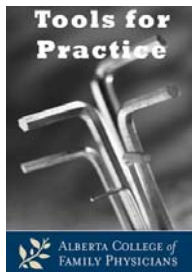


Tools for Practice is proudly sponsored by the Alberta College of Family Physicians (ACFP). ACFP is a provincial, professional voluntary organization, representing more than 2500 family physicians in Alberta. Established over fifty years ago, the ACFP strives for excellence in family practice through advocacy, continuing medical education and primary care research. www.acfp.ca

July 31, 2009



PPI's and clopidogrel: Never the twain shall meet?

Clinical Question:

Are there risks in giving a Proton Pump Inhibitor (PPI) with clopidogrel?

Evidence:

Two recent studies addressed this question.

- A Canadian Case-Control study of post-MI patients discharged on clopidogrel compared those who had a repeat MI within 90 days (730 patients) to those who did not (2000).
 - There was a statistically significant increase of repeat MI if a patient took any PPI, odds ratio = 1.27
 - Pantoprazole (the only PPI evaluated separately) did not increase the risk of MI.
 - When pantoprazole was excluded, the risk was higher with the other PPI medications (odds ratio 1.4).
- A US Veterans Cohort study of 8200 acute coronary syndrome (MI or unstable angina) patients discharged on clopidogrel was followed for 2.5 years.
 - There was a statistically significant increase in readmission for acute coronary syndrome if a patient took a PPI.
 - 15% if on PPI vs 7% if not taking PPI, Adjusted odds ratio = 1.86
 - Absolute difference 8% (Number needed to harm with PPI=13)
 - Pantoprazole not examined separately (numbers too low)

Context:

- Clopidogrel is a pro-drug:
 - Requires conversion (via cytochrome P450 2C19) to inhibit platelet function
 - PPI's inhibit P450 2C19 (except pantoprazole and perhaps rabeprazole)
- Up to 60% of patients discharged on clopidogrel also take a PPI.²
- Both studies are lower level evidence and so are not definitive; But...
 - They are well done
 - They are standard study designs to address questions of harm (like this)
 - They are supported by other evidence³

- Another review of the topic is available through Rx Files
<http://www.rxfiles.ca/rxfiles/uploads/documents/Clopidogrel-PPI-interaction-QandA.pdf>

Bottom-line: The available evidence indicates that most PPI's inhibit clopidogrel activity and lead to an increase in recurrent MI or Acute Coronary Syndrome in patients previously admitted for those conditions. In post MI or acute coronary syndrome patients on clopidogrel consider stopping a PPI or, if gastric protection/acid suppression is required, switching to pantoprazole or H2 Antagonist.

Authors: G Michael Allan MD CCFP & Michael Kolber MD CCFP

1. [CMAJ 2009; 180\(7\): 713-8.](#)
2. [JAMA 2009; 301\(9\): 937-944.](#)
3. [Ann Pharmacother 2009; 43:1266-74.](#)

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians. Archived articles are available on the Towards Optimized Practice website.

This communication reflects the opinion of the author and does not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.