Pharmacology

Theoretical

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**L.5**

**Calcium-Channel Blockers -----------------**

* Calcium channel blockers block voltage gated calcium channels and inhibits the influx of calcium ions into cardiac and smooth muscle cells. The decrease in intracellular calcium reduces the strength of heart muscle contraction, reduces conduction of impulses in the heart, and causes vasodilatation
* ***Therapeutic uses***
* Calcium-channel blockers have an intrinsic natriuretic effect and, therefore, do not usually require the addition of a diuretic.
* These agents are useful in the treatment of hypertensive patients who also have asthma, diabetes, angina, and/or peripheral vascular disease .
* ***Adverse effects***

Constipation occurs in 10 percent of patients treated with *verapamil*. Other example

* **Nifedipine**
* **Diltiazem**

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**Antiarrhythmic**

* The arrhythmias are simple dysfunctions cause abnormalities in impulse formation and conduction in the myocardium.
* For example, cardiac arrhythmias may cause the heart to beat too slowly (**bradycardia**) or to beat too rapidly (**tachycardia**), and to beat regularly (sinus tachycardia or sinus bradycardia) or irregularly (atrial fibrillation).
* **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.
* ***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.