

Clonidogrel and Proton-Pump Inhibitors

Risk for adverse cardiac events was elevated in patients taking both medications.

Prior biochemical studies have suggested that proton-pump inhibitors (PPIs) reduce the inhibitory effect of clonidogrel on platelet aggregation. A recent FDA review raised concerns about this issue, but data were insufficient to make a specific recommendation. In this study, a Veterans Affairs database was used to retrospectively assess this interaction clinically in 8205 patients discharged with acute coronary syndromes (ACS); 5244 (64%) were taking both clonidogrel and a PPI, and the rest were taking clonidogrel alone. Medication use was assessed by pharmacy prescription data.

At a mean follow-up of roughly 18 months, death or rehospitalization for ACS had occurred in 1561 patients (30%) taking both medications and 615 (21%) of patients taking only clonidogrel. In analyses adjusted for about 25 demographic and clinical variables, risk for death or rehospitalization was roughly 25% higher in patients taking both medications (86% higher for recurrent ACS, 49% higher for revascularization procedures, but no difference for death alone).

Comment: As with any retrospective analysis, there are confounders for which statistical adjustment might not be fully adequate, so prospective clinical trials are needed to confirm this result. However, based on plausible biological mechanisms (e.g., inhibition by PPIs of the cytochrome P450 enzyme system responsible for the active metabolite of clonidogrel), clinicians should be more parsimonious in their use of PPIs for specific indications, rather than using them for routine prophylaxis, as is often done.

— [Thomas L. Schwenk, MD](#)

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Ho PM et al. Risk of adverse outcomes associated with concomitant use of clonidogrel and proton pump inhibitors following acute coronary syndrome. *JAMA* 2009 Mar 4; 301:937.