Treatment of PU

Lecture 3

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Anticholinergic drugs

Mechanism

1. ↓Hcl secretion (mild effect). Usually in combination.
2. Antispasmodic. Usually in colic.
3. Decrease nocturnal pain.
4. Delay gastric emptying → prolonged exposure of ulcer to Hcl (this can be diminished by combination with antacids).

Preparations: atropine substitutes.

Adverse effects:

1. Dryness of secretions.
2. Constipation.
3. Tachycardia.
4. Contraindicated in old males to avoid glaucoma & retention of urine.

Sulpride

Mechanism

Selective dopamine D2 antagonist.

1. ↓ Hcl secretion & ↑ GIT motility.
2. Antiemetic.

Uses

1. DU.
2. Stress ulcer (mediated via central D2 receptors).

Adverse effects

1. Diarrhea.
2. Galactorrhea.

Mucosal protectives (Cytoprotectives)

1. Sucralfate

Mechanism

It is a complex salt of sucrose containing sulfate and poly aluminium hydroxide.

1. The negatively charged sulfate groups bind to the positively charged proteins in the ulcer base, forming a protective barrier against acid, bile and pepsin.

2.↑ mucus secretion.

↓ H+ diffusion.

↑ PG production.

3. Binds epidermal and fibroblast growth factors.

Uses

1. GU.
2. With NSAIDs.
3. Stress ulcer.
4. Smoker,s ulcer.

Dose

Orally, 1 gm before meals, 4 times daily for 4 weeks.

Adverse effects and disadvantages

1. Active only in gastric acid medium (forming aluminium and non absorbable anion), so if antacids or H2 blockers are given they should be at least I hour apart (after meals).

2. Constipation.

3. Dry mouth.

4. Nausea, vomiting, gastric discomfort and flatulence.

5. In renal diseases: aluminium toxicity, osteomalacia and encephalopathy.

6. Binds some drugs leading to decrease absorption, so given at least 2 hours apart.

Misoprostol

Mechanism :-

PG analogue → ……(mention…..). Potent selective cytoprotective.

Uses :-

For healing of GU but not DU.

Adverse effects :-

1. Severe colicky pain of stomach and intestine.
2. Diarrhea (treated by aspirin).
3. Severe uterine contractions.
4. Vaginal bleeding. Contraindicated in pregnancy
5. Decrease male and female fertility.

H pylori therapy

A) Acid - suppressives

1. Proton pump inhibitors.
2. Ranitidine.

B) Antimicrobials

1. Clarithromycin: most potent. Related to erythromycin but is more acid stable, better absorbed and more effective against H pylori. Dose: 500 mg twice daily orally.
2. Amoxicillin: 1gm twice daily.
3. Tetracyclines : 500 mg 4 times daily.
4. Levofloxacin.
5. Metronidazole: 250 mg 4 times daily. High resistance rate.
6. Nitroimidazole: to avoid metronidazole resistance.
7. Tinidazole.

Aim of combinations

1. Enhance H pylori cure.

2. Shorten duration of treatment (1- 4 weeks). In one week therapy high doses of 3- 4 drugs are used.

3. Decrease treatment failure.

4. Decrease recurrence rate.

Types of regimens

e.g. Triple therapy.

10 -14 days of :

PPI + 2 antimicrobials. 1 + (2,3 or 4) + (5,6 or 7).

Sequential therapy:

5 - 7 days of PPIs + amoxicillin.

5 - 7 days of PPIs + 2 other antimicrobials.

The lower M Wt., the more:

1. Potent. 2. Rapid onset. Advantages

3.Rebound. 3. Short duration. Disadvantages

A) Systemic : → alkalosis & alkaline urine.

Na HCO3 → CO2 gas.

B) Local :

1. **Ca CO3**
2. **Al (HO)3** : chemical + physical.

a. Demulcent.

b. Astringent.

c. Adsorbent : Fe, phosphates, anticholinergic drugs...

3. **Mg salts:** chemical & physical.

- 1 & 2 → constipation. 3 → diarrhea.
- In renal dysfunction:

1: ↑ Ca.

2: Encephalopathy.

3: CNS depression.

Antacids

They neutralize gastric Hcl, increasing pH of stomach leading to:

1. ↓ pain.
2. ↓ spasm.
3. Ulcer protection.

Systemic antacids (Na HCO3)

Advantages:

1. Potent.
2. Rapid onset.

Disadvantages:

1. Systemic alkalosis.
2. Alkalinization of urine → phosphate and oxalate stones.
3. Short duration.
4. Rebound hyperacidity.

Local antacids

1. Calcium carbonate

Advantages:

1. No alkalosis.
2. Rapid onset.
3. Potent.

Disadvantages:

1. Gastric distension.
2. Short duration
3. Rebound hyperacidity.
4. Constipation.
5. Milk alkali syndrome.
6. Phosphate stones by alkaline urine.
7. 40% of Ca++ is absorbed.

2. Aluminium hydroxide

Advantages:

1. Moderate potency, onset and duration.
2. No alkalosis.
3. No CO2 gas (no gastric distension).
4. Physical and chemical mechanism.

Disadvantages:

1. Constipation.
2. Encephalopathy in renal failure (little is absorbed).
3. Adsorption → ↓ absorption of iron, phosphate, tetracyclines, digoxin and anticholinergic drugs.
4. Hypophosphatemia → osteomalacia.

3. Magnesium salts

Advantages:

1. Long duration.
2. No rebound hyperacidity.
3. No alkalosis.
4. No gastric distension.

Disadvantages:

1. Mild action.
2. Delayed onset.
3. Diarrhea.
4. CNS depression in renal failure (little is absorbed).