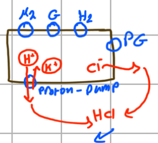
LECTURE 1

Physiology:-

- 2L of acid/day are secreted by the Parietal Cells.
- 

in the Canaliculi not inside the Cell.

- Enteric neurons (Vagus) → ACh → M1 → ↑ HCl; → G cells → Gastrin → ↑ HCl (→ ↑ Histamin)
- ECL (enterochromaffin-like) cells → Histamin → H_2 receptor → ↑ HCl
- G Cells → Gastrin → G receptor → ↑ HCl.
- Gastric PH<3 → Gastric D cells → somatostatin → Effects the Parietal Cells → ↓ HCl (Direct); → ↓ Histamine + ↓ Gastrin → ↓ HCl (indirect)

somatostatin ↓ acid secretion

Phases of gastric acid secretion:-

1. Cephalic Phase:-

- sighting, smelling, tasting or thinking. → ENS is active.
- The major effect of gastrin is indirect through the releasing of Histamine

2. Gastric Phase:-

- The Food stretch the stomach walls → Neural reflex → ↑ acid secretion.
- Peptides and amino acids → Stimulate G cells → ↑ Gastrin.
- Food acts as a buffer → ↑ PH → ↓ Somatostatin.

3. Intestinal phase:- chyme the duodenum → Negative Feedback → ↓ acid.

Peptic ulcer:-

stomach — duodenum

- Causes:- ↑NSAIDs, Smoking, H.Pylori (most common), stress, alcohol, Gastrinomas (↑ Gastric acid) and Zollinger Ellison Syndrom (ZES)
- ↑NSAIDs → ↓ Mucus, ↓ Bicarbonate, ↓ Blood Flow, ↓ Neutrophils, ↓ Cell restitution → Mucosal damage and ulceration.
- Symptoms → burning pain in the stomach between meals or at night, bloating, heartburn, nausea, vomiting, (In sever cases) → Dark stool (bleeding), Vomiting blood, weight loss and sever pain in the mid to upper abdomin.
- Complications → GI bleeding (can be life threatening), Cancer (H.Pylori), Perforation

Treatment:-

- ↓ acid secretion (M_1, H_2, PPIs)
- Neutralizing of HCl
- Protect the Mucosa
- Antibiotics for H. Pylori.

1. Neutralization of acid (Antacids):- مش علاج ، بس نخفيف ألم

- Non prescription (من غير وصفة) treats the heartburn and dyspepsia.
- Given 1 hour AFTER the meal. → work up to 2 hours.

- Mg and Al Hydroxide:-
  - Slow → No gas Formation. → Metabolic alkalosis is uncommon.
  - Mg causes diarrhea. → AL causes constipation. So they usually givin in combination (No Diarrhea or constipation)
  - AL interfer with absorption of many drugs → ما بنعطي مع أدوية ثانية بنفس الوقت.
  - Mg → Have laxative (مليّن) active, The diarrhea stimulate gastric secretion causing acid rebound.
  - Magnesium trisilicate → slow antacid.
  - Contraindicated (ممنوع) in renal insufficiency.

- Ca Carbonate:-
  - ↑ Ca → ↑ Gastrin → ↑ HCl ⇒ Acid rebound.
  - With chronic use, it may cause milk-alkali syndrom. ↑ calcium, ↑ phosphate, ↑ urea, ↑ nitrogen, ↑ creatinin and ↑ Bicarbonate.

- Sodium bicarbonate ($NaHCO_3$):-
  - ↑ Blood pressur. → counteracts diuretic (مدر للبول) therapy for hypertension.
  - Short duration of action. → Acid rebound.
  - Highly bsorbed → cause metabolic alkalosis.
  - CO_2 results in belching.

2. Antisecretory Drugs:-

- H_2 receptor antagonists:- 1970s - 1990s
  - Competitive. → ↓ basal and meal-stimulated acid secretion
  - ↓ volume of secretion and pepsin concentration.
  - it was the most common drug in the past.
  - Drugs → Cimetidine (Prototype, Many problems), Ranitidine, Famotidine (50% First-pass), Nizatidine (little First-pass metabolism).
  - Antagonist:
    - Histamin → X H_2 → ↓ HCl
    - gastrin → ↑ Histamin → X H_2 → ↓ HCl
    - Acetylcholine → X H_2 → HCl
  - Duration of action = 12 hours.
  - ↓ 60-70% of total 24h acid secretion.
    - 90% of nocturnal acid ← The presence of intraintestinal PH<4 during overnight Period fo at least 60 continuos minits.
    - 60% of day time, meal stimulated acid.
  - Uses:-
    1. Gastroesophageal Reflux →
       - Prophylactically
       - Before meals.
       - Afford healing for 50% of erosive esophagitis patients.
       - Proton Pump inhibitors are preferred.
    2. Non ulcer Dyspepsia.
    3. Stress Related Gastritis → Prevent bleeding. → given IV.
    4. Peptic ulcer disease:-
       - Replaced by PPI.
       - Healing Rate = greater than 80-90% after 6-8 weeks.
       - Not effect in the case of H.Pylori.
       - Not effect is NSAID is continued.
  - Side effects:-
    - Extremely safe drugs.
    - can cause diarrhea, hedache, fatigue myalagia and constipation.
    - CNS → Confusion, hallucination (هلوسة) → only if given IV to elderly patients in ICU.
    - Endocrine → (only Cimetidine) 1. inhibit estradiole metabolism. 2. ↑ prolactin serum levels.
    - can cross the placental barrier and appear in breast milk.
    - Rarely can cause bradycardia and hypotension.
  - Drug interactions:-
    - Cimetidine → inhibit cytochrom P450 enzymes (CYP1A2, CYP2C9, CYP2D6 and CYP3A4) ~so~ → can ↑ the half life of many drugs.
    - Ranitidine → binds 4-10 times less.
    - Nizatidine and Famotidine → binding is negligible.

Lecture 2

Proton pump inhibitors (PPIs) in 1990s

1. omeprazole (oral) 2. Rabeprazole (oral) 3. Lanzoprazole (oral) and (IV)

4. Pantoprazole (oral) and (IV) 5. Esmoprazole (oral) and (IV)

→ They are prodrugs that are released in the intestine (need an activation, and this activation happen in the intestine)

→ Immediate release suspension results in rapid response. (Less common)

→ Very efficacious and safe drugs.

→ Pharmacokinetics:

↳ they are lipophilic weak bases (pKa 4-5).

↳ Intestinal absorption → the drug diffuse across lipid membranes into acidified compartments (such as parietal cell canaliculus) → it undergoes a molecular conversion to the active form → Binds the H^+/K^+ ATPase enzyme and inactivates it.

↳ The prodrug becomes protonated and concentrated more than 1000-Fold within the parietal cells.

↳ Rabeprazole has immediate release. ↳ omeprazole has Fastest onsets of action.

↳ given 1 hour before meal. ↳ Have short half life But effect lasts for 24 hours due to irreversible inhibition.

→ Pharmacodynamics:-

↳ Block the Final common pathway (80-90% of 24-hour secretion) of acid secretion → inhibit Both Fasting and meal-Stimulated secretion.

→ Clinical uses:

1. Gastroesophageal reflux (GERD) → The most effective agents in all form of GERD and complications.

2. Nonulcer Dyspepsia → 10-20% more benficial than a placebo.

3. Stress-Related Gastritis →

↳ Patients with nasogastric tube → oral immediate-release omeprazole.

↳ Patients without a nasogastric tube → IV H_2-antagonists are preferred because of their proven efficacy.

4. Gastrinoma and other Hypersecretory conditions → High doses of omeprazole

5. Peptic Ulcer → The PPIs heal 90% of cases within 4-8 weeks.

↳ H. Pylori ulcers:-

- PPI eradicate (قضاء) H. pylori by Direct antimicrobial activity and by lowering MIC (the lowest concentration (inhibitory) of antimicrobial) of the antibiotics.
- Triple therapy → 1. PPI (omeprazole (20mg)) twice daily. 2. Clarithromycin 500 mg twice daily. 3. Amoxicillin (1gm (1000mg)) twice daily OR Metronidazole 500 mg twice daily.

↳ NSAIDs-associated ulcers: PIs promote ulcer healing Despite continued NSAID use and prevent ulcer complications of NSAIDs.

↳ Rebleeding peptic ulcers:

- oral or IV. - High pH may enhance coagulation and platelet aggregation.

→ Adverse Effects:-

1. Diarrhea. 2. Headache. 3. Abdominal pain. 4. Not teratogenic in animals but not used in pregnancy.

5. Reduce of Cyanocobalamine absorption. 6. ↑ risk of GI and pulmonary infection

7. ↑ serum gastrin levels → Hyperplasia of ECl cells.

8. Carcinoid tumors in rats. 9. ↑ proliferative rate of colonic mucosa.

10. Chronic inflammation in gastric body. 11. Atrophic gastritis (↳ inflammation of the lining of the stomach) and intestinal metaplasia.

12. ↓ B_{12} ↳ Help balance immune responses.

→ Drug interactions:

↳ May effect absorption of drugs like digoxin and ketoconazole by decreasing gastric acidity.

↳ omeprazol can inhibit metabolism of drugs such as diazepam and phenytoin (it decrease PMSA)

↳ Rabeprazole and pantoprazole have No significant interaction.

Lecture 38-

Drug Affecting GI Motality

Laxative (ملين) — Antidiarrheal

→ Nonpharmacologic Remedies (For constipation):-

1. High Fiber diet. 2. Adequate Fluid intake.

3. Regular exercise. 4. Responding to nature's call.

Laxatives:-

- Bulk-Forming laxatives.
- Stool Surfactant agents (Softeners).
- Osmotic laxatives (Purgatives).
- Stimulant laxatives (Cathartics).
- Tegaserod.

1. Bulk-Forming Laxatives:-

↳ indigestible.

↳ Hydrophilic colloids that absorb water → Forming a bulky (Emollient gel) → destends the colon and promotes peristalsis.

↳ Adverse effects → can cause bloating and flatus.

↳ Include → A Natural Plant Products (Psyllium, Sterculia (Nomacol) and Methylcellulose).

B. Synthetic Fibers → polycarbophil.

2. Stool Surfactant Agents (Softeners):-

↳ Mechanism → Permit water and lipid to penetrate stool → softer and easier to pass.

↳ Given orally and rectally.

↳ Examples → 1. Docusate 2. Glycerin suppository 3. Mineral oil.

↳ Mineral oil:-

- clear viscous oil, it lubricates fecal material, retarding water absorption from the stool.
- Prevent and treat fecal impaction.
- Aspiration can cause lipoid Pneumonia (when food of liquid is breathed into the airways of lungs, instead of being swallowed)
- Can impair absorption of Fat-soluble vitamins.

3. Osmotic Laxatives (Purgatives):

↳ Soluble nonabsorbable compounds.

↳ ↑ Stool liquidity due to an obligate increase in Fecal Fluid (↑ osmotic pressure → the water will go to the lumin → Immediately evacuation.)

↳ Examples:- Magnesium oxid, sorbitol, Lactulose and Balanced polyethylene Glycol.

↳ Magnesium oxide (Milk of Magnesia):

- can cause hypermagnesemia.
- Large doses of Mg citrate and Na phosphate can cause purgation which means rapid bowel evacuation within 1-3 hours ⟶ which may cause volume depletion.

↳ Lactulose: sugars metabolized by bacteria producing (side effects) sever Flatus and cramps.

↳ Balanced Polyethylene Glycol (PEG):

- Safe solution → No intravascular Fluid or electrolyte shifts.
- Doesn't cause cramps or Flatus. - used for complete colonic cleansing before endoscopy.
- it is an inert, nonabsorbable, osmotically active sugar.
- Sodium sulfate, chloride, bicarbonate and potassium chloride.
- For colonic cleansing → it should be ingested rapidly (4L over 2-4 hrs)
- For chronic constipation → powder is mixed with water or juice.

4. Stimulant Laxatives (Cathartics):- (إضافية) ممنوع تُستخدم للحوامل والمرضعات

- Direct stimulation of the enteric system (Neural plexus)
- Can lead to dependence and destruction resulting in colonic atony (ارتخاء) and dilation.
- it lead to Colonic electrolyte and Fluid secretion (Mechanism) → Local inflammation ⇒ ↑↑ water secretion.
- needed in neurologically impaired patients and in bed-bound patients in long term care facilities (مش في الحالات الطبيعية).
- Examples → 1. Anthraquinone Derivatives (Aloe, Senna (عشبة), cascara. 2. Castor oil.

- Cascara:-

↳ Poorly absorbed. ↳ After hydrolysis → Produce bowel movement in 6-12 hrs.

↳ cause brown pigmentation of the colon (Melanosis coli) → side effect.

↳ Not carcinogenic.

- Castor oil:-

↳ Hydrolyzed in upper intestine into ricinoleic acid → Local irritation.

↳ used as purgative to clean the colon before procedures.

5. Tegaserod:-

Normally ⟹ Gut distention → stimulates 5-HT (releas from EC cells)

- stimulate 5-HT3 receptors on extrinsic afferent nerves ↓ stimulate nausea, vomiting or Abdominal pain.
- stimulates 5-HT1P receptors of the intrinsic primary afferent nerves (IPANs) ↓ Activate the enteric neurons resposible for Peristaltic and secretory reflex activity.

↳ stimulating of 5-HT4 receptors (by Tegaserod) on presynaptic terminals of IPANs (→ of the submucosal) enhances the release of Ach and Calcitonin gene related peptide (CGRP) → promoting reflex activity

these neurons:

- via ach and substance P ↓ stimulate proximal bowel contraction.
- via NO and VIP ↓ stimulate distal relaxation.

↳ Tegaserod → Serotonin 5-HT4 partial agonist.

↳ The drug promotes gastric emptying and Small and large bowel transit But has NO effect on Esophageal motility.

↳ It also stimulate cAMP-dependent chloride secretion ~so→ ↑↑ stool liquidity

↳ Clinical uses → 1. chronic constipation. 2. Nonulcer dyspepsia. 3. Gastroparesis. 4. Irritable bowel syndrom.

↳ Adverse effects: Extremely safe.

1. Diarrhea in 9% of patients (resolves within days) 2. Expensive.

Antidiarrheal Agents

- Acute diarrhea (Mild-Moderate)
- infective diarrhea.
- Chronic diarrhea (irritable bowel syndrom or inflammatory bowel disease)

→ include:- 1. opioid Agonists. 2. Kaolin and pectin. 3. Bile-salt binding resins (colestyramine, colistipol) 4. Octreotide.

1. Opioid Agonist:-

↳ Inhibit presynaptic cholinergic nerves → ↓ Motility → ↑ colonic transit time and ↑ Fecal water absorption.

↳ ↓ Mass colonic movements and gastrocolic reflex.

↳ Have CNS effects and addiction (إدمان) potential Because of that it usually combined with atropine.

↳ Examples → 1. loperamide → Don't cross BBB (No analgesic on addiction)

2. Diphenoxylate → Can have CNS effects (May cross BBB).

2. Kaolin and Pectin:-

↳ Kaolin → a naturally occuring hydrated mg silicate.

↳ Pectin → an indigestible carbohydrated derived from apples.

↳ Both act to absorb bacteria, toxins and Fluid ~so→ taken far from other drugs.

→ ↓↓ Fluids → ↓ Diarrhea (these drugs called adsorbants)

↳ Usually combined (e.g. Kaopectate)

3. Bile Salt-binding resins: 1. cholestyramin. 2. Colistipol.

↳ in case of diarrhea because Malabsorption of bile salts (After surgical resection). ↳ it can bind bile salts.

↳ side effects → bloating, flatulence, constipation, Fecal impaction and drug and fat Malabsorption.

4. Octreotide: a synthetic octapeptide with actions similar to Somatostatin

* somatostatin → A 14 amino acid peptide, released in the GIT and pancreas from the hypothalamus, it:- 1. ↓ release of many hormones. 2. ↓↓ intestinal Fluid and pancreas secretions.

3. ↓ GI motility and gallbladder contraction.

4. Contracts blood vessels. 5. Inhibits secretion of some anterior pituitary hormones.

↳ Clinical uses: 1. Inhibition of endocrine tumor effects like carcinoid which can cause secretory diarrhea and systemic syndrome (flushing and wheezing).

2. Diarrhea due to vagotomy (cutting the branch of the vagus that stimulate gastric acid secretion) and dumping syndrome (when food (especially with high sugar) moves very fast to the small bowel) or AIDS.

3. (In small doses) can stimulate motility in small bowel bacterial overgrowth or intestinal pseudo-obstruction secondary to sclerodorma. (uncommon) تيبس الجلد

4. Pituitary tumors and GI bleeding.

Lecture 4:-

Treatment of Irritable Bowel Syndrome (IBS)

→ IBS → An idiopathic, chronic, relapsing disorder characterized by abdominal discomfort (pain, bloating, distention or cramps with alteration in bowel habits (diarrhea, constipation, or both).

↳ The therapies are directed at relieving abdominal pain and improving bowel function.

↳ Drugs:- 1. Antispasmodic or anticholinergic agents (Dicyclomine, Hyoscyamine)

2. Serotonin 5-HT3 receptor antagonist (Alosetrone) 3. Serotonin-4 agonist. (Tegaserod)

1. Antispasmodic or anticholinergic agents:- Dicyclomine + Hyoscyamine.

- Spasm is not an important symptom in IBS.
- Low doses. - Have minimal side effects.
- Inhibit muscarinic receptors in the enteric plexus and on smooth muscle.

2. Serotonin 5-HT3 receptor antagonists:-

- 5-HT3 receptors are present in 1. the afferent pain fibers in the extrinsic sensory neurons. 2. the terminals of the enteric cholinergic neurons.
- 5-HT3 is involved in the central respone to visceral afferent stimulation.
- Alosetrone:-

↳ Selective antagonist of 5-HT3 receptors. ↳ long duration of action.

↳ Approved for women with sever IBS with diarrhea is the prominent symptom.

↳ Efficacy in men is not established.

↳ Adverse effects → ischemic colitis (↓ blood flow to part of large intestine) severe constipation requiring hospitilization and surgery.

3. Tegaserod:- serotonin-4 agonist.

↳ For short term treatment of women with IBS who predominantly have constipation. ↳ It reduces pain, bloating and hardness of stool.

↳ Expensive.

→ IBS → Symptomatic treatment including stress management and education of the patient (first step)

- Constipation → ↑ dietary fiber and fluids → إذا ما فادة ↓ Add bulk-forming and antispasmodic agents. → إذا ما فادة ↓ Add serotonin-4 agonist
- Diarrhea → Lactose and caffein-free diet + education on other food and drugs to avoid → إذا ما فادة ↓ antispasmodic (loperamide) → إذا ما فادة ↓ serotonin-3 antagonist

→ Behavior modifications (↓ stress.)

Antivomiting

Antiemetic Agents:-

→ Conditions that cause nausea and vomiting:-

1. Adverse effect of medications. 2. Systemic disorders or infections. 3. Pregnancy. 4. Vestibular dysfunction. 5. CNS infection or pressure. 6. Peritonitis. 7. Hepatobiliary disorders. 8. Radiation or chemotherapy. 9. GIT obstruction, dysmotility or infections.

→ Cranial nerves VIII (8) and X (10) and neural networks in the nucleus tractus solitarius (control respiratory, salivatory and vasomotor centers) → will interaction with vomiting center (CN) in the brainstem → which cause vomiting.

→ Vomiting center contains high concentrations of: 1. M_1 receptors. 2. H_1 receptors (for histamine). 3. Neurokinin$_1$ receptors (NK_1) → for substance P. 4. 5-HT3 receptors (for serotonin). → Stimulation of these receptors will cause vomiting.

→ Vomiting is a protective reflexes that preven the ingestion of toxins.

→ Drugs:-

1. Serotonin 5-HT3 antagonists:- التقيؤ إلي بسبب تحفيزمن المعدة والأمعاء

↳ Examples → Odansetron, Granisetron.

↳ Block central and peripheral (main effect) 5-HT3 receptors

↳ Prevent emesis due to vagal stimulation and chemotherapy (+ surgery and radiotherapy)

↳ Poorly control other emetic stimuli as motion sickness.

↳ Uses → prevention of acute chemotherapy-induced nausea and emesis and postoperative nausea and vomiting → work in 5-HT3 receptor.

↳ Their efficacy is enhanced by combination therapy with Dexamethasone and NK_1-receptor antagonists.

↳ Adverse effects → Headache, dizziness (دوخة), and constipation.

2. NK_1 receptor antagonists:-

↳ Block NK_1 receptors in the are postrema.

↳ Example → Aprepitant. ↳ it used in combition with 5-HT3 receptor antagonist and corticosteroids for the prevention of acute and delayed nausia and vomiting from chemotherapy.

3. Cannabinoids:-

↳ Examples → Nabilone, Dronabilon. ↳ Psychoactive agents (زي الحشيش)

↳ Used for chemotherapy-induced vomiting.

↳ No understood mechanism (slides) → (بشتغل على CB1 receptor يلي موجود في الـ vomiting center وتحفيز هذا المستقبل بعمل Antiemetic effect (إضافة مني))

↳ Adverse effect → Euphoria, dysphoria, sedation, hallucinations, dray mouth and increased appetite (حشيش).

4. Antipsychotic drugs:-

↳ Exampils → Prochlorperazine, Promethazine, Droperidol.

↳ Blocking of dopamine (D_2) and muscarinic M_1 receptors.

↳ Adverse effects → Antihistamine activity → sedative effects

5. Benzodiazepines:-

↳ Examples → Lorazepam, Diazepam.

↳ ↓ Vomiting caused by anxiety. (قلق)

Lecture 5 :-

Antiprotozoal Drugs : For protozoal and helminthic.

→ they cause diseases in migrant workers or individual returning from an endemic area

→ Protozoal Diseases :-

1. Amebiasis:-

↳ by Entamoeba histolytica. ↳ endemic in parts of the US.

↳ it can present in the host as encysted or trophozoits.
- encysted ← in feces, infective, resistant
- encysted → trophozoits: excystation; trophozoits → encysted: encystation
- trophozoits → feeding, motile, replication.

↳ Asymptomatic or sever amebic dysentery (frequent passage of blood stained stools.

↳ Symptoms occurs after invasion of intestinal mucosa by trophozoite (protozoan)

↳ Trophozoits may go to the portal vein then → to the liver producing acute amebic hepatitis.

↳ Many people continue to secrete cysts for several years after recovery from the acute disease.

↳ Diseases by Entamoeba histolytica: Asymptomatic infection, mild to moderate colitis, sever infection (dysentry), Ameboma (tumor-like mass which results in a larg local lesion), liver abscess and other Extraintestinal infections.

↳ Treatment :-

Asymptomatic intestinal infection

↳ Treated by luminal amebicides:
1. Diloxanid Furoate. 2. Iodoquinol.
3. paromomycin.

↳ luminal amebicide is required in the treatment of all other forms of amebiasis.

Amebic Colitis

↳ Metronidazole + lumina amebicide ⟹ treatment of choice.

↳ Tetracyclines and erythromycin ⟹ Alternative drugs for moderate colitis but are not effective against extraintestinal disease.

↳ Dehydroemetine or emetine can also be used, but they are toxic so should be avoided.

2. Balantidium Coli :-

↳ The largest protozoans that infect humans.

↳ trophozoite form is covered with cilia (impart mobility).

↳ Ingestion of cyst-contaminated soil, food or water leads to in-ection.

↳ The trophozoite causes superficial necrosis or deep ulceration in the mucosa and submucosal of the large intestine.

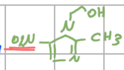
↳ Healthy persons commonly exhibit Nausea, Vomiting, abdominal pain and diarrhea.

↳ stressed patients may develop sever dysentery.

→ Classes of oral antiprotozoal drugs : commonly used
- antimalarial drugs
- Miscellaneous antiprotozoals.
  - Metronidazol
  - nifurtel
  - tinidazole

↳ Metronidazole and doxycycline are also used in bacterial infections.

1. Metronidazole : Flagyl / Metrogel



↳ Drug of choice in the treatment of extraluminal amebiasis.

↳ Kills trophozoites but not cysts. ↳ eradicate intestinal and extraintestinal infections

↳ Tinidazole has similar activity and better toxicity profile than metronidazol.

↳ Has (Metronidazol) activity against most anaerobic bacteria and several protozoa.

↳ It freely penetrates protozoal and bacterial cells but not mammalian cells.

↳ pyruvate-ferredoxin oxidoreductase (Enzyme found only in anaerobic organisms) → Reduces Metronidazole → The drug is active → it disrupts replication and transcription and inhibits DNA repair.

↳ Clinical uses :-

1. Amebiasis → Drug of choice for all tissue infection with E. histolytica.
   ↳ Not effective with liminal parasites.
2. Giardiasis → Drug of choice.
   ↳ Efficacy after a single treatment is 90% ↳ Tinidazole is equally effective.
3. Trichomoniasis → Drug of choice.
   ↳ single dose of 2g is effective.

↳ Adverse Effects and Cautions :-

1. Common → Nausea, headache, dry mouth, metalic taste.
2. Infrequent → Vomiting, diarrhea, insomnia, weakness, dizziness.
3. Rare → Pancreatitis and sever CNS toxicity (Tinidazole doesn't have this toxicity)

– congenital abnormalities have not clearly been associated with use in humans, but it is best avoided in pregnant or nursing women.

2. Tinidazole :-

↳ Has many of same side effects of metronidazole

↳ Can be given in a singil dose.

↳ nifuratel is an alternative drug to metronidazole or tinidazol in the treatment of trichomoniasis.