Drugs used in Helminth infections and Filariasis

Introduction

- *Anti* – against
- *Helminths* – worms

  - Vermicide – Drugs that kill worms
  - Vermifuge – expel infesting helminths

    Peristaltic movement of Intestine
    Cathartic and purgative action

Ideal anthelmintics

- Orally effective
- Effective in single dose
- Inexpensive
- Wide safety of margin with highest toxicity to worms, but lesser toxic to the host

Common Helminths

- **Roundworm:** Ascaris lumbricoides
- **Hookworm:** Ancylostoma duodenale and Necater americanus
- **Threadworm:** Enterobius vermicularis and Strongyloides stercoralis
- **Whipworm:** Trichuris trichiuria and Trichinella spiralis
- **Filaria:** W. Bancrofti, Brugia malayi
- **Tapeworms:** T. saginata, T. solium, H. nana
- **Hydatid disease:** E granulosus and E multilocuralis

Drugs…

Intestinal worms	Tissue worms
Mebebndazole	Diethylcarbamazine
Albendazole	Ivermectin
Thiabendazole	Praziquantel
Pyrantel Pamoate	
Piperazine	
Levamizole	

Benzimidazoles

- Albendazole
- Mebendazole
- Thiabendazole

  - Inhibit helminthic microtubular function
  - Inhibit glucose uptake by the worm
  - Broad spectrum of activity

Mebendazole

- Synthetic benzimidazole derivative

- **Mechanism of action**
  - Slow in action, takes 2-3 days to develop
  - Blocks glucose uptake in the parasite and depletion of glycogen store

Mebendazole …

- Pharmacokinetics : Minimal absorption
  75-90% is passed unabsorbed in the faeces
  Excreted mainly in urine as inactive metabolite
- **Adverse effects:** No adverse effects with short term therapy
- Mild GIT disturbanesnausea, diarrhoea and abdominal pain
- Allergic reactions
- Rare : Granulocytopenia, loss of hair and elevation of liver enzymes

- Pregnancy ??

Uses..

- 100% cure rate for round worm, hook worm, enterobius (less for Strongyloides) and trichuris
- 75% effective for tape worms but not for H. nana
- Hadatid cyst: prolonged treatment

Albendazole

- Congener of Mebendazole
- **Pharmacokinetics:**
- Fatty meals enhance absorption
- Its active and penetrates brain with t1/2 of 8-9 Hrs – **basis of tissue anthelmintic action**
- For intesinal worm given in empty stomach and for tissue action – with fatty meals

Uses..

- Single dose is enough in many cases. Eg: Ascariasis, Hookworm and Enterobiasis . (3 day treatment with mebendazole)
- Superior to Mebendazole in Strongyloidosis, Hydatid disease.
  But, inferior in Trichuriasis.
- Treatment of choice : Cutaneous larva migrans, Neurocysticercosis, Hydatid disease
- Filariasis: with DEC or Ivermectin – in lymphatic filariasis

Adverse effects..

- When used for 1-3 days, nearly free of significant adverse effects.
- Mild and transient epigastric distress, diarrhea, headache, nausea, dizziness, lassitude, and insomnia can occur.
- In long-term use can cause abdominal distress, headaches, fever, fatigue, alopecia,increases in liver enzymes, and pancytopenia.
- Caution in patients with hepatic or renal disease.

Thiabendazole

- First benzimidazole polyanthelmintic
- It inhibits development of eggs of worms & kills larvae
- It has **analgesic,antiinflammatory & antipyretic action**
- Mechanism of action similar as mebendazole
- Well absorbed from GI tract
- Adverse effects : Nausea,vomiting,loss of appetite,giddiness, itching,abd. pain,diarrhoea

Thiabendazole…

- Uses..
  - Symptomatic relief in Cutaneous larvae migrans, Guinea worm disease
  - In Strongyloidosis & Trichinosis

Muscle paralysers..

- Pyrantel pamoate
- Piperazine
- Levamizole

Pyrantel pamoate

- Originally for **pinworms** but extended to hook worm and round worms
  - Less active against necater, strongyoides and trichuris

- Mechanism of action
- Activation of nicotininic cholinergic receptors
- Persistent depolarization leding to contracture and spastic paralysis – expelling of worms

Pyrantel pamoate…

- **Pharmacokinetics:** Only 10-15% is absorbed

- **Adverse effects**
  - Usually free from ADRs
  - Mild GIT symptoms, tastelessness
  - Headache

- Note: Piperazine though used for same purpose it antagonize the action of pyrantel pamoate.

Piperazine

- Reversibly inhibit N-M transmission
- Uses : Round worm, Pin worm
- C/I in pregnancy, Epilepsy, Renal failure
- Adverse effects
  - GI Disturbances
  - Hypersensitivity
  - Drowsiness
  - Confusion
  - Rarely muscular incordination

Levamisole

- Nicotine like effect : Stimulation and subsequently blocking N-M transmission
- Uses : Round worm
- Adverse effects
  - GI disturbances <1 %
  - Blood dyscrasis occasionally

Drugs used in Intestinal Helminths

- **Roundworms (Ascariasis)**
  - *Mebendazole, Albendazole, Pyrantel, Piperazine, Levamizole*
- **Pinworm (Enterobiasis)**
  - *Mebendazole, Albendazole, Pyrantel, Piperazine*
- **Hookworm (Ankylostomiasis)**
  - *Mebendazole, Albendazole, Pyrantel*
- **Whipworm (Trichuriasis)**
  - *Mebebdazole, Albendazole*
- **Strongilodiasis**
  - *Thiabendazole, Albendazole*

Diethyl carbamazine citrate (DEC)

- Drug of choice for the treatment of filariasis, loiasis and tropical eosinophilia
- Mechanism of action
  - Modifies parasite & Susceptible to host's immune mechanism
  - Alteration of Mf membrane – to be readily phagocytosed by tissue monocytes
  - Since piperazine derivative – hyperpolarization and muscular weakness

DEC : Pharmacokinetics

- It is synthetic piprazine derivative
- Rapidly absorbed from gut
- It has a half life of 2-3 hours
- It is excreted in urine unchanged
- Dosage is reduced in urinary alkalosis and renal impairment

DEC…

- Adverse effects
  - Nausea, vomiting, loss of appetite
  - Febrile condition – rash, pruritus, enlargement of lymph nodes

    withdraw the drug and start antihistamines and corticosteroids
  - Can be minimized by starting low dose

Praziquantel

- Action: Mainly on Schisosomiasis and other Trematodes, cestodes but not nematodes
- Mechanism of action :
  - Rapidly taken up by worms
  - Leakage of intracellular Ca++ causing paralysis
  - Worms lose grip on intestinal wall

Praziquante…

- Pharmacokinetics
- Rapidly absorbed and enhanced by food
- High first pass metabolism
- Crosses BBB and attains therapeutic concentration in CSF
- Phenytoin, carbamazepine and steroids induce metabolism – failure of therapy

Praziquante…

- Adverse effects
- Bitter in taste, produce nausea and vomiting and abdominal pain
- Headache, dizziness and sedation
- Urticaria, rash, fever etc- destroyred flukes

Ivermectin

- Action:
  - Drug of choice for Onchocercosis and Strongyloides
  - Equal to DEC in Filaria
  - Also efective against cutaneous larva migrans and ascariasis
  - Also scabies and head lice

Tissue Helminths

- Filariasis & Loiasis : DEC
- Onchocerciasis : Ivermectin
- Trichnosis : Thiabendazole
- Dracontosis : Thiabendazole

Other Helminths

- Larva migrans : Thiabendazole, Albendazole
- Tapeworms : Praziquantel, Niclosamide
- Cystercercosis : Praziquantel
- Hydatid cyst : Albendazole (Adjunct to Sx)
- Schistosomiasis : Praziquantel
- Flukes : Praziquantel

THANK YOU