A) Treatment of GERD
B) Antiemetics

Lecture 4

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GERD

Clinical picture

1. Typical: heartburn, regurgitation, worse after fatty or sugar meals or recumbent position.

2. Atypical: Extraesophageal syndromes include chronic cough, laryngitis, hoarseness, pharyngitis, asthma , reflux chest pain

and dental erosions.

3. Complicated: pain, dysphagia, painful swallowing, bleeding,

wt. loss, anemia & choking.

Barrett,s esophagus is a complication of GERD for years.

Squamous → columnar → high grade dysplasia → adenocarcinoma.

Treatment

A) Life - style modification is more important.

B) Drugs: combinations are more effective.

Life - style modification

1. Remaining upright for 2 hours after meals.
2. Elevation of head of patient during sleep.
3. ↓ meal size.
4. ↓ body weight.
5. **Avoid:**

a. Drugs increasing Hcl (mention them).
b. Direct mucosal irritants: acidic food as citrus fruits & tomatoes.
c. Foods decreasing LESP:
Fatty & fried food, sugars, caffeine, chocolate, peppermint & spices.
d. Drugs decreasing LESP:
1. Anticholinergic drugs & related drugs as TCA.
2. Nitrates & slow calcium channel blockers.
3. β2 adrenoceptor agonists.
4. α1 adrenoceptor blockers.
5. Smoking, caffeine and alcohol.

Drug therapy of GERD

1. Antacids & alginic acid – containing **antacids**:

Antacids (aluminium hydroxide + Mg salts) neutralize Hcl → rapid relief.

Alginic acid forms a foam barrier for coating stomach and

anti-reflux layer over mucosa.

Not absorbed or metabolized.

Used in GERD & other acid - related disorders.

2. Sucralfate: in mild or moderate cases or in combinations.

3. Acid - suppressive drugs are the most effective means for symptom relief and healing. PPIs are more effective than H2 antagonists. Higher & more frequent doses are used.

4. H pylori therapy.

5. Prokinetics: they increase gastric motility & emptying and improve LES tone & esophageal motility. This ↓reflux and improves luminal clearance. e.g.

a. Benzamides (5-HT4 agonists) ??

b. Domperidone & metoclopramide.

c. Itopride is a benzamide prokinetic effective in functional dyspepsia. It inhibits D2 receptors and ChE enzyme.

It may be combined with pantoprazole in acid - related disorders, given 1 hour before meals specially in morning for up to 14 days.

d. Macrolides are prokinetics.

- **Eukinetics** ↓transient LES relaxations.

Rabeprazole

Compared to PPIs:

Pharmacodynamics:

More rapid conversion to active, more potent, ↑intragastric pH > 4, of longer duration.

More effective in nocturnal heartburn specially in GERD (nocturnal GERD).

Uses:

1. Short term ttt of GERD.
2. PU.

Dose: Orally, 20 mg, once daily, with or after meals.

Adverse effects:

More common & more severe than other PPIs. Also, specifically:

1. Diarrhea.
2. Allergy.
3. SLE.
4. Bone fractures.

Antiemetics

Vomiting center contains 5-HT3, M1& H1 receptors. Stimulated by:

1. Peripherally, fibers from GIT, liver and myocardium are rich in 5-HT3, M1, H1 & substance P receptors.

In chemo & radiotherapy and gastroenteritis.

2. CTZ (chemoreceptor trigger zone): outside BBB.

Rich in D2, 5-HT3, opioids, substance P & neurokinin (NK1) receptors. Stimulated by emetic drugs (opioids, digoxin, antiepileptics, antiparkinsonism, oral contraceptives, antiarrhythmic drugs, nicotine and anti ChE), toxins, uremia, acidosis and radiation.

3. Fibers from vestibular system (mediate motion sickness, vertigo & migraine) have high concentration of M1& H1 receptors.

4. High CNS centers: via sight, smells or emotional experiences.

1. Dopamine antagonists

Effective, commonly in vomiting induced via stimulation of CTZ by…..

e.g. domperidone and metoclopramide..

In postoperative nausea & vomiting corticosteroids and 5-HT3 antagonists have also efficacy, but combinations have additive benefits.

2. Antihistaminics (H1 antagonists)

e.g. diphenhydramine & meclizine are used mainly for motion sickness in long journeys, vertigo and migraine.

3. Anticholinergics

e.g. scopolamine (hyoscine) are used mainly for motion sickness in short journeys.

4. 5-HT3 antagonists

Block vomiting center, GIT & CTZ.

e.g. ondansetron, granisetron & tropisetron.

Used in nausea and vomiting due to postoperative, chemotherapy or radiotherapy.

Dose: 8 mg orally twice daily or slowly IVI.

Most potent and of long duration.

Adverse effects:

1. Headache.
2. Constipation.
3. Warm or flushing sensation in head or epigastrium.
4. QT prolongation.

5. Neurokinin (NK-1) antagonists

→ ↓ substance P release.

Uses: orally in vomiting due to chemotherapy and radiation

(+ 5- HT3 antagonists or corticosteroids).

e.g. aprepitant. Many adverse effects.

6. Cannabinoids

Uses as 5.

e.g. nabilone & dronabinol.

Adverse effects: euphoria, dysphoria, sedation & hallucination.

7. Sedatives as benzodiazepines for anticipatory & psychogenic nausea & vomiting. They act on higher CNS centers.

8. Vitamin B6. In pregnancy.

9. Corticosteroids. In combination with most antiemetics.

Metoclopramide

Mechanism :-

Central :blocking of dopamine (D2) receptors in CTZ (antiemetic).

Peripheral: ↑ cardiac tone and gastric peristalsis. It relaxes pyloric antrum and duodenal cap increasing gastric emptying.

Also cholinomimetic action.

Uses :-

1. Vomiting by drugs, uremia, toxins and radiation therapy.
2. Postoperative vomiting.
3. GERD. . Emergency anesthesia: clears gastric contents.
4. Endoscopy: facilitate passing of tube into GIT.
5. Radiological examination of GIT (barium meal).
6. Combination with paracetamol or aspirin increasing their absorption and analgesic activity e.g. in migraine.

Adverse effects:

1. Sedation.
2. Extrapyramidal.
3. Galactorrhea.
4. Gynecomastia.
5. Diarrhea.
6. Convulsion in children.

Domperidone has peripheral more than central actions (produces less adverse effects).

But →Q-T prolongation & cardiac arrhythmias.