

# RGH Pharmacy E-Bulletin

Volume 33 (8): March 30, 2009

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Clopidogrel and PPIs

Clopidogrel and proton pump inhibitors (PPIs) don't mix? Clopidogrel is a commonly used anti-platelet drug which prevents platelet aggregation by inhibiting the Adenosine Diphosphate (ADP) receptor. It is a prodrug that is converted to an active metabolite by the enzyme cytochrome P450 2C19 (CYP2C19) in the liver. There is growing evidence suggesting that reduction in CYP2C19 activity reduces blood concentration of the active form of clopidogrel leading to decreased platelet inhibition and an increased rate of major cardiac events. Recent focus has centred on individuals with genetic polymorphisms that reduce the activity of CYP2C19 and individuals with concomitant use of CYP2C19 inhibitors.

The combination of clopidogrel and a proton pump inhibitor (PPI) is commonly seen in clinical practice, particularly in patients who are also treated with aspirin and/or a non-steroidal anti-inflammatory drug, the aim of PPI treatment in this context is often to reduce the risk of gastrointestinal bleed. This is of concern as a number of PPIs are strong inhibitors of CYP2C19. Selected evidence for how this may affect the efficacy of clopidogrel is summarised below:

- A study conducted in patients undergoing percutaneous coronary intervention treated with aspirin and clopidogrel found that the use of omeprazole significantly decreased the anti-platelet activity of clopidogrel. A case-series of patients taking clopidogrel showed that patients who were also taking PPIs had a threefold increase in risk of acute myocardial infarction relative to those who were not taking PPIs. However, these studies were small and there were many potential confounding factors.
- A recent large retrospective cohort study found that concurrent use of clopidogrel and a PPI after patients discharged from hospital for acute coronary syndrome (ACS) was associated with an increase in all-cause mortality or rehospitalisation for ACS (odds ratio 1.25, 95% confidence interval, 1.11-1.41).
- A population-based study in patients receiving clopidogrel after acute myocardial infarction found that the current use of PPI, other than pantoprazole, was associated with an increase risk of reinfarction, odds ratio 1.27 (95% CI, 1.03-1.57).

In summary, the findings of these studies suggest that PPIs, with possible exception of pantoprazole, may attenuate the anti-platelet benefits of clopidogrel. Hence it seems appropriate that PPIs should be used only if there is a clear indication instead of using them routinely as a prophylaxis. If the patients are on clopidogrel, the alternative treatment option with aspirin alone, if clinically appropriate, may be considered. In the cases where a medication for acid suppression is required, ranitidine or pantoprazole may be considered in preference to the concomitant use of clopidogrel and a PPI such as esomeprazole, lansoprazole, rabeprazole or omeprazole.

Acknowledgment – This E-Bulletin is based on work by Wassana Sorich, Senior Clinical Pharmacist, RGH. The advice and assistance of Dr Andrew Russell is also acknowledged.

**FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: [chris.alderman@gh.sa.gov.au](mailto:chris.alderman@gh.sa.gov.au)**  
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