Inorganic pharmaceutical chemistry

Gastrointestinal Agents: acidifying agents- antacid-

Lecture five

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Gastrointestinal agents

- Inorganic agents used to treat gastrointestinal disorders include:

1. Products for altering gastric PH.
2. Protectives for intestinal inflammation.
3. Adsorbents for intestinal toxins.
4. Cathartic or laxative for constipation.

- Most of GI agents do not require a prescription which places the responsibility directly on the pharmacist.

Acidifying Agents

- Achlorhydria is the absence of hydrochloric acid in the gastric secretions.
- Patients with this condition fall into one of two groups:

  (1)Those who remain free of gastric hydrochloric acid after stimulation with histamine phosphate.

  (2)Those in whom there is normally a lack of gastric hydrochloric acid but who respond to stimulation by histamine.

- Patients with the first type of achlorhydria include those with a subtotal gastrectomy, atrophic gastritis (chronic gastritis with atrophy of the mucous memb. and glands), carcinoma of the stomach or gastric-polyps.

- The second type, in which the patients are initially free of gastric hydrochloric acid but will secrete it upon histamine stimulation, include those with chronic alcoholism, tuberculosis, hyperthyroidism, and parasitic infestations.
- It is common in otherwise normal individuals after age 50.

- Gastric hydrochloric acid functions by killing the bacteria in ingested food and drink, softening fibrous food, and promoting formation of the proteolytic enzyme, (pepsin).
- Pepsin is formed by pepsinogen being converted to pepsin when the pH of gastric content drops below 6.
- Thus, a lack of hydrochloric acid could reasonably be expected to cause gastrointestinal disturbances.

- The symptoms of achlorhydria can vary with the associated disease, but they generally include mild diarrhea or frequent bowel movements, epigastric (upper middle portion of the abdomen) pain, and sensitivity to spicy foods.

- Because pepsin possesses its greatest proteolytic activity below pH 3.5, this usually is not considered to be a problem, since the many proteolytic enzymes in the intestinal tract are still present and fully functional.
- It is not uncommon (common) for patients with achlorhydria to have pernicious anemia due to a lack of intrinsic factor, the protein necessary to carry vitamin B_{12} across the intestinal wall.

- In an attempt to relieve the gastrointestinal symptoms caused by achlorhydria, diluted hydrochloric acid (HA) has been utilized.
- The usual 5-ml dose of Diluted HA added to 200 ml of water provides about 15 mEq of acid.

- In order to avoid exposure of dental enamel to hydrochloric acid, the use of:

1. Drinking straw laid well back on the tongue has been recommended.
2. The use of equivalent (but more expensive) products such as glutamic acid hydrochloride (Acidulin®) which is administered in capsules.

Antacids


Diovol
Plus
Pepto-
Bismol
Pepto-
Bismol
TUMS
Rolaids
Alka-
Seltzer
Gelusil
Maalox

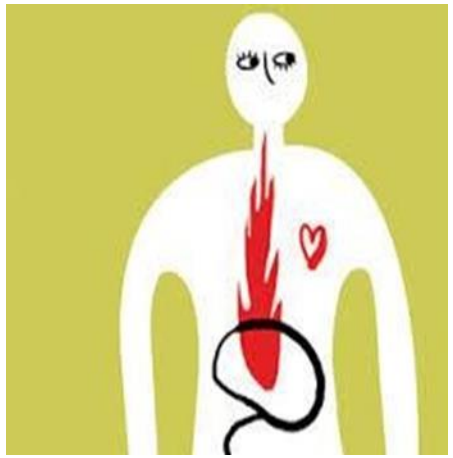
When the general public asked why it takes antacids?

the answer will include:

1.That uncomfortable feeling from overeating.

2. Heart burn.

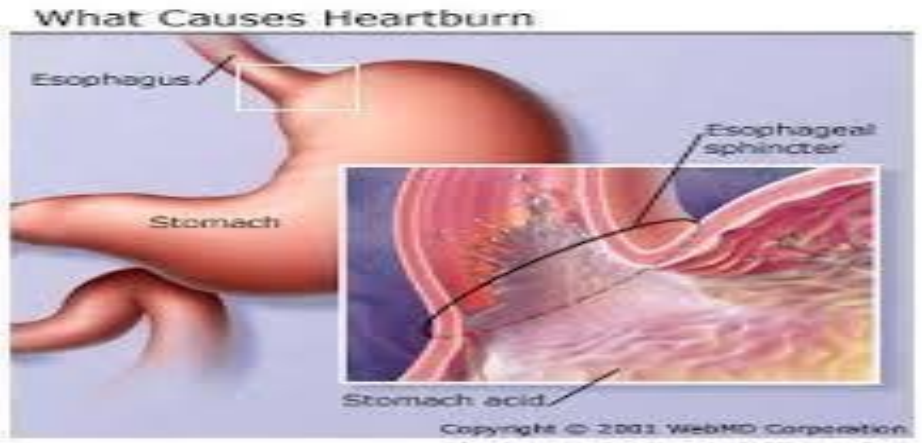
3. A growing hungry feeling between meals.



The chief indication for administering an antacid is:

1. To neutralize excess gastric hydrochloric acid which may be causing pain and possible ulceration.
2. To inactivate the proteolytic enzyme, pepsin.

Depending upon the extent of hyperacidity an anticholinergic agent may be indicated, and depending on the degree and extent of ulceration , bed rest and surgery may also be required



- The stomach pH can range from (1-7) when food is present.
- The low acid pH is due to the presence of endogenous HCl which is always present under physiologic conditions.
- When hyperacidity develops the result can range from gastritis to peptic ulcer.
- Esophageal ulcer occurs when the esophageal sphincter is defective, causing heartburn.

Antacid therapy:

- Antacids are alkaline bases used to neutralize the excess gastric HCl associated with gastritis and peptic ulcer.
- This in turn inactivates pepsin which functions optimally at low pH although some antacids may inhibit pepsin independently of the pH effects.

Antacids side effects:

1. Acid rebound which has been viewed as over titration by the parietal cells. Theoretically, if the gastric PH is raised too much, acid rebound may occur as an effort to maintain a lower pH, the stomach secrets additional HCl which consumes the antacids.

2. Sodium content of the antacid.

Those patients who are on sodium restricted diets should be advised of this when an antacids is recommended.

3. Systemic alkalosis: if the antacid is sufficiently water soluble and is composed of readily absorbable ions, the antacids may be absorbed and exert its alkaline effects on the body's buffer systems. example sodium bicarb.

4. The local effect in the GIT: antacids containing calcium and aluminum salts after being converted to soluble salts by gastric acids tend to be constipating while those containing magnesium salts tend to have a laxative effect.

- It is currently thought that antacids are effective in the reduction of pain associated with peptic ulcer, even in the absence of excessive acid through:

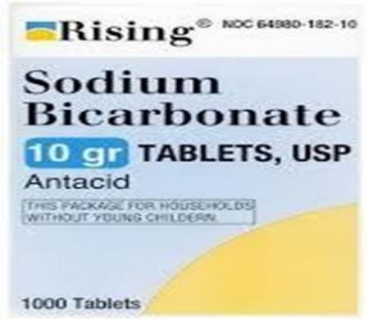
1. Increase in gastric pH and subsequent buffering.
2. An inhibition of the proteolytic action of pepsin by either adsorption by the antacid or increase of gastric pH.
3. Protective coating action on the ulcerative tissue.

- While no antacid is "ideal," there have been certain criteria that have been developed. These are:

1. The antacid should not be absorbable or cause systemic alkalosis.
2. The antacid should not be a laxative or cause constipation.
3. The antacid should exert its effect rapidly and over a long period of time.
4. The antacid should buffer in the pH 4-6 range.
5. The reaction of the antacid with gastric hydrochloric acid should not cause a large evolution of gas.
6. The antacid should probably inhibit pepsin.

Antacids products:

1. Sodium containing antacids.
2. Aluminum containing antacids.
3. Calcium containing antacids.
4. Magnesium containing antacids.



1. Sodium containing antacids.

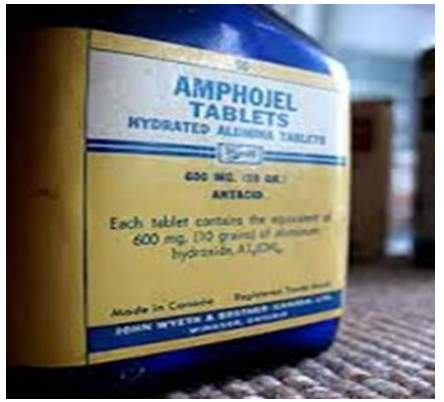
- **Sodium Bicarbonate as an antacid**
- It can cause a sharp increase in gastric pH up to or above pH 7.
- Because of the evolution of carbon dioxide in the presence of acid, sodium bicarbonate can cause belching and flatulence.
- $NaHCO_3 + HCl \longrightarrow NaCl + CO_2 + H_2O$

- It is readily absorbed, and sodium retention can result with continued use.
- Sodium bicarb. is not indicated for patients needing antacid therapy for even limited periods of time.
- It will inhibit the absorption of tetracycline from the GIT.

2. Aluminum containing antacids.

- The aluminum containing antacids are widely used.
- They are non systemic.
- buffering range in PH 3-5 region.
- They tend to be constipating because of liberation of astringent aluminum cations.

Aluminum Hydroxide



- It is recognized by the current U.S.P. in two physical forms plus one dosage forms.

(1) Aluminum hydroxide Gel (Amphogel) is a white viscous suspension, from which small amounts of clear liquid may separate on standing.

(2) Dried Aluminum Hydroxide Gel is not a typical gel but is a white odorless, tasteless amorphous powder. Also found as dried aluminum hydroxide gel tablets

- Both forms are assayed in terms of their aluminum oxide (Al_2O_3) content and their acid-consuming capacity.
- A problem with the gels is that of a loss of antacid properties on aging, this more frequent occur with the dried gel and seems to be related to the manufacturing process.

- The most acid reactive gels are those in which the conc. of a monovalent anion, such as chloride or bicarbonate, approaches 1mole per mole aluminum or those in which a bivalent anion, such as sulfate, approaches 0.5 mole per mole of aluminum.
- The aluminum hydroxide gels are non absorbable and exert little, if any, systemic effect.

Aluminum Phosphate

- Aluminum Phosphate is official as Aluminum Phosphate Gel (Phosphagel).
- It is a white, viscous suspension from which small amounts of water may separate on standing.
- It may contain suitable preservatives.

- It is assayed in terms of aluminum phosphate ($AlPO_4$) content.
- This non absorbable antacid has been used in place of aluminum hydroxide gel where loss of phosphate may be a problem to the patient.

Dihydroxyaluminum aminoacetate

It is recognized by the national formulary in two physical forms and one dosage form.

1. Dihydroxyaluminum aminoacetate.

2.Dihydroxyaluminum aminoacetate magma, it is a white viscous suspension from which small amounts of water may separate on standing, but may be readily reformed upon shaking.

- All dihydroxyaluminum aminoacetate preparations are assayed in terms of aluminum oxide content.
- Dihydroxyaluminum acetate is manufactured by reacting aluminum isopropoxide with glycine.

Dihydroxyaluminum Sodium carbonate

- It is assayed in terms of aluminum oxide.
- It is made by the reaction of aluminum isopropoxide and an aqueous solution of sodium bicarbonate.
- Potential drawbacks to this preparation would be the presence of sodium, evolution of carbon dioxide, and the usual problems associated with the aluminum antacids.

Calcium containing antacids

- They differ from the aluminum antacids in that their action is dependent upon their basic properties and not on any amphoteric effect.
- Studies show that calcium antacids raise the stomach pH to nearly 7.
- Calcium containing antacids particularly calcium carbonate are considered by some the antacids of choice.

- Uncommon serious side effect is the milk-alkali syndrome (brunett syndroum) caused by taking too much of sodium bicarbonate or calcium carbonate together with large amounts of milk.
- The calcium antacids tend to be constipating and are usually found in combination with magnesium antacids.

Calcium carbonate:

- Calcium carbonate is official as precipitated calcium carbonate.
- It is a fine white odorless, tasteless, microcrystalline powder which is stable in air.
- It is practically insoluble in water, but its solubility is increased by the presence of any ammonium salt or carbon dioxide.

- Because of its fast action, calcium carbonate is one of the most popular antacids.
- Its action is limited by the amount of salt that will go into solution thus as gastric HCl consumes the solubilized calcium carbonate more goes into solution.
- Because of calcium constipation effect, most calcium carbonate preparation will be found in combination with a magnesium antacid.

Tribasic calcium phosphate

- It is occasionally used as antacid.
- The principle of its action is that the phosphate ion reacts with the water present in stomach liberating hydroxide which then reacts with the gastric hydrochloric acid.

4. Magnesium containing antacids

- There are a large number of official antacids containing magnesium.
- With the possible exception of magnesium trisilicate, they all function in the same manner.
- They are poorly soluble salts which only go into solution as acid consumes the small amount of anion already in solution.

- The magnesium cation causes this group of antacids to be laxative for this reason, they are usually found in combination with aluminum and calcium antacids in an attempt to equalize the constipated and laxative actions.

- Although the magnesium antacids are considered non systemic and most of the magnesium is excreted in the feces as insoluble magnesium salts; Small amounts of magnesium cation may be absorbed.

- Since the absorbed magnesium is excreted by the kidneys, the magnesium-containing antacids contraindicated in patients with impaired renal function, otherwise magnesium retention can occur, leading to magnesium poisoning.

Magnesium carbonate

- Consist of a hydrated mixture of Magnesium carbonate ($MgCO_3$) and magnesium hydroxide [$Mg(OH)_2$], and is assayed in term of magnesium oxide (MgO).
- The antacid properties of magnesium carbonate are due to carbonate and hydroxide anions reacting with the gastric HCl.
- Bufferin is an antacid consist of magnesium carbonate and dihydroxyaluminium aminoacetate.

Other magnesium containing antacids:

1. Magnesium citrate solution.
2. Magnesium hydroxide.
3. Magnesium oxide.
4. Magnesium phosphate.
5. Magnesium trisilicate.

Combination antacid preparations

- Because no single antacid meets all the criteria for an ideal antacid, several products are on the market containing mixtures of antacids.
- Most of these combination products are an attempt to balance the constipative effect of calcium and aluminum with the laxative effect of magnesium.
- Some of these products are also mixture of an antacid with rapid onset of action and one with a longer duration of action.

Official antacid combinations

1. Aluminum Hydroxide Gel-Magnesium Hydroxide Combinations.
2. Aluminum Hydroxide Gel-Magnesium Trisilicate Combinations.
3. Simethicone containing antacids.

Because many people with gastric hyperacidity complain of being “gassy” the defoaming agent simethicone has been added to some antacids.

Calcium carbonate containing antacids mixtures:

- Calcium carbonate can be found in combination with aluminum hydroxide gel to yield products that have rapid onset with prolonged action.
- It can also be found with magnesium containing antacids in an attempt to balance the constipative effect of calcium with the laxative effect of magnesium.
- Three part combinations of calcium carbonate, aluminum hydroxide gel and a magnesium containing antacid are available.

Alginic acid-sodium bicarbonate containing antacid mixtures:

- This type of preparation was formulated in an attempt to provide symptomatic relief of reflux esophagitis.
- The tablet is chewed and as the contents come in contact with water the alginic acid react with sodium bicarbonate forming sodium alginate and carbon dioxide.
- The latter causes formation of foam within the solution.

- As long as the patient remains upright, the antacid contained in the foam remains near the gastroesophageal junction and suppose to be the first material passed into the esophagus when reflux of the gastric contents occurs.

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