

[Antiprotozoal Drugs]

Drugs for amoebiasis

1) Tissue amebicides:

a) **For both intestinal and extra intestinal amoebiasis:**

- Metronidazole and tinidazole
- Emetine and dehydroemetine(use is declined because of cardiac toxicity)

b) **For extra intestinal amoebiasis :** chloroquine

Metronidazole

Spectrum of activity:

- 1-protozoa: *E. histolytica* ,*giardia lamblia*, *trichomonas vaginalis*
- 2-anaerobic bacteria: *Cl difficile*, *Cl perfringes*, *H.pylori*, *fusobacterium*, *bacteroides fragilis* and *gardenerella vaginalis*

Mechanism of action: inside the anaerobic bacteria and sensitive protozoa . metronidazole is converted into an active form by reduction of its nitro group ;this binds to DNA and prevents nucleic acid synthesis; it is bacteriostatic.

It is effective against trophozoites but not the cysts of *E.histolytica* .

Kinetics: It

is well absorbed after oral or rectal administration. achieves sufficient concentration to eradicate infection in intestinal wall, pelvic tissues, liver, brain, CSF, semen and vaginal fluid and it can cross the placenta is metabolized in liver and is excreted in urine, inducing a harmless dark -brown color. Plasma t1/2 is 8 hrs; administered 8 hourly.

Uses:

- 1) amoebiasis including acute intestinal amoebic dysentery, amoebic hepatitis and amoebic liver abscess.
- 2) giardiasis
- 3) urogenital trichomoniasis in both sexes
- 4) anaerobic bacterial infections as: postsurgical infections, intra-abdominal infections , septicaemia , osteomyelitis, brain and lung abscess
- 5) anaerobic vaginosis
- 6) pseudomembraneous colitis (caused by *Cl. Difficile*), due to use of some antibiotics.
- 7) acute ulcerative gingivitis and dental infections
- 8) eradication of *H. pylori* associated with peptic ulcer
- 9)cutaneous leishmaniasis

Side effects

- 1-GIT: nausea, vomiting, metallic taste, furred tongue

2- CNS: headache, dizziness, vertigo, ataxia, peripheral neuropathy, high doses may cause seizures

3- Disulfiram-like effect with alcohol(nausea , vomiting, sweating, flushing, tachycardia, hypotension).

4- carcinogenic in rodents and mutagenic in bacteria so it is not recommended during 1st trimester of pregnancy and cautiously used later on.

5-Inhibits metabolism and Potentiates anticoagulant effect of warfarin.

Tinidazole

Similar to metronidazole in efficacy and spectrum of activity but:

- It has longer duration of action, allowing once daily administration .
- single (2g) dose is effective for giardiasis, trichomoniasis and acute ulcerative gingivitis.
- lower side effects

Chloroquine

is an antimalarial drug; highly concentrated in liver ; used for prevention and treatment of amebic liver abscess.

2) Lumenal amebicides

-act in intestinal lumen but do not have tissue amoebicidal action

- must be administered with or after tissue amoebicides during treatment of acute intestinal dysentery or liver abscess, **to eradicate cysts (the infective stage of the parasite)** from the colon and prevent carriers.

- Cure the asymptomatic cyst passers.

a) Diloxanide furoate

Mechanism of action: Oral dose is hydrolyzed by intestinal flora into diloxanide and furoic acid; about 90% of the diloxanide is absorbed, metabolized in liver and excreted in the urine. The unabsorbed fraction reaches colon and acts as a luminal meboecide; kills trophozoites responsible for production of cysts and eradicates cysts in the lumen of the colon.

dverse effects: flatulence, nausea, abdominal pain, proteinurea and rashes.

b)Iodoquinol is an iodinated hydroxyquinolone. Kills the cyst-forming trophozoites

Other uses: Trichomoniasis ,giardiasis

Side effects: Thyroid enlargement, optic atrophy, visual loss, skin rash, anorexia, diarrhea, abdominal pain.

c)Antibiotics:Paromomycin, Tetracycline , Doxycycline**Paromomycin :**

is an aminoglycoside antibiotic ,given orally, doesn't absorbed, reaches colon in large amounts. It has a direct action on the cyst membrane causing leakage of intracellular components and indirect action as it inhibits colonic flora on which the amoeba feed so reduces proliferation of the amoeba in intestinal lumen.

Other Uses:

- Cutaneous and visceral Leishmaniasis

Adverse Effects: abdominal cramps, nausea and vomiting

Tetracycline & Doxycycline**Mechanism:**

They eradicate colonic flora on which amoeba feed so reduce proliferation of the amoeba in intestinal lumen which reduces the risk of intestinal invasion, perforation and peritonitis.

Drugs for TOXOPLASMOSIS

1)Spiramycin (macrolide antibiotic) for toxoplasmosis in pregnant women.

2) Combination of pyrimethamine with either sulphadiazine , clindamycin, clarithromycin or azithromycin.

DRUGS FOR LEISHMANIASIS**Sod.stibogluconate:**

is pPoorly absorbed orally; administered IV , IM or intralesionally has a cumulative effect on repeated administration because it remains stored in tissues.

Side effects: pain and stiffness at injection site, bradycardia and ECG changes.

Pentamidine:administered i.m. or i.v

Mechanism: unknown.

Side effects: hypotension, fainting and dyspnea, due to histamine releas

OTHERS:amphotercin B, metronidazole , paromomycin