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A review: Pharmacology of Antacids

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ABSTRACT
Acidity caused by common gastric conditions such as non-ulcer dyspepsia, duodenal ulcer, gastric ulcer, stress gastritis, gastroesophageal reflux disease (GERD), pancreatic insufficiency, bile acid-mediated diarrhoea, biliary reflux, and constipation.
Antacids are a group of drugs that have been used for many years. They were initially first-line defence against peptic ulcer disease.
Antacids are symptomatic relief from hyperacidity as well as other associated conditions by neutralizing the gastric acid directly, thereby raising the gastric pH, attenuating the pepsin activity, restoring acid-base balance, and increasing prostaglandin and bicarbonate secretion.
Antacids show therapeutic efficacy even at low dosage with less side effects, persistent increase in gastric pH, faster and longer duration of pain relief, and fast relief from gas.
This activity reviews the indications,their types with examples, mechanisms of action, pharmacodynamics, pharmacokinetics,adverse effects, drug interactions, contraindications, toxicity,, and other key elements of antacid therapy in the clinical setting as relates to the essential points needed for managing the care of patients with heartburn and mild GERD.
KEYWORDS: Antacids , Gastric pH , gastroesophageal reflux disease (GERD), Pharmacological action,, Etc.

I. INTRODUCTION

Antacids are the common class of of over-the-counter (OTC) medicines,it neutilize the acid present in the stomach, heartburn, indigestion and upset stomach.

It is the combination of various salts such as magnesium, calcium, or aluminum that provide symptomatic relief from hyperacidity and also other associated conditions by neutralizing the gastric acid directly, as a result , increase the gastric pH,reduce pepsin activity, restoring acid-base balance, and increasing the secretion of bicarbonate and prostaglandin. [1, 2]

Antacids neutralize excess hydrochloric acid (HCl) in gastric juice and inhibit the proteolytic enzyme pepsin.[3] The normal range of gastric pH of the stomach is 1.5 to 3.5. [4]

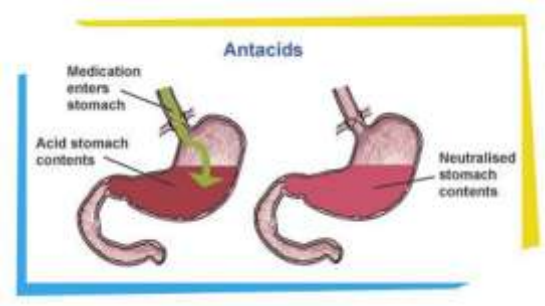

Figure 1 : antacids enter the stomach and it neutralised stomach contents.

The antacids quickly relieve occasional heartburn which is the major symptom of gastroesophageal reflux disease (GERD). It is specifically related to the reflux of gastric acid through the lower esophageal sphincter,which is a typical symptom of gastroesophageal reflux disease (GERD). [5]

The effectiveness of antacids is determined by its acid neutralizing capacity (ANC) and buffering capacity. Antacids efficiency is evaluated by their ANC which is expressed in mEq of hydrochloric acid that is neutralized by a standard dose of antacids raising the pH to approximately 3.5 during a predetermined time (usually – about 15 minutes).[6]

Antacids are also used after administration of Anaesthesia or to reduce post operational acidity and it is effective in relieving abdominal bloating .

A few studies state that some antacids can be safely used during pregnancy owing to their local action rather than systemic effects. [7, 8]

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INDICATIONS

Antacids are OTC drugs Which don't require a prescription; it is also called self-prescribed. Antacids are a combination of various compounds with various salts of calcium, magnesium, and aluminum as active ingredients. The antacids neutralizing the gastric acid in the stomach and by inhibiting pepsin, which is a proteolytic enzyme. Each of these cationic salts possess characteristic pharmacological properties that determine its clinical use.

THERAPEUTIC USES

- Heartburn symptoms in GERD
- Duodenal and gastric ulcers
- Stress gastritis
- Pancreatic insufficiency
- Non-ulcer dyspepsia
- Diarrhoea caused by bile-acid
- Biliary reflux
- Constipation
- Osteoporosis
- Urinary alkalinization
- Phosphate binding in chronic renal failure [9]

TYPES OF ANTACIDS

It has two types of antacids based on digestive absorption .

Absorbable Antacids

These are soluble, readily absorbable and capable of producing systemic electrolyte abnormalities. Properties include:

- Absorbed into the systemic circulation.[10, 11]
- Their cationic group that does not form insoluble basic compounds with a bicarbonate ion (HCO3-) hence the HCO3- can be absorbed. [10, 11]

Non-absorbable antacids

These avoid the above mentioned complications. Properties include:

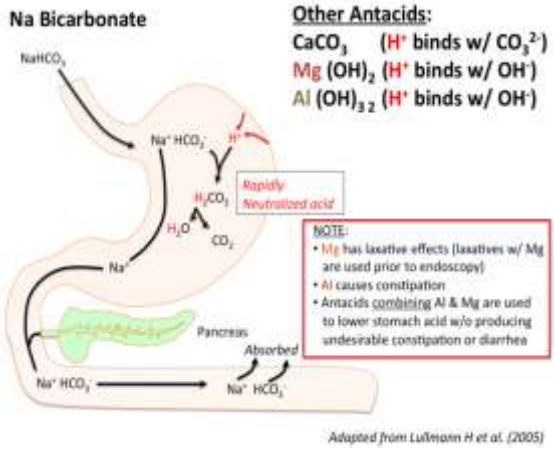
- Not absorbed into the systemic circulation.
- Their anionic group neutralises the hydrogen ions (H+) in gastric acid. This releases their cationic group which combines with HCO3- from the pancreas to form an insoluble basic compound that is excreted in faeces.
- They do not produce metabolic alkalosis.
- Accumulation of calcium (Ca2+), magnesium (Mg2+) and aluminium (Al2+). Dangerous with use in renal insufficiency with aluminium compounds being contraindicated in renal insufficiency. [10, 11,12]

Absorbable	Non-absorbable
Sodium carbonate (baking soda)	Aluminum phosphate
Magnesium oxide (magnesia)	Aluminum hydroxide
Magnesium carbonates	Magnesium silicate
Calcium carbonates	Magnesium hydroxide
Bourget mixture (sodium bicarbonates, sulphate, phosphate)	Aluminium-magnesium combination
Rennie mixture (calcium carbonates, magnesium carbonates)	Aluminum-magnesium combination with other Active ingredients (anaesthetics, antiflatulents, alginates, etc.)
Tums mixture (calcium carbonates, magnesium oxide).	

Table 1 : Examples of Absorbable and Non-absorbable Antacids. [9]

MECHANISM OF ACTION OF ANTACIDS

Weak bases that react with gastric acid(HCl) to form salt and water, thus decreasing the acidity in the stomach. [6]



Adapted from Lullmann H et al. (2005)

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Figure 2: Antacids for rapid acid neutralization. Each compound in solution dissociates into a metal ion (Na, Ca, Mg, Al) and an acid binding group. The pancreas secretes bicarbonate in the duodenum, which can precipitate Ca and Al so that they are largely excreted in the faeces (not shown). Many antacids combine both Al and Mg, ions which counteract each other's action to prevent unwanted constipation or diarrhoea. Al by itself produces constipation due to an astringent action, and $Mg(OH)_2$ produces diarrhoea by an osmotic mechanism. Since food has a buffering effect, antacids should be taken between meals (e.g. 1 hour before, or 3 hours after, and at bedtime).[13]

• Each antacid has a specific active ingredient. This ingredient whether metallic or non-metallic has a different effect on the gastric acid. Antacids act similar to when an acid reacts with a hydroxide; a salt and water are formed, as in the following equation: [11]

HCl (aq) + NaOH (aq) → NaCl (aq) + H2O

• Sodium bicarbonate: HCl (aq) + NaHCO3 (aq) → NaCl (aq) + H2O + CO2

• Calcium carbonate: HCl (aq) + CaCO3 (aq) → CaCI2 (aq) + H2O + CO2.

• Magnesium compounds: MgO + H2O → Mg (OH)2; HCl (aq) + Mg (OH)2 → MgCl2 + H2O

• Aluminum compounds: Al(OH)3 + HCl → AlCl3 + H2O.

PHARMACODYNAMICS

Absorbable antacids are rarely used in clinical practice because they have a large number of systemic side effects. Such antacids come into direct neutralization reactions with hydrochloric acid in the stomach. They are characterized by quick onset of therapeutic action and short-term effects, because after the administration of absorbable antacids, the pH level of intragastric increases up to 7 or more in a short period of time (15-20 min) that provokes secondary acid hypersecretion (the «rebound» syndrome)

Non-absorbable antacids have less systemic adverse effects than absorbable antacids. Their main mechanism of action is associated with the absorption of hydrochloric acid. Non-absorbable antacids begin acting later (within 10-30 minutes), however, they have longer periods of therapeutic action – nearly 2.5-3 hours .Their Buffer (neutralizing) capacity is higher than that of the absorbable. Their neutralizing activity remains until the pH does not exceed 3.0-4.0 (the physiological pH when there is a normal digestion and hydrochloric acid act as an antimicrobial action). [10]

PHARMACOKINETICS

Absorbable antacids are rapidly dissolving substances that immediately react with hydrochloric acid in the stomach forming carbon dioxide and water. Carbon dioxide causes gastric distention which stimulates gastroesophageal reflux and stimulates gastric secretion enhancement.

The non-absorbable antacids are mostly used in medical practice, without systemic pharmacokinetics.[10]

ADMINISTRATION

Dosage forms of antacids are tablets and suspensions.

- Antacids react with hydrogen ions in solute form of suspension(smaller particles have large surface area)and they dissolve faster in an acidic environment when compared to tablets. Antacids are more effective in the form of suspension than tablets.
- The average therapeutic dose of an antacid is 10–15 ml of liquid or one to two tablets 3-4 times a day.
- Administration of antacids on an empty stomach are rapidly emptied into the duodenum, in addition their effect is negated because food acts as a buffer for antacids. Antacids should be prescribed 1–1.5 hours after meals.
- Periodic monitoring of calcium and phosphorus levels is recommended in patients on chronic therapy. Careful dosing done in those with hepatic and renal impairment.[11,1]

METABOLISM

- Antacids have small volumes of distribution, undergo at least hepatic metabolism and are excreted in faeces.[11]

ADVERSE EFFECTS

Side effects of long term use of antacids

- Hyperacidity and milk-alkali syndrome may be caused due to antacids; it depends on its dose concentration.
- Antacids which contain aluminum hydroxide [Al (OH)3] may cause hypophosphatemia, aluminium- intoxication, constipation and osteomalacia.
- Magnesium contained in antacids has a laxative effect which may cause diarrhoea.

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- The renal failure patients are not able to eliminate magnesium from the body with urine as a result increased magnesium levels in the blood.
- Antacids containing sodium are harmful for the patients on sodium prohibited diet while calcium contains antacids it may cause formation of kidney stones. [14]

DRUG INTERACTIONS

Antacids which contain calcium, magnesium and aluminium ions are chelators. They are bound to a large number of drugs such as digitoxin, tetracycline, indomethacin, aspirin, cimetidine, ranitidine, famotidine, theophylline, etc.

- The bioavailability of drugs like barbiturates, sulphonamides, and penicillin are decreased due to antacids.
- For better results and to avoid harmful interactions, antacids are prescribed before or after two hours taking any medication.[10]

CONTRAINDICATIONS

To any compounds of the formulation; the common contraindication is hypersensitivity. The followinga caution of use of antacids in patients with :

- Renal failure
- Heart failure
- Edema
- Cirrhosis
- Low-sodium diets
- Uremia
- GI haemorrhages
- Hyperparathyroidism
- Renal calculus or kidney stones
- Achlorhydria [1]

TOXICITY

No data is found related to toxicities caused by aluminium- and calcium-containing antacids. However, in the above mentioned high risk populations antacids should be used cautiously. [1]

OTHER KEY ELEMENTS OF ANTACID THERAPY

Antacids are over-the-counter (OTC) drugs ,which means that drugs do not need a prescription to obtain them. The only medications give effect of symptomatic relief, which may protect an underlying disorder, The delay in diagnosis of health conditions like GERD, peptic ulcer, gastric ulcer, and hiatal hernia may occur due to the lack of awareness in people. Such conditions lead to inappropriate use of these drugs and reduced symptoms.Patients need to educate on the importance of proper mode of administration, time of administration, and dosage for immediate and long-term relief of symptoms. Although these drugs do not cause toxicity at high doses , understanding their interactions with other drugs is essential, especially when the patients are involved in polypharmacy. [15]

II. CONCLUSION

Antacids are used in the treatment of gastric disorders to provide prolonged relief and quick action with low dose administration.Therapeutic efficacy even at low doses with less side effects, sustained increase in gastric pH, faster and longer duration of pain relief, and quick relief from gas. Antacids containing combinations of aluminum hydroxide, magnesium hydroxide, and other ingredients showed significant clinical results in vitro, thus restoring the confidence of clinicians. The role of antacids suggests that treating physicians may use antacids with high neutralizing capacity to achieve rapid symptomatic relief.

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