of MACE ranged from 24.3% to 29.2%, while the increases in risk ranged from 39% to 61%. All of the associations were highly statistically significant.

Discussion

In addition to confirming already existing evidence that PPIs interfere with clopidogrel and render them less effective, our study sheds further light on this question by showing that this interaction is apparent with each of the most commonly prescribed PPIs.

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