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GASTROINTESTINAL - ACID SUPPRESSION DRUGS: EVIDENCE, TIPS AND PEARLS

B. Schuster - © www.RxFiles.ca - Feb 07

Five Key Decision Points in the Approach to Patients with Uninvestigated Dyspepsia (pain or discomfort in upper abdomen) [3]

1. Are there other possible causes for the symptoms? Consider cardiac, hepatobiliary, medication-induced, lifestyle or dietary indiscretion
2. Is the patient >50yrs, or does the patient have alarm symptoms? Alarm features and increased age identify patients at higher risk of organic causes, including cancer and ulcers.
   Alarm symptoms - ***VBAD⇨*** (**V**omiting, **B**leeding/anemia, **A**bdominal mass/uninvestigated wt loss, **D**ysphagia) ⇨ warrant prompt investigation
3. Is the patient regularly using conventional NSAIDs (including ASA)? Stop therapy if possible
4. Is the dominant symptom heartburn or acid regurgitation, or both? If yes, these are reliable indicators of GERD (gastroesophageal reflux disease)
5. Is the patient infected with *Helicobacter pylori*? Considering this question last will assist in legitimate indications for *H.pylori* testing

GERD

- symptomatic response to antisecretory therapy with proton pump inhibitors (**PPI**) or H2 antagonists (**H2RA**) is generally considered to support the presumptive diagnosis of GERD.
- mild symptomatic GERD can often be managed with lifestyle and dietary modifications along with OTC antacids or H2RAs

PHARMACOLOGICAL CONSIDERATIONS

Initial therapy

- Standard dose PPI is more efficacious than H2RA[1]; double dose PPI is generally no more efficacious than standard dose for initial therapy in erosive esophagitis [1]

Reassess therapy at 4 wks

- if response STOP therapy. If recurrence, repeat original therapy
- if symptoms not resolved,
  →if not on a PPI, switch to a PPI X 4-8 weeks
  →if on a PPI give bid x 4-8 weeks or consider investigation;
  {Ensure PPI taken 15-30 minutes before am meal; or at hs if primarily nocturnal symptoms}
- if symptoms respond to 4-8weeks of therapy STOP therapy, if symptoms recur repeat original therapy

Long-term therapy

- REASSESS NEED FOR THERAPY
  "patients should earn the right to be on long-term therapy"
- Tailor the dose and frequency to control symptoms. Patients should be maintained on the lowest dose of therapy that was adequate to provide symptom relief.

On-Demand PPI after response to initial PPI

- patients who respond to initial PPI therapy, subsequent "on-demand" PPI is more efficacious than continuous H2RA, but less efficacious than standard dose PPI {in uninvestigated GERD}[1]

STANDARD DOSES OF PPIs

There are no clinically important differences among standard doses of PPIs in treatment of symptomatic GERD, ENRD and esophagitis [1] **Patient variation in response may be seen.**
{Standard dose: Omeprazole, rabeprazole & esomeprazole 20mg od;
lansoprazole 30mg od; pantoprazole 40mg od}.

PPIs are **not efficacious** in **asthma** associated with GERD, in improving **laryngeal** symptoms associated with reflux or improving **chronic cough** with or without GERD[1]

PUD & *H.pylori* (Non-NSAID PUD)

- ≈90% of DU & 70% of GU may be *H.pylori* positive
- the standard of care for all patients with GU/DU is *H.pylori* testing and treating if positive
- smoking cessation improves ulcer healing rates and reduces ulcers not related to *H.pylori* infection

H.pylori TESTING – Noninvasive

- diagnostic testing for *H. pylori* should only be performed in pts suspected of having *H pylori*-related conditions such as PUD and if treatment is intended. (test and treat strategy)

Urea Breath Test (UBT)

- should be used for routine diagnosis, unless endoscopy is indicated for another reason
- excellent sensitivity, specificity and ease of use
- to prevent false –'ve results patients should be off antibiotics & bismuth for at least 4wks & off PPIs/H2RA for at least 1wk

Serology:

- appropriate if no access to UBT or endoscopy, higher rate of false positives results (≈20%)

Repeat H.pylori testing after *H.pylori* eradication

- for uncomplicated DU, confirmation of *H.pylori* eradication is not required unless symptoms persist
- serology cannot be used to determine cure from infections (IgG antibodies detectable after 6-12 months after eradication)

***H.pylori* Regimens** (see *H.pylori* Chart; all PPIs equally effective)

- *H.pylori* regimens 1-2-3 =**1** week, **2** times a day, **3** drugs commonly used, but four drug regimens an option
- single and two drug regimens not recommended
- 7 & 10 regimens equally effective, but 14 day regimens more efficacious than 7 days regimens [1]
- consider the following when selecting regimen: allergy history, recent metronidazole use or EtOH intake (avoid metronidazole), potential compliance issues (1-2-3 regimens, Hp-PAC®), DIs
  [See also RxFiles H. Pylori Eradication chart http://www.rxfiles.ca/acrobat/CHT-Hpylori.pdf]

PPI treatment after *H.pylori* eradication

- for uncomplicated duodenal ulcer, once HP has been eradicated, continued PPI use does not produce higher ulcer healing rates and is generally not indicated[1]
  {Note: PPI may be indicated for acute healing of gastric ulcer}

PUD & NSAIDs - Prevention

- NSAIDS are responsible for the majority of HP negative PUD
- routine concomitant antiulcer prophylaxis is not warranted for all pts taking NSAIDs; assess patient risk

Preventing NSAID Induced Ulcer in High Risk Patients [+]

High Risk: age >60, hx of ulcers/UGIB, warfarin, steroids, 2x normal dose NSAID. Those with several risk factors are at highest risk for NSAID-induced GI toxicity (up to 9%[@6 months])

- avoid NSAID if possible (use acetaminophen)
- if NSAID must be used, use lowest dose & shortest duration
- **GI Prophylaxis**
  →standard dose PPI (all PPIs, similar efficacy) [1]
  →misoprostol 200ug tid-qid $38-49 (GI upset & diarrhea)
  {H2RAs are not recommended for GI prophylaxis in NSAID pts}

HP Eradication and NSAID Use

- *H.pylori* & NSAID additive on the risk of PUD/UGIB
- Prior to initiating chronic NSAIDS or low dose ASA, experts recommend *H.pylori* testing & treating if positive. Those at greatest risk (hx of peptic ulcers, dyspepsia, steroids, and/or warfarin) most likely to benefit.

COXIBs:

- The GI sparing effect of COXIBs is compromised when used concurrently with low dose ASA, therefore the GI advantage of a COXIB [especially at high-dose] is lost. When a COXIB is used with warfarin concurrently, the risk is similar to NSAIDS.
- COXIB risks are dose dependent {e.g. cardiac, renal, gastric}
- COXIB vs {NSAID + PPI} appear to have similar efficacy in prevention and recurrence of ulcer/bleeding in patients with previous NSAID associated UGIB[1]

TREATMENT OF NSAID INDUCED ULCER

- Discontinue NSAID, *H.pylori* test & treat if positive, treat like a non-NSAID ulcer {e.g. PPI or H2RA (x4wk in DU); (x8wk in GU)}
- Healing rates: standard dose PPI x4-8weeks is more efficacious than H2RA or misoprostol [1]

If NSAID MUST BE CONTINUED

- secondary prevention PPI more effective than H2RA, but similar efficacy to misoprostol 400-800ug/day [endoscopic evidence 1]
- *H.pylori* –'ve pts [(ulcer bleeding history)] on **low dose ASA+PPI** have lower risk of ulcer complications vs clopidogrel alone[1]

COXIBs= Selective cyclooxygenase 2 inhibitors **DI**=drug interactions **DU**=duodenal ulcer **ENRD**=endoscopic negative reflux disease **EtOH**=alcohol **GERD**=gastroesophageal reflux disease **GI**=gastrointestinal **GU**=gastric ulcer ***H.pylori***=*helicobacter pylori*
H2RAs=2-receptor antagonist **NSAIDS**=nonsteroidal anti-inflammatory drugs **OTC**=over the counter **PPI**=proton pump inhibitor **PUD**=peptic ulcer disease **UBT**=urea breath test **UGIB**=upper GI bleed. [See also http://www.rxfiles.ca/acrobat/CHT-AcidSuppression.pdf]

References

1. Canadian Agency for Drugs and Technologies in Health. *Evidence for PPI use in gastroesophageal reflux disease, dyspepsia and peptic ulcer disease* [Scientific report]. DRAFT. Ottawa: The Agency; 2006 Dec 6.
2. 2006 UpToDate® • www.uptodate.com [See also RxFiles NSAID/COXIB chart: http://www.rxfiles.ca/acrobat/CHT-NSAID-Cox2.pdf]
3. Veldhuyzen van Zanten SJ, Flook N, Chiba N, Armstrong D, Barkun A, Bradette M, et al. An evidence-based approach to the management of uninvestigated dyspepsia in the era of Helicobacter pylori. Canadian Dyspepsia Working Group. CMAJ 2000;162(12 Suppl):S3-S23.
4. e-therapeutics www.e-therapeutics.ca
5. Preventing NSAID-Induced Ulcers.. Pharmacist's Letter/Prescriber's Letter 2002; 18(3):180306.
6. Armstrong A, Marshall JK, Chiba N et al. Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults – update 2004. Can J Gastroenterol 2005;19(1):15-35.
7. Hunt RH, Fallone CA, Thomson, ABR. Canadian Helicobacter Study Group. Canadian Helicobacter pylori Consensus Conference Update: Infections in Adults. Can J Gastroenterol 1999;13(3): 213-217.
8. Hunt R, Thomson ABR. Canadian Helicobacter pylori Consensus Conference. Can J. Gasteroenterol 1998;12(1):31-41.

[+] **NSAID Ulcer Risk Factors (x=↑in odds ratio risk):** ●hx ulcer complications x13.5 ●multiple NSAIDS x9 ●high dose NSAID x7 ●concomitant anticoagulant use x6.4 ●age≥70 x5.6 ●age ≥60 x3.1 ●concomitant steroids x2.2 ●heart disease x1.8