Risk of Adverse Cardiovascular Outcomes Associated with Concomitant Use of Clopidogrel and Proton Pump Inhibitors in Elderly Medicare Beneficiaries

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OBJECTIVES: Evidence regarding the effect of concomitant use of clopidogrel and proton pump inhibitors (PPIs) on adverse cardiovascular outcomes remains inconclusive. The purpose of the current study was to examine the effect of concomitant use of clopidogrel and PPI in a national sample of elderly Medicare beneficiaries (age ≥ 65 years).

METHODS: The study used a nested case-control design. A cohort of Medicare beneficiaries taking clopidogrel for any period between July 1, 2006 and December 31, 2008 was identified from a 5% national sample of Medicare claims data using prescription drug records. Within this cohort, cases (beneficiaries who experienced a major adverse cardiovascular event (MACE, composite of acute myocardial infarction, coronary artery bypass graft, percutaneous coronary intervention, stroke, and mortality) and controls (beneficiaries who did not experience MACE) were identified from Medicare inpatient and outpatient claims. Concomitant use of clopidogrel and PPI was ascertained using prescription drug records. Each case was matched to a control on age and time entering the cohort using a greedy match algorithm. Conditional logistic regression was conducted on the matched sample to determine the risk of experiencing a MACE. Sensitivity analyses were performed using propensity score matching between cases and controls.

RESULTS: A cohort of 52,420 clopidogrel users was identified. 18,461 of them (35.22%) used clopidogrel and PPI concomitantly at any time during the study period. 9790 cases were identified and matched to equal number of controls. Beneficiaries using clopidogrel and PPI concomitantly were more likely to experience a MACE as compared to beneficiaries receiving
clopidogrel only (cdds ratio: 1.085, 95% Confidence Interval: 1.019 – 1.154). The propensity score matching approach yielded similar results.

**CONCLUSIONS:** Concomitant use of clopidogrel and PPI was associated with a slightly increased risk of experiencing a cardiovascular adverse event. Caution should be exercised when co-prescribing the two medications to elderly patients.