Antihelmintic Drugs

- May act by :

A ) Paralyzing the worm .

B ) Damaging the worm leading to partial digestion or rejection by immune mechanism .

C ) Interfering with the metabolism of the worm .

* Humans are the primary hosts for the most of helminthic infections

* Most worms produce in human sexually by producing eggs and larvae
* These pass out of body and infect the secondary host .
* Immature forms invade humans via skin or GIT and mature to adult worms with characteristic tissue distribution.
* Worms or larva live in other tissues of the host like muscles , viscera , meninges , lungs , or subcutaneous tissue .
* Adult filariae live in the lymphatics , connective tissue , or mesentery of the host and they produce live embryos or microfilariae , which go to the blood stream .

- The Antihelmintic Drugs are :

1. Albendazole
2. Mebendazole
3. Thiabendazole
4. Pyrantel Pamoate
5. Piperazine
6. Niclosamide
7. Diethylcarbamazine
8. Ivermectin
9. Bithionol

ALBENDAZOLE

* A broad spectrum drug .

- Pharmacokinetics :

* It’s a benzimidazole carbamate .
* Erratically absorbed after oral administration. Absorption increases with fatty meals.
* Metabolized in the liver into an active metabolite ( albendazole sulfoxide )

* T1/2 = 8-12 hours.
* Sulfoxide is mostly protein bound , and distributed well to tissues and enters bile , CSF , and hydatid cysts . It passes the BBB and excreted in urine .

- Mechanism of action :

* It inhibits microtubule synthesis ( by binding to β tubulin ) in nematodes , and also irreversibly impairs glucose uptake , so the intestinal parasites are immobilized & die slowly
* It is larvicidal in hydatid , cysticercosis , ascariasis , and hook worm infections.
* It’s also ovicidal (Kills the eggs of ) hookworms , ascaris , and trichuris .

- Clinical Uses :

* Used on empty stomach when used against intraluminal parasites but with fatty meal when against tissue parasites.
1. In ascaris , trichuriasis , hookworm , and pinworm infections : a single dose of 400 mg orally .
2. Hydatid diseases ( Echinococcosis ) : drug of choice , a dose of 400 mg twice with meals for one month or longer .
3. Neurocysticercosis : Corticosteroids are usually given with albendazole to decrease inflammation caused by dying organisms and it also reduces the duration of course i.e. 400 mg twice daily for 21 days .
4. Other infections : Drug of choice in cutaneous and visceral larvea migrans , intestinal cappillariasis , trichinosis , giardiasis , gnathostomiasis , and taeniasis .

- Adverse Effects :

- In short term use (1-3 days) : mild epigastric pain , diarrhea , nausea , headache , and insomnia .

- In long term use ( when used in hydatid cyst & cysticercosis ) : abdominal pain , headache , fever , fatigue , alopecia , pancytopenia . Blood count & liver enzymes should be followed .

* Not given during pregnancy and in hypersensitive people.

MEBENDAZOLE

* a synthetic benzimidazole .
* has wider spectrum and is safer than albendazole .

- Mechanism of action :

* same as that of albendazole .

- Pharmacokinetics :

* Less than 10% of orally administered drug is absorbed .
* Absorption increases with fatty meal.
* Absorbed drug is 90 % protein bound
* It is converted to inactive metabolites rapidly in liver.
* It has a half life of 2-6 hours , and is primarily excreted in urine.

- Clinical uses :

* It is taken orally before or after meals , the tablets should be chewed before swallowing

* Pinworm infection : 100 mg as a single dose, to be repeated after 2-3 weeks .
* Ascaris lumricoides , trichuris trichura , hookworm , and trichostrongylus infections : 100 mg twice for 3 days in adults and children over 2 years of age .
* In adults and children over 2 years cure rate is 90-100 % except hook worm it’s less
* Other infections : intestinal capillaries , trichinosis , taeniasis , and strongyloidosis .

- Adverse effects :

* Short term therapy : Mild GI disturbances .
* With high doses : Hypersensitivity reactions , agranulocytosis , alopecia , elevation of liver enzymes
* Hepatic parenchymal disease .

- Cautions & Contraindications :

* Used with caution under 2 years of age may cause convulsion

* Enzyme inducers and inhibitors affect plasma level of the drug.
* Contraindicated in pregnant women .

THIABENDAZOLE

* It is a benzimidazole , and is a chelating agent that forms stable complexes with metals including iron , but does not bind with calcium .
* It’s an alternative to ivermectin for strongyloidiasis (roundworm) and cutaneous larva migrans .

- Pharmacokinetics :

* Taken orally , and is rapidly absorbed .
* Almost completely metabolized in the liver , and is excreted in the urine .
* Has a half life of 1.2 hours & can be absorbed from the skin .

- Mechanism of action : similar to other benzimidazoles.It is ovicidal for some paracites .

- Clinical Uses :

* Should be given after meals with the tablets being chewed .
1. Strongyloidiasis .
2. Cutaneous larva migrans : Thiabendazole cream can be applied topically or the local frug given for 2 days .

- Adverse effects :

* More toxic than other benzamidazoles

* Dizziness , anorexia , nausea , and vomiting are common

* Less frequent problems include epigastric pain , abdominal cramps , diarrhea , pruritus , headache , and neuropsychiatric symptoms .
* Irreversible liver failure , and fatal Steven-Johnson Syndrome

- Cautions & Contraindications :

* Limited in children weighing less than 15 Kg

* Shouldn’t be used in pregnancy .
* Not used in the presence of hepatic or renal failure .

PYRANTEL PAMOATE

* A broad specturm anthelmintic drug .

- Pharmacokinetics :

* Poorly absorbed from GIT ( active mainly against luminal organisms ) .

* Half of the drug is excreted unchanged in the feces .

- Mechanism of action :

* It’s a depolarizing neuromuscular blocking agent

* Causes the release of Ach , and inhibition of cholinesterase . This results in the paralysis & expulsion of the worms

- Efficacy :

* Not effective against trichuriasis (whip worms) , or strongyloidiosis .
* Oxalate pamoate is effective in the treatment of trichuriasis

* Not effective against migratory stages in the tissues or against ova .

- Clinical Uses :

* Enterobius vermicularis (pin worm) : single dose to be repeated in 2 wks.
* Ascaris lumbricoides (common round worm) : single dose to be repeated after 2wks .
* Ankylostoma dudenale (hook worm) : single dose for light infection but a 3 days course is necessary for heavy infection. Especially N americanus ( picture ) .

- Adverse effects :

* GIT disturbances .

* Dizziness , drowsiness , headache , and insomnia .
* Rash & fever .

- Cautions & Contraindications :

* Used with caution in patients with liver dysfunction .
* Limited in pregnant women & children under age of 2 years .

PIPERAZINE

* An alternative in the treatment of ascariasis

- PK : Absorbed from the GIT , metabolized in the liver , and excreted in the urine .

- Mechanism of action :

* Causes paralysis of ascaris by blocking Ach at the myoneural junction; unable to maintain their position in the host , live worms are expelled by normal peristalsis .
* Not recommended for other helminth infections .

- Clinical uses :

* For ascariasis : 75 mg/kg/day orally for 2 days at breakfast .
* For heavy infections , treatment should continue for 3-4 days , or repeated after one week .

- Adverse effects :

* GIT disturbances .
* Neurotoxicity : Serum Sickness Like Syndrome ( Type II hypersensitivity reaction )

- Cautions & Contraindications :

* Patients with history of epilepsy

* Patients with impaired liver or renal functions .
* Patients with severe malnutrition or anemic patients .
* Patients with chronic neurological diseases .
* Pregnant women .

NICLOSAMIDE

* 2nd line drug for the treatment of most tapeworm infections .

- Pharmacokinetics :

* Despite the fact the it’s minimally absorbed from the GIT , it’s taken orally

* Neither the drug nor its metabolites have been recovered from the blood or urine .

- Mechanism of action :

* Adult worms ( BUT NOT OVA ) are rapidly killed , presumably due to inhibition of oxidative phosphorylation or stimulation of ATPase activity .

- Clinical Uses :

* T.saginata , T.solium , and Diphyllobothrium latum :
* For D.latium & T.saginata : a single dose of 2g is given in the morning on an empty stomach .
* It’s probably equally effective against T.solium .
* Cysticercosis is theoretically possible after the treatment of T.solium infections, because viable ova are released into the gut lumen following digestion of segments. The drug should be given 2 hours later to eliminate mature & adult parasites.
* Hymenolepis nana : it’s effective against adult parasites .

- Adverse effects :

* GIT disturbances .
* Headache , skin rashes , and pruritus .

- Cautions & Contraindications :

* Alcohol consumption should be avoided on the day of treatment and one day afterward .
* Not used in children under the age of 2 , and not in pregnant women .

DIETHYLCARBAMAZINE

* It’s a synthetic peperazine derivative.
* drug of choice for the treatment of filariasis , loiasis , and tropical eosinophillia

- Pharmacokinetics :

* Rapidly absorbed from the GIT , metabolized in the liver , and excreted in the urine unchanged .
* Has a wide distribution including the CSF .
* Has a half life of 2-3 hours which increases in alkaline urine to 10 hours .
* Dosage is reduced in urinary alkalosis and renal impairment .

- Mechanism of action :

* It immobilizes microfilariae and alters its surface structure , displacing them from tissues and making them susceptible to destruction by host defense mechanisms

* It has an immunosuppressive effect .

- Clinical uses :

* Wuchereria bancrofti , Brugia malayi , Brugian timori , and Loa loa :
* Microfilariae of all species are rapidly killed; adult parasites are killed more slowly.
* The drug is highly effective against Loa loa .
* Dose : 2mg/kg tid for 3 weeks .
* For W.bancrofti infections , to decrease the incidence of allergic reactions to dying Microfilariae , a single dose is administered on the 1st day , 2 doses on the 2nd day , and 3 doses on the 3rd day .
* For Loa loa ( with risk of encephalopathy ) or B.Malayi infection , individual doses should start at 1 mg/kg once on the 1st day , and gradually increases over 5-6 days .
* Antihistamines & Corticosteroids are given in allergic manifestations .
* Blood should be checked for Microfilariae several weeks after treatment , a course maybe repeated after 3-4 weeks . Complete cure may require several courses of treatment over 1-2 years .
* The drug may also be used for chemoprophylaxis ( 300 mg weekly ) .
* Tropical Eosinophilia : 2mg/kg tid for 7 days .

Cont’d :

- Adverse effects :

A ) Drug induced reactions :

* Frequent : Headache , malaises , anorexia , and weakness .
* Less often : nausea , vomiting , and sleeplessness .

 B ) Reactions induced by the dying parasite :

* Fever , malaise , popular rash , headache , GIT symptoms , cough , and chest , muscle , or joint pain .
* Leukocytosis is common .
* Retinal hemorrhage .
* Encephalopathy .
* Lymphangitis & lymph abscess

- Cautions & Contraindications :

* Caution is advised when using the drug in patients with hypertension or renal disease .
* Patients suspected to have malaria should be treated before given the drug for fear of relapse .
* Patients with lymphangitis should be treated with Quiescent ( enough to treat ) periods .
* It’s not teratogenic , but should be used with caution

IVERMECTIN

* A semisynthetic macrocyclic lactone .

- Pharmacokinetics :

* It’s only given orally , metabolized by the liver , and is exclusively excreted in the feces

* Widely distributed , but NOT to the CSF

* Has a half life of 16 hours .

- Mechanism of action :

* It intensifies GABA-mediated transmission of signals in peripheral nerves .
* Which leads to the paralysis of the nematodes & arthropods .
* In onchocerciasis , Ivermectin is microfilaricidal . It doesn’t effectively kill adult worms but blocks the release of microfilariae for some months after therapy .

- Clinical Uses :

* Onchocerciasis ( River Blindness ) : [ Drug of choice ]

* Single dose of 150mcg/kg with water on an empty stomach . Doses are repeated every 3 months for a year .
* After acute therapy , treatment is repeated at 12-month intervals until the adult worms die , which may take 10 years of longer .
* Strongyloidiasis : [ Drug of choice ]

* Treatment consists of 2 daily doses of 200mcg/kg . Stool analysis should be repeated 3 times at month interval .
* Bancroftian Filariasis : it’s microfilarial only .
* Scabies & cutaneous larva migrans .

- Adverse effects :

* In strongyloidiasis treatment : infrequent fatigue , dizziness , and GIT disturbances .

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Cont’d :

* In onchocercosis treatment :
1. Mazotti reaction ( a hypersensitivity reaction ) : fever , rashes , pruritus , headache , dizziness , somnolence (or "drowsiness") , weakness , diarrhea , arthralgia , hypotension , reflux tachycardia , lymphadenitis , and peripheral edema .
* Due to killing microfilaria , steroid may be necessary for several days .
1. Swelling and abscesses occasionally occur at sites of adult worms .
2. Corneal opacities ( Corneal opacity is a disorder of the cornea, the transparent structure on the front of the eyeball, which can cause serious vision problems. Corneal opacity occurs when the cornea becomes scarred. This stops light from passing through the cornea to the retina and may cause the cornea to appear white or clouded over ) .

- Cautions & Contraindications :

* Concomitant use of ivermectin and other drugs that enhance GABA activity such as Barbiturates, bnezodiazepines, and valproaic acid

* Should not be used in pregnancy .
* Impaired BBB e.g. meningitis .
* Safety in children under 5 years of age has not been established .

BITHIONOL

* An alternative drug for the treatment of pulmonary paragonimiasis

* The drug of choice for the treatment of fascioliasis ( sheep liver fluke )

- Pharmacokinetics :

* It is orally administered and excreted in urine .

- Clinical use :

* Used for the treatment of paragonimiasis and -

Fascioliasis , the dosage is 30-50 mg/kg in 2 or 3

Divided doses , given orally after meals on alternate days for 10 - 15 days .

- Adverse effects :

* Diarrhea & abdominal cramps are the most common

* Anorexia , nausea , and vomiting .
* Pruritus & urticaria .
* Dizziness & headache .
* Leucopenia .

- Cautions & Contraindications :

* Used with caution for children under the age of eight .
* Patients whom their liver functions and hematological tests show hepatitis & leucopenia .

