

Session Title: Medication Mayhem - Down the Hole

Track: Abdominal Disorders

Session Overview

It's been taken as dogma that certain medications will NOT be used in a surgical patient....but is that true? The speaker will review the literature to provide clarity.

Objectives

1. Review the literature on a myriad of medications long since believed to worsen the outcome of the presenting GI patient - morphine, NSAIDs, PPIs.
2. Discuss how to disseminate this update to colleagues across the hall.
3. Demonstrate incorporation of the literature in case-based scenarios including patients with an acute Appendicitis.

Pain Management

Background

Abdominal pain is the most common reason for patients to present to the ED ([CDC 2015](#)). As early as 1921, in Cope's Early Diagnosis of the Acute Abdomen, it was believed that providing analgesia to patients with acute abdominal pain could interfere with the assessment and diagnosis. Can analgesia affect surgical consultation?

Important studies demonstrating no negative effect of early analgesia

- [Zoltie and colleagues \(1986\)](#) conducted a prospective double blind trial with 288 abdominal pain patients receiving buprenorphine 200 mcg, buprenorphine 400 mcg, or placebo. Physical signs altered in proportion to dosage, but this had no effect on clinical diagnosis. [Adults]
- [Attard et al. \(1992\)](#) studied 100 consecutive patients and administered IM opioid or IM saline. Incorrect diagnoses and management decisions were made in 2 patients who received opioid analgesia and in 9 patients who received saline. [Adults]
- [Thomas et al. \(2003\)](#) performed a prospective, randomized, placebo-controlled study of 74 patients found no instance of masking physical findings after IV morphine. [Adults]
- [Kim and colleagues \(2002\)](#) conducted a randomized, double-blind trial in 60 patients aged 5-18 administered IV morphine or an equal volume of IV saline. There was no significant difference in diagnostic accuracy between the groups. Children requiring laparotomy were identified and no significant complications were found in those who received morphine. [Pediatric]
- [Green et al \(2006\)](#) performed a multicenter, randomized, controlled trial in 108 patients receiving IV morphine or placebo and found no difference in diagnostic accuracy. [Pediatric]
- Other studies: [Gallagher, Ann Emerg Med 2006](#); [Pace, Acad Emerg Med 1996](#); [Bailey, Ann Emerg Med 2007](#); [Kokki, Arch Pediatr Adolesc Med 2005](#)

Cochrane and other systematic reviews

- Effect on diagnostic efficiency of analgesia for undifferentiated abdominal pain ([Br J Surg 2003](#))
- Do opiates affect the clinical evaluation of patients with acute abdominal pain? ([JAMA 2006](#))
- Analgesia in patients with acute abdominal pain ([Cochrane 2011](#))
- Opioids for acute pancreatitis pain ([Cochrane 2013](#))
- Opioid analgesia for acute abdominal pain in children ([Acad Emerg Med 2014](#))
- Nonsteroidal anti-inflammatory drugs and non-opioids for acute renal colic ([Cochrane 2015](#))
- Non-steroid anti-inflammatory drugs for biliary colic ([Cochrane 2016](#))

What is our ED practice?

A 2004 ED study in 330 abdominal pain patients found a pain medication was given to 47%; 39% received a narcotic, 6% received an NSAID, 2% received a narcotic and an NSAID. ([Edwards, Ann Emerg Med 2004](#)) Patients experiencing moderate or severe pain were 2.1 times more likely to receive a pain medication (60% versus 28%, adjusted odds ratio [OR] 3.9, $P=.01$) and were 2.6 times more likely to receive a narcotic (51% versus 20%, adjusted OR=3.9, $P=.01$). Patients with cholecystitis were 2.6 times more likely to receive a pain medication (51% versus 20%, adjusted OR=3.9, $P=.01$), and there was a trend for patients with cholecystitis to receive a narcotic (48% versus 32%, adjusted OR=1.7, $P=.06$).

The Surgery Perspective

Nissman et al surveyed 60 EM physicians and found 59 of 60 (98.3%) respondents reported that it is their practice to administer analgesia prior to surgical evaluation. ([Nissman, Am J Surg 2003](#)). Of these, only 9 of 59 (15.3%) reported always informing the surgeon prior to dosing the patient. Their MEDLINE search through 2002 identified 4 studies supporting the practice of analgesia first, but with which they cited significant flaws. A rebuttal was published a year later. ([Abboud, Am J Surg 2004](#)) This was also before much of the newer literature was available.

Bridging the Gap

- Have a plan/protocol in place ahead of time with our surgical colleagues. Most may be ok with analgesia before consultation, but some may not.
- Establish common goals (ie, reduce pain to manageable levels, possibly improving the accuracy of the abdominal examination by minimizing voluntary guarding)
- Shared conference/journal club with EM/surgical residents/attendings to review literature together

Pain Management Options

- Opioids (surgical or non-surgical abdomen)
- Ketamine (surgical or non-surgical abdomen)
- Acetaminophen (surgical or non-surgical abdomen) - several routes available (IV expensive)
- NSAIDS (non-surgical abdomen if GI bleeding ruled out)
- Lidocaine (renal colic)

NSAID 'Ceiling' Effect

For acute pain, parenteral ketorolac is generally administered as 30 mg IV or 60 mg IM. Dr. Chris Bond ([@socbmobem](#)) has written about the '[ceiling effect](#)' of NSAIDS. The question is: are we using too much ketorolac without getting additional pain benefit? A randomized, double-blind trial from Dr. Sergey Motov's group ([@painfreeED](#)) addresses this question. ([Motov 2017](#))

What they did: 240 patients with acute pain in a 711-bed urban community teaching hospital ED were randomized to receive 10 mg, 15 mg, or 30 mg of IV ketorolac as a single-dose.

- Age 18 to 65 years
- Acute flank, abdominal, musculoskeletal, or headache pain with an intensity of 5 or greater on a standard 0 to 10 numeric rating scale
- Patients who would routinely be treated with IV ketorolac
- Pain scores, vital signs, adverse effects recorded at baseline and 15, 30, 60, 90, and 120 minutes
- IV morphine 0.1 mg/kg available as rescue at 30 min

Outcome: Reduction in numeric rating scale pain score at 30 minutes from medication administration

What they found

1. No difference in reduction of pain scores between the groups
 - 10 mg – 7.7 to 5.2
 - 15 mg – 7.5 to 5.1
 - 30 mg – 7.8 to 4.8
2. No differences between the groups with respect to use of rescue morphine analgesia at any time
3. No concerning changes in vital signs and no clinically significant adverse effects at any dose

Limitations: No placebo group and the box plot (Figure 2) revealed wide variability in all treatment arms

Implications for Clinical Practice

- Well-conducted study found no pain score reduction difference for various doses of IV ketorolac
- Doses of 10 mg or 15 mg are just as effective in most cases as 30 mg (or 60 mg) and should be used preferentially over higher doses ([Reuben 1998](#), [Staquet 1989](#), [Minotti 1998](#), [Brown 1990](#))

- Higher doses can cause more adverse effects, especially if more than one dose is administered ([Quan 1994](#), [Corelli 1993](#), [Gallagher 1995](#), [Dordoni 1994](#))

Proton Pump Inhibitor (PPI) for Upper GI Bleeding

Undifferentiated UGI Bleeding

PPI treatment initiated before endoscopy might reduce the proportion of participants with stigmata of recent hemorrhage (active bleeding, non bleeding visible vessel or adherent clot) at index endoscopy and significantly reduces requirement for endoscopic therapy during index endoscopy. However, there is no evidence that PPI treatment affects clinically important outcomes, namely mortality, rebleeding, or need for surgery. ([Cochrane 2010](#); [The Number Needed to Treat](#))

PPI therapy is useful only in a selected group of patients with acute non-variceal UGI bleeding, namely those with peptic ulcers having endoscopic high-risk stigmata for rebleeding. ([Khuroo, J Gastroenterol Hepatol 2005](#))

Peptic Ulcer Bleeding

H2 Receptor Antagonists - do not lower the rate of ulcer rebleeding. ([Gisbert, Aliment Pharmacol Ther 2001](#))

PPIs - lower the rate of rebleeding (odds ratio [OR] 0.46, 95% CI 0.33-0.64) and the need for surgery (OR 0.59, 95% CI 0.46-0.76) compared with placebo or H2 receptor antagonists, but there is no effect on all-cause mortality ([Leontiadis, BMJ 2005](#); [Cochrane 2006](#); [The Number Needed to Treat](#))

How PPIs Work in UGI Bleeding

Elevation of gastric pH, which stabilizes blood clots ([Green, Gastroenterology 1978](#))

Adverse Effects of PPIs

Most adverse effects associated with long-term use. Adverse effects potentially concerning in the ED patient:

1. *C. Difficile* infection ([Cao, J Hosp Infect 2018](#))
2. Acute Interstitial Nephritis ([Geevasinga, Clin Gastroenterol Hepatol 2006](#); [Muriithi, Am J Kidney Dis 2014](#))
3. Pneumonia??? ([Eom, CMAJ 2011](#); [Jena, J Gen Intern Med 2013](#); [Filion, Gut 2014](#))

PPI Dosing in the ED

Guidelines recommend bolus + infusion. However, intermittent PPI therapy is comparable to the current guideline-recommended regimen of IV bolus plus a continuous infusion of PPIs in patients with endoscopically treated high-risk bleeding ulcers. ([Sachar, JAMA Intern Med 2014](#))

IV Options:

1. Pantoprazole IV 80 mg once, followed by 40 mg BID (or 40 mg BID without bolus)
2. Esomeprazole IV 80 mg once, followed by 40 mg BID (or 40 mg BID without bolus)

Most of the studies looked at PPI dosing regimens following endoscopy rather than initiation prior to endoscopy. It seems likely that initiation after endoscopy would give a similar result since the benefit is likely due to pH changes. Small studies suggest that intermittent dosing and continuous infusion have similar effects on gastric pH for the first 12 hours after the initial bolus is given. ([Laterre, Crit Care Med 2001](#); [Hung, ANZ J Surg 2007](#)) A 2007 trial randomized 638 patients with UGI bleeding to either IV omeprazole (80 mg IV bolus followed by an 8 mg/hr infusion) or placebo before endoscopy. ([Lau, NEJM 2007](#)) Patients who received omeprazole were less likely to have signs of active bleeding (6 vs 15%) or to require endoscopic hemostatic therapy (19 vs 28%).

Approach to the UGI Bleeding Patient in the ED

1. ED patients with UGI bleed should be given IV pantoprazole or esomeprazole 40 mg or 80 mg X 1
2. If the patient has an emergent endoscopy, continued therapy (IV or PO) should be directed by endoscopy results
3. If the patient has a delayed endoscopy while boarding in ED or after admission, BID dosing of IV PPI is ok to continue until bleeding peptic ulcer is ruled out