Antiamoebic

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Amebiasis

- A parasitic disease of worldwide public health importance
- Second to malaria in mortality due to protozoan parasites
- Invasive amebiasis results in up to 100,000 deaths / year
- Amebiasis is infection with *Entamoeba histolytica*.
- Approximately 40-50 million people infected with *E. histolytica*, develop *amebic colitis* or extraintestinal abscesses
- Infection commonly acquired by ingestion of food or water contaminated with *E. histolytica cysts*
- Amebiasis is transmitted through gastrointestinal tract.
Ameba has two stages of development: cyst and trophozoite.
Clinical Forms of Amebic Colitis

**Amebic dysentery**
- diarrhea with visible blood and mucus
- (+) *E. histolytica trophozoites with ingested* red blood cells (hematophagous trophozoite) in stools or tissues
- **Sigmoidoscopic examination:** inflamed mucosa with or without discrete ulcers

**Nondysenteric amebic colitis**
- recurrent bouts of diarrhea with or without mucus but no visible blood
- (+) *E. histolytica cysts or trophozoites with* no ingested red blood cells (nonhematophagous trophozoite) in stools
- **sigmoidoscopic examination:** normal
Drug Treatment of Amebic Colitis

- **Tissue Amebicide**: active against invasive forms in the tissues; inconsistent activity against cyst forms
  - **Drug of Choice**: Metronidazole 35-50mg/kg/day TID x 7-10 days
  - **Alternative**: Tinidazole 50 mg/kg/day (max 2 g) OD x 3 days
    - Secnidazole

- **Luminal agents** - eradicate remaining cysts in the intestinal lumen; recommended after giving a tissue amebicide
  - Diloxanide furoate 20 mg/kg/day TID x 10 days
  - Iodoquinol 30-40 mg/kg/day TID x 20 days
  - Paromomycin 25-35 mg/kg/day TID x 10 days
  - Tetracycline
Four Principal Steps in the Management of Children with Bloody Diarrhea

• **F - Fluids**
  - Prevent dehydration with oral or IV rehydration fluids

• **F - Follow-up**
  - Re-evaluate clinical status after 48 hrs

• **F - Feeding**
  - Continue provision of *nutritious food*: breastfeeding; small frequent meals

• **A - Antimicrobial therapy**
  - Ideally, antimicrobial treatment should be based on suspected or identified specific bacterial pathogen
Metronidazole

• A nitroimidazole

• **Pharmacokinetics**
  – Oral metronidazole is readily absorbed and permeates all tissues by simple diffusion.
  – Protein binding is low (<20%)
  – Metabolizing in liver.
  – Excreted mainly in the urine.

• **Pharmacological Effects and Clinical Uses**
  1. **Anti-amebiasis:**
     • **kills all tissue infections with *E. histolytica* trophozoites but not cysts.**
     • **No effect against luminal parasites** and so must be used with a luminal amebicide to ensure eradication of the infection.
  2. **Anti-trichomoniasis:**
  3. **Anti-giardiasis:**
MOA

Metronidazole kills protozoa & is bactericidal for anaerobic bacteria.

- Metronidazole is a prodrug. It requires reductive activation of the NITRO group.
- This occurs in sensitive anaerobic protozoa & anaerobic bacteria by Ferredoxins; which are electron transport proteins.
- These proteins can donate electrons to Metronidazole, which serves as electron acceptor.
- The reduced product is cytotoxic, it targets DNA & other bio-molecules/proteins, resulting in cell death. Hence, it kills the micro-organisms.
• **Adverse Effects and Cautions**

  – Nausea, headache, dry mouth, a metallic taste in the mouth.
  
  – **Infrequent**: vomiting, diarrhea, rashes, insomnia, neutropenia,

  – **Rare**: severe CNS toxicity (ataxia, encephalopathy, seizures)——drug withdrawal
Tinidazole

• It is a second-generation Nitroimidazole.
• Congener of Metronidazole
• It is similar to Metronidazole in spectrum of activity, MOA, absorption, A/E & D/I.
• It is also effective against cysts of *E. histolytica*.
• It is longer acting – once daily dose.
• Short course – 2gm daily, single dose -- for 3 days.

Secnidazole

• Longer acting, Single 2gm dose is given
Emetine and Dehydroemetine

• **Emetine** (an alkaloid derived from ipecac), and **dehydroemetine** (a synthetic analog), are **effective** against tissue trophozoites of *E. histolytica*.

• Because of major toxicity concerns they have been almost completely replaced by metronidazole.

• Administered **subcutaneously** (preferred) or i.m. (but never i.v.) because oral preparations are absorbed erratically.

**Mechanisms**

• Inhibiting peptidyl-tRNA transposition → inhibiting elongation of peptide chain → inhibiting protein synthesis → interfering cleavage and breeding of trophozoites
**Adverse Effects and Cautions**
- Mild when used for 3-5 days. Toxicity increase with length of therapy.
  1. **Cardiac toxicity**: arrhythmias, CHF, hypotension, ECG changes
  2. **Neuromuscular blockade**: muscle weakness and discomfort
  3. **Local stimulation**: pain and tenderness in the area of injection.
  4. **Gastrointestinal tract discomfort**: nausea, vomiting
- Not be used in patients with cardiac or renal disease, in young children, or in pregnancy.

**Pharmacological Effects and Clinical Uses**
- kills *E. histolytica* trophozoites of histolytic tissues but no effect against luminal trophozoites, a luminal amebicide should also be given.
- Used to treat amebic dysentery for the minimum period because of toxicity.
- Occasionally as alternative therapies for amebic liver abscess.
Chloroquine

- **Tissue Amebicide** specially against Amoebic Hepatitis & Liver Abscess.
- Concentrated in liver; kills trophozoits of *E. histolytica*
- Not effective for amebic colitis or luminal amebae because absorbed in upper intestine.

**Use:**
- Amebic liver abscess.
- Hepatic amebiasis / abscess; not responding to Metronidazole
- Not effective in the treatment of intestinal or other extrahepatic amebiasis.
Diloxanide Furoate

• Diloxanide furoate is a dichloroacetamide derivative.
• Effective luminal amebicide but is not active against tissue trophozoites.
• The unabsorbed diloxanide in the gut is the active antiamebic substance.
• DOC for asymptomatic luminal infections.
• It is used with a tissue amebicide, usually metronidazole.

Adverse Effects:
flatulence, nausea, abdominal cramps, rashes, abortion.

Precautions:
Pregnancy
IODOQUINOL

• Iodoquinol (Diiodohydroxyquine) is a halogenated hydroxyquinoline.
• An effective luminal amoebicide used with metronidazole to treat amebic infections.
• Only effective against trophozoits in lumen.

Pharmacokinetics: Poorly understood
• 90% unabsorbed → amebicide.
• 10% absorbed → Metabolized to Glucronides, excreted in urine.
• Half life 11-14 hrs
ADVERSE EFFECTS

- Diarrhea, anorexia, nausea, vomiting, abdominal pain, headache
- **Iodism**: Dermatitis, urticaria, pruritis, fever.
- Some idoquinol can produce severe neurotoxicity on prolonged use & high doses---so used with caution

CAUTIONS

- Taken with meals.
- With caution in: optic neuropathy, Non-amebic Hepatic disease, Renal or Thyroid disease.

Contraindication

- in intolerance to Iodine
Paromomycin

• Aminoglycoside antibiotic.
• Not significantly absorbed from the GIT.
• Only as a luminal amebicide and has no effect against extraintestinal amebic infections.
• Less toxic than other agents
• inhibiting protein synthesis → kill trophozoites

Adverse Effects:
• Abdominal distress and diarrhea
Tetracyclines

• Used as Luminal amebicide.
• Does not kill bacteria directly but disturbs the symbiosis between normal intestinal flora & *E. histolytica*.
• The amebae grow at expense of normal intestinal flora.
• Tetracyclines are broad spectrum antibiotics & kill these flora leading to death of *E. histolytica* also.
• Used in resistant cases
THANK YOU