

Journal Club Block 4: Oct 14, 2015

What is the efficacy of proton pump inhibitors in upper GI bleeds?

Hosted by Drs. Jon Henderson, Sara Birdsong and James Brown

Clinical Scenario: You're working a shift when you pick up a 63 year old woman with a chief complaint of "bloody emesis." She takes daily Voltaren for chronic knee pain. Two days ago she began having epigastric pain and last night she had 2 episodes of dark emesis followed by an episode of bloody emesis this morning.

In the ER, she looks a bit pale but is not actively vomiting. She is mildly tachycardic but vital signs are otherwise stable. On exam her abdomen is mildly distended with epigastric tenderness. Lab work demonstrates hemoglobin of 9, coags are not elevated. While you are waiting for the labs she has 1 episode of coffee ground emesis. Type and cross for 2 U pRBCs is ordered and a NG is placed. You call the hospitalist for admission and the GI team for an emergent endoscopy. Your ED attending asks you to order a protonix bonus and drip. You wonder what the evidence says regarding the use of PPIs in management of acute UGIB.

PICO question:

What is the outcome difference in adult patients with undifferentiated acute upper GI bleeding treated with a proton pump inhibitor (either IV or PO) vs placebo in regards to mortality, rebleeding rates, need for surgery, need for blood transfusion.

Introduction:

The use of proton pump inhibitors (PPI) in the setting of acute upper GI bleeding (UGIB) has been debated in the medical literature for the past 25 years. In our clinical practice today it is expected that we initiate a PPI for patients with active UGIB before admitting them to the hospitalist or GI teams. The thought process behind this therapy is to neutralize the pH of the stomach to allow formation and stabilization of clots to control bleeding.

Articles:

Background Article:

Dorward S, Sreedharan A, Leontiadis GI, Howden CW, Moayyedi P, Forman D. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. *Cochrane Database Syst Rev.* 2006 Oct 18;(4):CD005415. Review. Update in: *Cochrane Database Syst Rev.* 2010;(7):CD005415.

Article 1:

Hawkey GM, Cole AT, McIntyre AS, Long RG, Hawkey CJ. Drug treatments in upper gastrointestinal bleeding: value of endoscopic findings as surrogate end points. *Gut.* 2001 Sep;49(3):372--- 9.

Article 2:

Lau JY, Leung WK, Wu JC, Chan FK, Wong VW, Chiu PW, Lee VW, Lee KK, Cheung FK, Siu P, Ng EK, Sung JJ. Omeprazole before endoscopy in patients with gastrointestinal bleeding. *N Engl J Med*. 2007 Apr 19;356(16):1631-40.

Article 3:

Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: a systematic review and meta-analysis. Sachar H, Vaidya K, Laine L. *JAMA Intern Med*. 2014 Nov;174(11):1755-62. doi: 10.1001/jamainternmed.2014.4056. Review. PubMed PMID: 25201154; PubMed Central PMCID: PMC4415726.

The Cochrane review article last revised in 2010 concluded that although the visualization of active or recent hemorrhage during endoscopy was reduced if the pt was pretreated with a PPI, there was no statistically significant improvement in patient-based outcomes including mortality, delayed rebleeding, need for surgery or need for blood transfusion. The endorsement toward the use of PPI in these patients is thus based on the weight of surrogate clinical markers over patient centered outcomes. The Hawkey article in *Gut* 2001 and the Lau article in *NEJM* in 2007 confirm an improved appearance of gastric mucosa on endoscopy following pretreatment with a PPI but again demonstrated no change in the mortality, rebleeding or surgery rates.

The Sachar article published in *JAMA* 2014 discusses the importance of intermittent dosing of a PPI vs a bolus dose followed by a drip. In these patients who often have poor venous access and may require blood products for acute anemia or anticoagulation reversal, the non-inferiority of a intermittent dosing may help free up valuable resources in the ED to allow administration of other resuscitative medications without sacrificing any potential benefits of a PPI.

Discussion:

Our journal club discussion centered around 2 themes: the importance of recognizing the clinical limitations of surrogate clinical markers and focusing on managing limited resources in your ED. Surrogate outcomes are attractive because they are often easier to measure and more “black and white” than complicated patient outcomes like attempting to attribute mortality to a single clinical intervention. However, it is important to remember that there is not always a clear correlation between an improvement in a surrogate marker and a true improvement in the patient.

The second point of discussion was developing an awareness of your nursing resources, vascular access and medication availability in the ED. While the gastroenterologists we work with may request a bolus and drip for a patient with an acute UGIB, the reality of the patient care environment at any given moment in the ED may not allow for the allocation of resources (nursing time, use of a IV line, increased boarding time) to perform this in the ED. This concept can be extrapolated to other patient care scenarios requiring higher levels of resource allocation. The importance of communicating with the admitting team to ensure the patient

receives all intended care while encouraging smooth and rapid transition out of the ED is part of the art of emergency medicine.

Bottom line: In clinical practice, PPIs are inexpensive, likely do not cause harm and may be beneficial to the patient so we will continue to use them in patients with acute UGIB with the understanding that the science behind their use may be limited.