The Medical Letter®

On Drugs and Therapeutics

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Volume 52 (Issue 1333)
March 8, 2010

www.medicalletter.org

Primary Prevention of Ulcers in Patients Taking Aspirin or NSAIDs

Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) are common causes of peptic ulcer disease. Patients infected with *Helicobacter pylori* who take aspirin or another NSAID have an especially high risk.[1] Drugs that have been tried for prevention of ulcers in patients taking NSAIDs including H_2-receptor antagonists, proton pump inhibitors (PPIs), aluminum- or magnesium-containing antacids, the prostaglandin misoprostol (*Cytotec,* and others), and antibiotics to eradicate *H. pylori*.[2]

H_2-RECEPTOR ANTAGONISTS — NSAIDs are more likely to cause gastric than duodenal ulcers. High doses of an H_2-receptor antagonist have been shown to prevent NSAID-related gastric ulcers. In a 6-month study in patients on long-term NSAID therapy, famotidine 40 mg twice daily was significantly superior to placebo in preventing gastric ulcers found on endoscopy, which occurred in 20% of placebo-treated patients and 8% of those on famotidine.[3] In a 12-

Table 1. Some Drugs for Prevention of Peptic Ulcers

Drug	Formulation	Dosage	Cost[1]
Proton Pump Inhibitors			
Esomeprazole[2-4] - *Nexium* (AstraZeneca)	20, 40 mg caps[5]	20-40 mg once daily	$195.06
Lansoprazole[2-4,6-8] – generic	15, 30 mg tabs, caps, ODT	15-30 mg once daily[9]	176.93
Prevacid (Takeda)			179.94
Omeprazole[4,6-8] – generic	10, 20, 40 mg caps	20-40 mg once daily[9]	119.40
Prilosec (AstraZeneca)			169.75
Zegerid	20, 40 mg caps[5,10]		167.74
Pantoprazole[11] – generic			122.70
Protonix (Wyeth)	20, 40 mg tabs	20-40 mg once daily	137.10
Rabeprazole[4,6] – *Aciphex* (Eisai)	20 mg tabs	20 mg once daily	188.39
H_2-Receptor Antagonists[6-8,12]			
Cimetidine – generic	200, 300, 400, 800 mg tabs	200-400 mg bid	52.20
Tagamet (GlaxoSmithKline)			104.83
Famotidine – generic	20, 40 mg tabs	20-40 mg bid	4.00[13]
Pepcid (Merck)			116.80
Nizatidine – generic	150, 300 mg caps	150 mg once daily-bid	71.50
Axid (Lilly)	150, 300 mg caps[5]		96.38
Ranitidine – generic	150, 300 mg tabs, caps[5]	150 mg once daily-bid	4.00[13]
Zantac (GlaxoSmithKline)	150, 300 mg tabs[5]		122.83
Other Drugs			
Misoprostol[14] – generic	100, 200 mcg tabs	200 mcg bid-tid[14]	71.95
Cytotec (Searle)			113.82

ODT = orally disintegrating tabs.
1. Cost for 30 days' treatment at the lowest dosage, according to AWP listings of prescription formulations in *Redbook* 2009 and *Redbook Update* February 2010.
2. FDA-approved for treatment of GERD.
3. FDA-approved for risk reduction of NSAID-associated gastric ulcers.
4. FDA-approved for *H. pylori* eradication to reduce risk of duodenal ulcer recurrence.
5. Also available as an oral suspension, syrup or solution.
6. FDA-approved for treatment of duodenal ulcers.
7. FDA-approved for treatment of gastric (benign) ulcers.
8. Also available over the counter, often at a much lower cost.
9. Lower dose is for GERD and duodenal ulcer; higher dose is for gastric ulcer.
10. Both strengths contain sodium bicarbonate 1.1 g; therefore, two 20-mg caps are not equivalent to a 40-mg cap.
11. FDA-approved for treatment of erosive esophagitis associated with GERD.
12. Twice the dose once daily in the evening is effective.
13. Price at some chain pharmacies.
14. FDA-approved only for prevention of NSAID-associated gastric ulcers.

week randomized, double-blind trial comparing famotidine 20 mg twice daily to placebo in 404 adult patients taking aspirin 75-325 mg daily with or without clopidogrel *(Plavix)* or dipyridamole (*Persantine*, and others), the prevalence of gastric ulcers found on endoscopy was 15% with placebo and 3.4% with famotidine, and that of duodenal ulcers was 8.5% and 0.5%, respectively.[4] However, continued use of these agents leads to pharmacologic tolerance and loss of effectiveness over time.[2]

PROTON PUMP INHIBITORS (PPIs) — A randomized, double-blind trial in 169 patients taking NSAIDs compared omeprazole 20 mg once daily with placebo. After 6 months, the incidence of ulcers seen at endoscopy was 3.6% in the patients on omeprazole and 16.5% in those on placebo.[5] A more recent 2-year study (VENUS) found that esomeprazole 20 or 40 mg once daily for 6 months was superior to placebo in preventing ulcers in NSAID users who had additional risk factors such as advanced age or a past history of ulcer; among 844 such patients, endoscopic ulcers developed in 20% with placebo, 5% with esomeprazole 20 mg, and 4% with esomeprazole 40 mg.[6] Another trial compared esomeprazole 20 or 40 mg once daily with placebo in patients who were taking aspirin 75-325 mg daily and had one or more additional risk factors for ulceration, such as age over 65 or a past history of peptic ulcer disease; after 26 weeks, endoscopic ulcers were present in 7.4% of placebo-treated patients and in 1.1% and 1.5% of those on esomeprazole 20 or 40 mg, respectively.[7]

PPIs have been shown to be more effective than H_2-receptor antagonists in prevention of NSAID-related ulcers and at least as effective as misoprostol.[8,9]

MISOPROSTOL — Misoprostol (*Cytotec*, and others), a synthetic prostaglandin E1 analog, can prevent gastric and duodenal ulcers in patients on chronic NSAID therapy. It may be as effective as a PPI, but requires multiple daily dosing and is not as well tolerated. Abdominal pain and dose-related diarrhea are the most common adverse effects of misoprostol. Nausea can also occur. Misoprostol is an abortifacient and is contraindicated during pregnancy.[10]

***H. PYLORI* ERADICATION —** A meta-analysis of five prospective trials of *H. pylori* eradication showed a statistically significant reduction in the risk of endoscopic ulcers in patients who had not yet begun NSAID treatment, but not among those already taking an NSAID.[11] The American College of Gastroenterology now recommends considering routine testing for *H. pylori* before starting long-term therapy with an NSAID.[1]

ANTACIDS — There is no convincing evidence that long-term use of aluminum- or magnesium-containing antacids can prevent development of peptic ulcers in patients taking aspirin or NSAIDs. Other problems with antacid use are the requirements for multiple daily doses and adverse effects on bowel habits: constipation with aluminum-containing products and diarrhea with magnesium.

CONCLUSION — Taking a proton pump inhibitor can prevent aspirin- or NSAID-associated ulcers detected on endoscopy. To what extent it prevents clinical symptoms or bleeding remains to be determined. □

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 ISSN 1523-2859