Pharmacology

Theoretical

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**L.6**

 **Gastrointestinal and Antiemetic Drugs**

Drugs Used to Treat Peptic Ulcer Disease …………..

* ***several major causative factors are recognized***:
* nonsteroidal anti-inflammatory drug (NSAID) use,
* infection with gram-negative Helicobacter pylori,
* increased hydrochloric acid secretion,
* and inadequate mucosal defense against gastric acid.

----- types of drugs used : -----------

* ***1. Antimicrobial agents***
* Optimal therapy for 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 utilized,
* Eradication of H. pylori results in rapid healing of active peptic ulcers and low recurrence rates

Use of triple therapy to treat H. pylori which consisting of

 **Proton Pump Inhibitors (PPI)**

 **Omeprazole**

 **+**

 ***metronidazole* or *amoxicillin***

 ***+***

 ***Clarithromycin***

* 2-week course.

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* ***2. H2-receptor antagonists***
* antagonists of the histamine **H2** receptor block the actions of histamine at all H2 receptors, their chief clinical use is to inhibit gastric acid secretion, example

 ***Cimetidine***

* given orally, distribute widely throughout the body (including into breast milk and across the placenta), *Cimetidine* inhibits cytochrome ***P450*** and can slow metabolism

***Ranitidine*** *:*longer acting and is 5- 10 more potent than *Cimetidine .* it does not inhibitP450 and, thus, does not affect the concentrations of other drugs

* ***3.Inhibitors of the H+/K+-ATPase proton pump***
* *Omeprazole* is the first of a class of drugs that bind to the H+/K+-ATPase enzyme system (proton pump) of the parietal cell, thereby suppressing secretion of hydrogen ions into the gastric lumen.
* *Omeprazole* inhibits the metabolism of *warfarin, phenytoin, diazepam*, and *cyclosporine*. However, drug interactions are not a problem with the other PPIs.
1. ***Antacids***
* Antacids are weak bases that react with gastric acid to form water and a salt, thereby diminishing gastric acidity. Because pepsin is inactive at a pH greater than 4, antacids also reduce pepsin activity.
* Commonly used antacids are salts of **aluminum** and **magnesium**, such as *aluminum hydroxide* or *magnesium hydroxide* either alone or in combination. And ***sodium bicarbonate*** [NaHCO3]

***5.Mucosal protective agents***

* These compounds, known as cytoprotective compounds, have several actions that enhance mucosal protection mechanisms, thereby preventing mucosal injury, reducing inflammation, and healing existing ulcers.
* **Sucralfate :** This complex of *aluminum hydroxide* and sulfated sucrose binds to positively charged groups in proteins of both normal and necrotic mucosa.

 By forming complex gels with epithelial cells, *sucralfate* creates a physical barrier that impairs diffusion of HCl and prevents degradation of mucus by pepsin and acid.

***Antiemetic drugs***

* An **antiemetic** is a drug  that is effective against vomiting and nausea .
* Antiemetics are typically used to treat motion sickness and the side effects of opioid analgesics, general anaesthetics, and chemotherapy directed against cancer.
* Antiemetics are also used for morning sickness,

Types of antiemetics

1. 5-HT3 receptor antagonists

 these block serotonin receptors in the central nervous system and gastrointestinal tract. As such, they can be used to treat post-operative and cytotoxic drug nausea & vomiting. However, they can also cause constipation or diarrhea, dry mouth, and fatigue

 **Ondansetron** (**Zofran**)

1. Dopamine antagonists

 act in the brain and are used to treat nausea and vomiting

Prochlorperazine (**Stemetil**)

Metoclopramide  ( plasil )

1. Antihistamines (H1 histamine receptor antagonists)

 effective in many conditions, including motion sickness, morning sickness in pregnancy,

Cyclizine

1. Anticholinergics

Hyoscine (also known as scopolamine)

**Antidiarrheals**

* Increased motility of the gastrointestinal tract and decreased absorption of fluid are major factors in diarrhea.
* Antidiarrheal drugs include antimotility agents, adsorbents, and drugs that modify fluid and electrolyte transport
* ***A. Antimotility agents***
* opioid-like actions
* *diphenoxylate* and *loperamide*
* activating presynaptic opioid receptors in the enteric nervous system to inhibit acetylcholine release and decrease peristalsis.
* they lack analgesic effects.
* Side effects include drowsiness, abdominal cramps, and dizziness.
* ***B. Adsorbents***
* Adsorbent agents, such as *bismuth subsalicylate, methylcellulose* and *aluminum hydroxide* are used to control diarrhea.
* these agents act by adsorbing intestinal toxins or microorganisms and/or by coating or protecting the intestinal mucosa.
* They are much less effective than antimotility agents.
* They can interfere with the absorption of other drugs.
* ***C. Agents that modify fluid and electrolyte transport***
* *Bismuth subsalicylate*, used for traveler's diarrhea, decreases fluid secretion in the bowel.
* Its action may be due to its salicylate component as well as its coating action.

**Laxatives**

* Laxatives are commonly used to accelerate the movement of food through the gastrointestinal tract.
* They all have a risk of being habit-forming.
* increase the loss of pharmacologic effect of poorly absorbed, delayed-acting, and extended-release oral preparations by accelerating their transit through the intestines.
* They may cause electrolyte imbalances when used chronically.
* ***A. Irritants and stimulants***
* *Senna* is a widely used stimulant laxative. Its active ingredient is a group of sennosides, a natural complex of anthraquinone glycosides. it causes evacuation of the bowels within 8 to 10 hours. causes water and electrolyte secretion into the bowel.
* *Bisacodyl is* potent stimulant of the colon. tly on nerve fibers in the mucosa
* *Castor oil* is broken down in the small intestine to ricinoleic acid, which is very irritating to the gut, and increases peristalsis.
* ***B. Bulk laxatives***
* hydrophilic colloids
* They form gels in the large intestine, causing water retention and intestinal distension, thereby increasing peristaltic activity.
* *Bran*
* ***C. Saline and osmotic laxatives***
* Saline cathartics, such as *magnesium citrate, magnesium sulfate,*
* are nonabsorbable salts (anions and cations) that hold water in the intestine by osmosis and distend the bowel, increasing intestinal activity and producing defecation in a few hours.
* Electrolyte solutions containing *polyethylene glycol* (PEG) are used as colonic lavage solutions to prepare the gut for radiologic or endoscopic procedures.