CHAPTER 49

Acid-Controlling Agents

NDEG 26 A
Pharmacology I
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Types of Acid-Controlling Agents

- Antacids
- H_2 antagonists
- Proton pump inhibitors

Acid-Related Pathophysiology

The stomach secretes:

- Hydrochloric acid (HCl)
- Bicarbonate
- Pepsinogen
- Intrinsic factor
- Mucus
- Prostaglandins

Glands of the Stomach

- Cardiac
- Pyloric
- Gastric*

* The cells of the gastric gland are the largest in number and of primary importance when discussing acid control

Cells of the Gastric Gland

- Parietal
- Chief
- Mucoid
- Endocrine
- Enterochromaffin

Cells of the Gastric Gland (cont'd)

Parietal cells

- Produce and secrete HCl
- Primary site of action for many acid-controller drugs

Cells of the Gastric Gland (cont'd)

Chief cells

- Secrete pepsinogen, a proenzyme
- Pepsinogen becomes *pepsin* when activated by exposure to acid
- Pepsin breaks down proteins (proteolytic)

Cells of the Gastric Gland (cont'd)

Mucoid cells

- Mucus-secreting cells (surface epithelial cells)
- Provide a protective mucous coat
- Protect against self-digestion by HCl

Hydrochloric Acid

- Secreted by the parietal cells when stimulated by food
- Maintains stomach at pH of 1 to 4
- Secretion also stimulated by:
  - Large fatty meals
  - Excessive amounts of alcohol
  - Emotional stress

Acid-Related Diseases

- Caused by imbalance of the three cells of the gastric gland and their secretions
- Most common: hyperacidity
- Lay terms for overproduction of HCl by the parietal cells
  - indigestion, sour stomach, heartburn, acid stomach

Acid-Related Diseases (cont'd)

- PUD: peptic ulcer disease
- GERD: gastroesophageal reflux disease
- *Helicobacter pylori (H. pylori)*
  - Bacterium found in GI tract of 90% of patients with duodenal ulcers, and 70% of those with gastric ulcers
  - Antibiotics are used to eradicate *H. pylori* (tetracycline)

Antacids: Mechanism of Action

Promote gastric mucosal defense mechanisms

- Secretion of:
  - Mucus: protective barrier against HCl
  - Bicarbonate: helps buffer acidic properties of HCl
  - Prostaglandins: prevent activation of proton pump

Antacids: Mechanism of Action (cont'd)

- Antacids DO NOT prevent the overproduction of acid
- Antacids DO neutralize the acid once it's in the stomach

Antacids: Drug Effects

Reduction of pain associated with acid-related disorders

- Raising gastric pH from 1.3 to 1.6 neutralizes 50% of the gastric acid
- Raising gastric pH 1 point (1.3 to 2.3) neutralizes 90% of the gastric acid
- Reducing acidity reduces pain

Antacids

- OTC formulations available as:
  - Capsules and tablets
  - Powders
  - Chewable tablets
  - Suspensions
  - Effervescent granules and tablets

Antacids (cont'd)

Used alone or in combination

- Aluminum salts
- Magnesium salts
- Calcium salts
- Sodium bicarbonate

Antacids: Aluminum Salts

- Forms: carbonate, hydroxide
- Have constipating effects
- Often used with magnesium to counteract constipation
- Examples
  - Aluminum carbonate: Basaljel
  - Hydroxide salt: AlternaGEL
  - Combination products (aluminum and magnesium): Gaviscon, Maalox, Mylanta, Di-Gel

Antacids: Magnesium Salts

- Forms: carbonate, hydroxide, oxide, trisilicate
- Commonly cause diarrhea; usually used with other agents to counteract this effect
- Dangerous when used with renal failure—the failing kidney cannot excrete extra magnesium, resulting in accumulation

Antacids: Magnesium Salts (cont'd)

- Examples
  - Hydroxide salt: magnesium hydroxide (MOM)
  - Carbonate salt: Gaviscon (also a combination product)
  - Combination products such as Maalox, Mylanta (aluminum and magnesium)

Antacids: Calcium Salts

Forms: many, but carbonate is most common

- May cause constipation
- Their use may result in kidney stones
- Long duration of acid action may cause increased gastric acid secretion (hyperacidity rebound)
- Often advertised as an extra source of dietary calcium
  - Example: Tums (calcium carbonate)

Antacids: Sodium Bicarbonate

- Highly soluble
- Buffers the acidic properties of HCl
- Quick onset, but short duration
- May cause metabolic alkalosis
- Sodium content may cause problems in patients with HF, hypertension, or renal insufficiency

Antacids and Antiflatulents

- Antiflatulents: used to relieve the painful symptoms associated with gas
- Several agents are used to bind or alter intestinal gas and are often added to antacid combination products

Antacids and Antiflatulents (cont'd)

OTC antiflatulents

- Activated charcoal
- Simethicone
  - Alters elasticity of mucus-coated bubbles, causing them to break
  - Used often, but there are limited data to support effectiveness

Antacids: Side Effects

Minimal, and depend on the compound used

- Aluminum and calcium
  - Constipation
- Magnesium
  - Diarrhea
- Calcium carbonate
  - Produces gas and belching; often combined with simethicone

Antacids: Drug Interactions

- Adsorption of other drugs to antacids
  - Reduces the ability of the other drug to be absorbed into the body
- Chelation
  - Chemical binding, or inactivation, of another drug
  - Produces insoluble complexes
  - Result: reduced drug absorption

Antacids: Drug Interactions (cont'd)

Increased stomach pH

- Increased absorption of basic drugs
- Decreased absorption of acidic drugs

Increased urinary pH

- Increased excretion of acidic drugs
- Decreased excretion of basic drugs

Antacids: Nursing Implications

- Assess for allergies and preexisting conditions that may restrict the use of antacids, such as:
  - Fluid imbalances
  - Renal disease
  - HF
  - Pregnancy
  - GI obstruction
- Patients with HF or hypertension should use low-sodium antacids such as Riopan, Maalox, or Mylanta II

Antacids: Nursing Implications

- Use with caution with other medications due to the many drug interactions
- Most medications should be given 1 to 2 hours after giving an antacid
- Antacids may cause premature dissolving of enteric-coated medications, resulting in stomach upset

Antacids: Nursing Implications

- Be sure that chewable tablets are chewed thoroughly, and liquid forms are shaken well before giving
- Administer with at least 8 ounces of water to enhance absorption (except for the “rapid dissolve” forms)
- Caffeine, alcohol, harsh spices, and black pepper may aggravate the underlying GI condition

Antacids: Nursing Implications

- Monitor for side effects
  - Nausea, vomiting, abdominal pain, diarrhea
  - With calcium-containing products: constipation, acid rebound
- Monitor for therapeutic response
  - Notify heath care provider if symptoms are not relieved

Histamine Type 2 (H_2) Antagonists

- Reduce acid secretion
- All available OTC in lower dosage forms
- Most popular drugs for treatment of acid-related disorders
  - cimetidine (Tagamet)
  - famotidine (Pepcid)
  - ranitidine (Zantac)
  - nizatidine

H_2 Antagonists: Mechanism of Action

- Block histamine (H_2) at the receptors of acid-producing parietal cells
- Production of hydrogen ions is reduced, resulting in decreased production of HCl

H_2 Antagonists: Drug Effect

Suppressed acid secretion in the stomach

H_2 Antagonists: Indications

- GERD
- PUD
- Erosive esophagitis
- Adjunct therapy in control of upper GI bleeding
- Pathologic gastric hypersecretory conditions

H_2 Antagonists: Side Effects

- Overall, less than 3% incidence of side effects
- Cimetidine may induce impotence and gynecomastia
- May see:
  - Headaches, lethargy, confusion, diarrhea, urticaria, sweating, flushing, other effects

H_2 Antagonists: Drug Interactions

- cimetidine
  - Binds with P-450 microsomal oxidase system in the liver, resulting in inhibited oxidation of many drugs and increased drug levels
  - All H_2 antagonists may inhibit the absorption of drugs that require an acidic GI environment for absorption

H_2 Antagonists: Drug Interactions (cont'd)

SMOKING has been shown to decrease the effectiveness of H_2 blockers

H_2 Antagonists: Nursing Implications

- Assess for allergies and impaired renal or liver function
- Use with caution in patients who are confused, disoriented, or elderly
- Take 1 hour before or after antacids
- For intravenous doses, follow administration guidelines

Proton Pump

- The parietal cells release positive hydrogen ions (protons) during HCl production
- This process is called the “proton pump”
- H_2 blockers and antihistamines do not stop the action of this pump

Proton Pump Inhibitors: Mechanism of Action

- Irreversibly bind to H^+/K^+ ATPase enzyme
- This bond prevents the movement of hydrogen ions from the parietal cell into the stomach
- Result: achlorhydria—ALL gastric acid secretion is blocked
  - In order to return to normal acid secretion, the parietal cell must synthesize new H^+/K^+ ATPase

Proton Pump Inhibitors: Drug Effect

- Total inhibition of gastric acid secretion
  - lansoprazole (Prevacid)
  - omeprazole (Prilosec)*
  - rabeprazole (Aciphex)
  - pantoprazole (Protonix)
  - esomeprazole (Nexium)

*The first in this new class of drugs

Proton Pump Inhibitors: Indications

- GERD maintenance therapy
- Erosive esophagitis
- Short-term treatment of active duodenal and benign gastric ulcers
- Zollinger-Ellison syndrome
- Treatment of *H. pylori*–induced ulcers

Proton Pump Inhibitors: Side Effects

- Safe for short-term therapy
- Incidence low and uncommon

Proton Pump Inhibitors: Nursing Implications

- Assess for allergies and history of liver disease
- pantoprazole is the only proton pump inhibitor available for parenteral administration, and can be used for patients who are unable to take oral medications
- May increase serum levels of diazepam, phenytoin, and cause increased chance for bleeding with warfarin

Proton Pump Inhibitors: Nursing Implications

Instruct the patient taking omeprazole:

- It should be taken before meals
- The capsule should be swallowed whole, not crushed, opened, or chewed
- It may be given with antacids
- Emphasize that the treatment will be short term

Other Drugs

- sucralfate (Carafate)
- misoprostol (Cytotec)

sucralfate (Carafate)

- Cytoprotective agent
- Used for stress ulcers, erosions, PUD
- Attracted to and binds to the base of ulcers and erosions, forming a protective barrier over these areas
- Protects these areas from pepsin, which normally breaks down proteins (making ulcers worse)

sucralfate (Carafate) (cont'd)

- Little absorption from the gut
- May cause constipation, nausea, and dry mouth
- May impair absorption of other drugs, especially tetracycline
- Binds with phosphate; may be used in chronic renal failure to reduce phosphate levels
- Do not administer with other medications

misoprostol (Cytotec)

- Synthetic prostaglandin analog
- Prostaglandins have cytoprotective activity
  - Protect gastric mucosa from injury by enhancing local production of mucus or bicarbonate
  - Promote local cell regeneration
  - Help to maintain mucosal blood flow

misoprostol (Cytotec) (cont'd)

- Used for prevention of NSAID-induced gastric ulcers
- Doses that are therapeutic enough to treat duodenal ulcers often produce abdominal cramps, diarrhea

CHAPTER 50

Antidiarrheals and Laxatives

Diarrhea

- Abnormal frequent passage of loose stools

  or
- Abnormal passage of stools with increased frequency, fluidity, and weight, or with increased stool water excretion

Diarrhea (cont'd)

Acute diarrhea

- Sudden onset in a previously healthy person
- Lasts from 3 days to 2 weeks
- Self-limiting
- Resolves without sequelae

Diarrhea (cont'd)

Chronic diarrhea

- Lasts for more than 3 weeks
- Associated with recurring passage of diarrheal stools, fever, loss of appetite, nausea, vomiting, weight loss, and chronic weakness

Causes of Diarrhea

Acute Diarrhea	Chronic Diarrhea
Bacterial	Tumors
Viral	Diabetes
Drug induced	Addison's disease
Nutritional	Hyperthyroidism
Protozoal	Irritable bowel syndrome

Antidiarrheals: Mechanism of Action

Adsorbents

- Coat the walls of the GI tract
- Bind to the causative bacteria or toxin, which is then eliminated through the stool
- Examples: bismuth subsalicylate (Pepto-Bismol), kaolin-pectin, activated charcoal, attapulgite (Kaopectate)

Antidiarrheals: Mechanism of Action (cont'd)

Anticholinergics

- Decrease intestinal muscle tone and peristalsis of GI tract
- Result: slowing the movement of fecal matter through the GI tract
- Examples: belladonna alkaloids (Donnatal), atropine, hyoscyamine

Antidiarrheals: Mechanism of Action (cont'd)

Intestinal flora modifiers

- Bacterial cultures of *Lactobacillus* organisms work by:
  - Supplying missing bacteria to the GI tract
  - Suppressing the growth of diarrhea-causing bacteria
- Example: *L. acidophilus* (Lactinex)

Antidiarrheals: Mechanism of Action (cont'd)

Opiates

- Decrease bowel motility and relieve rectal spasms
- Decrease transit time through the bowel, allowing more time for water and electrolytes to be absorbed
- Examples: paregoric, opium tincture, codeine, loperamide, diphenoxylate

Antidiarrheal Agents: Side Effects

Adsorbents

- Increased bleeding time
- Constipation, dark stools
- Confusion, twitching
- Hearing loss, tinnitus, metallic taste, blue gums

Antidiarrheal Agents: Side Effects (cont'd)

Anticholinergics

- Urinary retention, hesitancy, impotence
- Headache, dizziness, confusion, anxiety, drowsiness
- Dry skin, rash, flushing
- Blurred vision, photophobia, increased intraocular pressure
- Hypotension, hypertension, bradycardia, tachycardia

Antidiarrheal Agents: Side Effects (cont'd)

Opiates

- Drowsiness, sedation, dizziness, lethargy
- Nausea, vomiting, anorexia, constipation
- Respiratory depression
- Bradycardia, palpitations, hypotension
- Urinary retention
- Flushing, rash, urticaria

Antidiarrheal Agents: Interactions

- Adsorbents decrease the absorption of many agents, including digoxin, clindamycin, quinidine, and hypoglycemic agents
- Adsorbents cause increased bleeding time when given with anticoagulants
- Antacids can decrease effects of anticholinergic antidiarrheal agents

Antidiarrheal Agents: Nursing Implications

- Obtain thorough history of bowel patterns, general state of health, and recent history of illness or dietary changes, and assess for allergies
- DO NOT give bismuth subsalicylate to children younger than age 16 or teenagers with chickenpox because of the risk of Reye's syndrome

Antidiarrheal Agents: Nursing Implications

- Use adsorbents carefully in geriatric patients or those with decreased bleeding time, clotting disorders, recent bowel surgery, confusion
- Anticholinergics should not be administered to patients with a history of glaucoma, BPH, urinary retention, recent bladder surgery, cardiac problems, myasthenia gravis

Antidiarrheal Agents: Nursing Implications

- Teach patients to take medications exactly as prescribed and to be aware of their fluid intake and dietary changes
- Assess fluid volume status, I&O, and mucous membranes before, during, and after initiation of treatment

Antidiarrheal Agents: Nursing Implications

- Teach patients to notify their physician immediately if symptoms persist
- Monitor for therapeutic effect

Laxatives

Constipation

- Abnormally infrequent and difficult passage of feces through the lower GI tract
- Symptom, not a disease
- Disorder of movement through the colon and/or rectum
- Can be caused by a variety of diseases or drugs

Laxatives: Mechanism of Action

- Bulk forming
- Emollient
- Hyperosmotic
- Saline
- Stimulant

Laxatives: Mechanism of Action (cont'd)

Bulk forming

- High fiber
- Absorbs water to increase bulk
- Distends bowel to initiate reflex bowel activity
- Examples:
  - psyllium (Metamucil)
  - methylcellulose (Citrucel)
  - polycarbophil

Laxatives: Mechanism of Action (cont'd)

Emollient

- Stool softeners and lubricants
- Promote more water and fat in the stools
- Lubricate the fecal material and intestinal walls
- Examples:
  - Stool softeners: docusate salts (Colace, Surfak)
  - Lubricants: mineral oil

Laxatives: Mechanism of Action (cont'd)

Hyperosmotic

- Increase fecal water content
- Result: bowel distention, increased peristalsis, and evacuation
- Examples:
  - polyethylene glycol (GoLYTELY)
  - sorbitol
  - glycerin
  - lactulose (Chronulac)

Laxatives: Mechanism of Action (cont'd)

Saline

- Increase osmotic pressure within the intestinal tract, causing more water to enter the intestines
- Result: bowel distention, increased peristalsis, and evacuation

Laxatives: Mechanism of Action (cont'd)

- Saline laxative examples:
  - magnesium sulfate (Epsom salts)
  - magnesium hydroxide (MOM)
  - magnesium citrate
  - sodium phosphate (Fleet Phospho-Soda, Fleet enema)

Laxatives: Mechanism of Action (cont'd)

Stimulant

- Increases peristalsis via intestinal nerve stimulation
- Examples:
  - castor oil
  - senna
  - cascara
  - bisacodyl

Laxatives: Indications

Laxative Group	Use
Bulk forming	Acute and chronic constipation
	Irritable bowel syndrome
	Diverticulosis
Emollient	Acute and chronic constipation
	Softening of fecal impaction; facilitation of BMs in anorectal conditions

Laxatives: Indications (cont'd)

Laxative Group	Use
Hyperosmotic	Chronic constipation
	Diagnostic and surgical preps
Saline	Constipation
	Diagnostic and surgical preps
	Removal of helminths and parasites

Laxatives: Indications (cont'd)

Laxative Group	Use
Stimulant	Acute constipation
	Diagnostic and surgical bowel preps

Laxatives: Side Effects

- Bulk forming
  - Impaction
  - Fluid overload
- Emollient
  - Skin rashes
  - Decreased absorption of vitamins
- Hyperosmotic
  - Abdominal bloating
  - Rectal irritation

Laxatives: Side Effects (cont'd)

- Saline
  - Magnesium toxicity (with renal insufficiency)
  - Cramping
  - Diarrhea
  - Increased thirst
- Stimulant
  - Nutrient malabsorption
  - Skin rashes
  - Gastric irritation
  - Rectal irritation

Laxatives: Side Effects (cont'd)

All laxatives can cause electrolyte imbalances!

Laxatives: Nursing Implications

- Obtain a thorough history of presenting symptoms, elimination patterns, and allergies
- Assess fluid and electrolytes before initiating therapy
- Patients should not take a laxative or cathartic if they are experiencing nausea, vomiting, and/or abdominal pain

Laxatives: Nursing Implications

- A healthy, high-fiber diet and increased fluid intake should be encouraged as an alternative to laxative use
- Long-term use of laxatives often results in decreased bowel tone and may lead to dependency
- All laxative tablets should be swallowed whole, not crushed or chewed, especially if enteric coated

Laxatives: Nursing Implications

- Patients should take all laxative tablets with 6 to 8 ounces of water
- Patients should take bulk-forming laxatives as directed by the manufacturer with at least 240 mL (8 ounces) of water

Laxatives: Nursing Implications

- Bisacodyl and cascara sagrada should be given with water due to interactions with milk, antacids, and H_2 blockers
- Patients should contact their physician if they experience severe abdominal pain, muscle weakness, cramps, and/or dizziness, which may indicate possible fluid or electrolyte loss

Laxatives: Nursing Implications

- Monitor for therapeutic effect

CHAPTER 51

Antiemetic and Antinausea Agents

Definitions

- Nausea
  - Unpleasant feeling that often precedes vomiting
- Emesis (vomiting)
  - Forcible emptying of gastric, and occasionally, intestinal contents
- Antiemetic agents
  - Used to relieve nausea and vomiting

VC and CTZ

- Vomiting center (VC)
- Chemoreceptor trigger zone (CTZ)
  - Both located in the brain
  - Once stimulated, cause the vomiting reflex

TABLE 51-1
NEUROTRANSMITTERS INVOLVED IN NAUSEA AND VOMITING

Neurotransmitter	Site in the Vomiting Pathway
Acetylcholine (ACh)	VC in brain; vestibular and labyrinth pathways in inner ear
Dopamine (D2)	GI tract and CTZ in brain
Histamine (H_1)	VC in brain; vestibular and labyrinth pathways in inner ear
Prostaglandins (PGs)	GI tract
Serotonin (5-HT3)	GI tract; CTZ and VC in brain

VC, Vomiting center; *GI,* gastrointestinal; *CTZ,* chemoreceptor trigger zone.

Table 51-1 Neurotransmitters involved in nausea and vomiting

Mechanism of Action

- Many different mechanisms of action
- Most work by blocking one of the vomiting pathways, thus blocking the stimulus that induces vomiting

Indications

- Specific indications vary per class of antiemetics
- General use: prevention and reduction of nausea and vomiting

Mechanism of Action and Indications

- Anticholinergic agents (ACh blockers)
  - Bind to and block acetylcholine (ACh) receptors in the inner ear labyrinth
  - Block transmission of nauseating stimuli to CTZ
  - Also block transmission of nauseating stimuli from the reticular formation to the VC
  - scopolamine
  - Also used for motion sickness

Mechanism of Action

Antihistamine agents (H_1 receptor blockers)
- Inhibit ACh by binding to H_1 receptors
- Prevent cholinergic stimulation in vestibular and reticular areas, thus preventing N&V
- dimenhydrinate, diphenhydramine, meclizine, promethazine
- Also used for nonproductive cough, allergy symptoms, sedation

Mechanism of Action (cont'd)

Neuroleptic agents
- Block dopamine receptors on the CTZ
- chlorpromazine, perphenazine, trifluprom azine
- Also used for psychotic disorders, intractable hiccups

Mechanism of Action (cont'd)

Prokinetic agents
- Block dopamine in the CTZ
- Cause CTZ to be desensitized to impulses it receives from the GI tract
- Also stimulate peristalsis in GI tract, enhancing emptying of stomach contents
- metoclopramide, cisapride
- Also used for GERD, delayed gastric emptying

Mechanism of Action (cont'd)

Serotonin blockers
- Block serotonin receptors in the GI tract, CTZ, and VC
- dolasetron, granisetron, ondansetron
- Used for N&V for patients receiving chemotherapy and postoperative nausea and vomiting

Mechanism of Action (cont'd)

Tetrahydrocannabinoids
- Major psychoactive substance in marijuana
- Inhibitory effects on reticular formation, thalamus, cerebral cortex
- Alter mood and body's perception of its surroundings

Mechanism of Action (cont'd)

Tetrahydrocannabinoids (cont'd)
- dronabinol (Marinol)
- Used for N&V associated with chemotherapy, and anorexia associated with weight loss in AIDS patients

Side Effects

- Vary according to agent used
- Stem from their nonselective blockade of various receptors

Nursing Implications

- Assess complete nausea and vomiting history, including precipitating factors
- Assess current medications
- Assess for contraindications and potential drug interactions

Nursing Implications

- Many of these agents cause severe drowsiness; warn patients about driving or performing any hazardous tasks
- Taking antiemetics with alcohol may cause severe CNS depression
- Teach patients to change position slowly to avoid hypotensive effects

Nursing Implications

- For chemotherapy, antiemetics are often given ½ to 3 hours before a chemotherapy agent
- Monitor for therapeutic effects
- Monitor for adverse effects