

Gastro Intestinal Drugs

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OVERVIEW

- common medical conditions involving the gastrointestinal tract:
 1. Peptic ulcers.
 2. Control of chemotherapy-induced emesis.
 3. Diarrhea and constipation.

Drugs used to treat peptic ulcer disease

- pathogenesis of peptic ulcer disease:
 1. infection with gram-negative *Helicobacter Pylori*.
 2. increased hydrochloric acid secretion.
 3. inadequate mucosal defense against gastric acid.

Treatment approaches in peptic ulcer disease

- (1) eradicating *H. Pylori* infection.
- (2) reducing secretion of gastric acid or neutralizing the acid after it is released.
- (3) providing agents that protect the gastric mucosa from damage.

Antimicrobial agents

- Optimal therapy of patients with peptic ulcer disease (both duodenal and gastric ulcers) who are infected with *H Pylori*. □ requires antimicrobial treatment.
- To document infection with *H Pylori*. □ endoscopic biopsy of the gastric mucosa or various noninvasive methods are available, including
 - serologic tests and
 - breath tests for urea.

Antimicrobial agents

- Eradication of *H. Pylori* results produce rapid healing of active peptic ulcers and low recurrence rates (less than 15% compared to 60 to 100% per year for patients compared with initial ulcers healed by traditional antisecretory therapy). Successful eradication of *H. pylori* (80 to 90%) is possible with various combinations of antimicrobial drugs.

Antimicrobial agents

- two-week course of triple therapy with bismuth, metronidazole and tetracycline (about 90% eradication rate).
- combinations of two antimicrobial agents (metronidazole, amoxicillin or clarithromycin) with an antisecretory agent (preferably omeprazole)(second line).
- Treatment with a single antimicrobial drug is less effective (20 to 40% eradication rates).

Regulation of gastric acid secretion

- Gastric acid secretion by parietal cells of the gastric mucosa is controlled by:
 1. acetylcholine.
 2. histamine.
 3. prostaglandins E_2 and I_2 .
 4. gastrin.

DRUGS USED IN PEPTIC ULCER THERAPY

- **The cause of PU is thought to be related to mucosal exposure to gastric acid & pepsin with very strong association with helicobacter pylori infection.**

Proton pump inhibitors

- Are drugs that inhibit H ions, K ions activated adenosine triphosphate in gastric cell , the final common pathway for acid secretion , it include:
- 1- esomeprazole
- 2-lansoprazole
- 3-omeprazole
- 4-pantoprazole
- 5-rabeprazole
- side effects:
- Headache , diarrhea , nausea

H2 – receptor antihistamines

- Cimetidine
- **Prolonged & high doses of it lead to antiandrogenic effects (impotence , gynecomastia)**
- **It has the ability to decrease the hepatic oxidative biotransformation of some drugs like lidocaine & diazepam**

antibiotics

- Pu disease is directly linked to infection by the gram -ve bacteria (*Helico bacter pylori*) , so routinely antibiotic therapy is added for eradication of peptic ulcer e.g. amoxicillin & clarithromycin

Gastric antacids

- Are weak base that buffer gastric hydrochloride acid , also it enhance ulcer healing by enhancing the gastric mucosal defense mechanism through the stimulation of prostaglandin production which inhibit gastric acid secretion & exert cytoprotective properties .
- Antacids have rapid onset of action & antacids suspensions dissolve more easily than tablet or powder
- Duration of action in the stomach is influenced by the gastric emptying time which slowed by food in the stomach.
- Types of antacids:
 - Sodium bicarbonate
 - Magnesium salts
 - Aluminum salts
 - calcium carbonate

prostaglandins

- Misoprostol which is synthetic PGE1 analogue , have direct cytoprotective effects on the gastric mucosa , it inhibit gastric acid secretion.
- Side effects :
- Abdominal pain
- diarrhea

Anti sialagogues

- Salivary secretion is inhibited by antimuscarinic drugs , the prototype of this class are atropine & scopolamine .
- **Side effects :**
 - 1-difficult in swallowing because of excessive dryness in mouth & throat.
 - 2-inhibition of sweating
 - 3-impairment of psychomotor activity .
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 - Other antisialagogues are synthetic anticholinergic drugs like
 - propantheline
 - glycopyrrolate

Emetics

Emergencies may arise that might be handled by an agent That induce a forceful emptying of the stomach .

If an emetic is desired , syp. of ipecac is a popular choice :

It is amixture of plant alkaloids (emetine) that act centrally On the chemoreceptor trigger zone & locally by irritation of Stomach , vomiting occure 15-30 min.

Side effects:

Diarrhea , lethargy , prolonged vomiting .

Antiemetics:

- Phenothiazine:
- Are dopamine antagonists & inhibit stimulation of chemoreceptor trigger zone , used in nausea of pregnancy , postoperative emesis, vomiting induced by chemotherapy
- Metoclopramide:
- Dopamine receptor antagonist , very useful in Rx of vomiting
- Induced by chemotherapy , it acts peripherally by stimulation
- Of Ach release & act centrally by blocking the dopamine 2 receptor in CTZ.
- **Side effects:**
- **Sedation , extra pyramidal symptoms**

Antiemetics

- **Diphenhydramine , meclizine & cyclizine:**
- **Are useful in Rx of nausea & vomiting associated with motion sickness , pregnancy & postoperative**
- **State.**
- **Note:**
- **Combination of antiemetics are more effective because of multiple sites of action & also because**
- **Of the synergistic effects of several antiemetic**
- **With different mechanism of action.**

Antidiarrheal agents

- **1-Attapulgate:** are Mg – Al silicate that allow for a large surface area that adsorb up to 8 times its weight in water .
- **2-Opioids :**e.g. codeine which inhibit propulsive contraction of GIT muscles
- **3-Loperamide:** is long acting derivative act on opioid receptors (centrally & peripherally) so alter the motor function in intestine .
- **Side effects of loperamide:**
- **Abdominal pain , nausea , vomiting , dry mouth , dizziness.**

Laxatives:

- Are used to relieve acute & chronic constipation , Rx of
- Hemorrhoids & prepare the bowl for examination (colon scopy)
- TYPES
- 1-stimulants: are local irritant of intestinal mucosa that increase propulsive activity or they may increase motility.
e.g. castor oil , bisacodyl
- 2- lubricants:e.g.docusate sodium & docusate calcium act like detergent & are used to soften the stool
- 3- saline cathartics are salt solution that are poorly absorbed from GIT e.g. Mg salts , Na salts
- Salt solutions osmotically increase water content of feces & fluid in intestinal lumen which will increase intra luminal pressure & exert a mechanical force to stimulate peristalsis
- 4- bulk forming agents : those include polycarbophil & other natural & semi synthetic cellulose derivatives , they absorb water & expand there by increase the bulk of intestinal contents which stimulate peristalsis .

General adverse reactions of GIT to drugs

- **1- opioid analgesics : constipation , nausea , vomiting.**
- **2- aspirin : gastric distress , fecal blood loss , ulceration**
- **3-sedative hypnotics : gastric irritation**
- **4-antibiotics: nausea , diarrhea**