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The Pharmacological Implications of The Drug Used for Parasitic and Antihelminhic Infections-Overview

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ABSTRACT

Nematodes, they are worms which mostly have disease causing ability. Many nematodes in the phyla nematoda causes serious disease conditions. Most of them are parasitic in nature. Nematodes like Necator americanus (hookworm) the Ancylostoma duodenale (hookworm), Ascaris lumbricoides, Enterobius vermicularis (pinworm), the Trichuris trichiura species (whipworm), and Strongyloides stercorali, they target various parts of human body. To get rid of these nematodal infection drugs like Albendazole, Praziquantel, Mebendazole etc

KEYWORDS: *Nematodes, worms, Albendazole, Praziquantel, Mebendazole*

INTRODUCTION

The phyla nematodes mainly has several diverse worms, which have varying strata of pathogenicity. Nematodes like *Necator americanus* (hookworm), the *Ancylostoma duodenale* (hookworm), *Ascaris lumbricoides, Enterobius vermicularis* (pinworm), the *Trichuris trichiura species* (whipworm),*Taenia* (tape worm)and *Strongyloides stercoralis.*All these organisms causes varying disease, their target of infections is different.

Nematodes

Nematodes or the roundworms phyla are the most common human parasites in the world. The intestinal nematodes that most commonly infect the humans are *Necator americanus* (hook worm), the *Ancylostoma duodenale* (hookworm), *Ascaris lumbricoides, Enterobius*

vermicularis (pinworm), the *Trichuris trichiura species* (whipworm), and *Strongyloides stercoralis.* Although all are members of the phyla Nematoda, they have varying disease processes that are clinically manifested and treated uniquely in humans (Schultz-Key et al.,1986).

Hookworm

The Nematodes in the Ancylostomatidae family are commonly known as hookworms. The species that generally affect the humans are *Necator americanus* and *Ancylostoma duodenale. Ancylostoma braziliense* is the causative species for the specific type of infection called cutaneous larva migrans (CLM).

Together Asia and sub-Saharan Africa have the much largest number of cases of hookworm annually. Since there is no reporting or surveillance in North America for the hookworm, the prevalence is unknown. The risk of infection and overall worm burden rises with aggrandizing age, with the highest prevalence in middle-aged persons (Roux et al.,1989).

Hookworm infections are acquired by the humans through soil penetration of the skin or through ingestion. The larvae stage are most commonly transmitted to those working in agricultural settings and on the exposure of bare feet to soil. Larval hookworms can live in the soil for weeks and will mainly resume development once in contact with human serum and tissues. After 5 to 8 weeks of entering the human hosts, the hookworm is sexually mature and will begin producing thousands of eggs each day. The *A duodenale* can live in the human intestine for about 1 to 3 years and *N americanus* for 3 to 10 years(Schultz-Key et al.,1985).

The Clinical presentation of *A duodenale* and *N americanus* may include pruritis of the skin typically in the hands and the feet accompanied by a papulovesicular rash. Acute infection with *A braziliense* results in the CLM presenting as folliculitis or burrows in the feet, buttocks, and abdomen. The CLM is more common among travelers to the Caribbean and residents of the Atlantic and Gulf coasts of the United States. The Hookworm larvae migrate through the pulmonary vasculature and lung parenchyma resulting in the cough, sore throat, and fever, which may be accompanied by the eosinophilic infiltrates. Once the larvae leave the lungs through coughing and enter the gastrointestinal tracts, epigastric pain may occur. The gastrointestinal symptoms seen, including pain, flatulence, and nausea, the peak between

30 and 45 days after infection. The Blood eosinophils peak at the onset of gastrointestinal symptoms. Diagnosis is made mainly by identifying hookworm eggs in a stool sample (Rougemont,,1982).

The major clinical manifestation of hookworm infection is iron deficiency anemia and protein energy malnutrition from the blood loss. Blood loss from the gastrointestinal tract is secondary to the hookworm attachment to the intestinal mucosa, which ruptures capillaries and arterioles. The risk for anemia is much highest in pregnant women and children. If there is an unusually high worm burden, protein loss can pave to malnutrition (Rothova et al.,1989).

Two anthelmintics currently available in the country of United States have been studied for the treatment of hookworm: albendazole and the pyrantel pamoate. A systematic review and meta-analysis assessing the efficacy of the drug albendazole single-dose regimens evaluated 14 randomized placebo-controlled trials encompassing 742 patients. The effect of albendazole on *A duodenale* and *N americanus* was evaluated and assesed. The mean cure rate was 72%, while the egg reduction rate ranged from 64.3% to 100%. Pyrantel pamoate was evaluated in the same systematic review and by meta-analysis. Four randomized, placebo-controlled trials of 152 patients were encompassed. The mean cure rate was 32%, and the egg reduction rate ranged from 56.6% to 75% (Rivas Alcala et al., 1987). Praziquantel may be effective for reducing hookworm burden but the cure rates have not been established. Mebendazole (cure rate of 15%) and levamisole (cure rate of 10% to 12.0%) are modestly effective but not available in the United States (Richards et al., 1989).

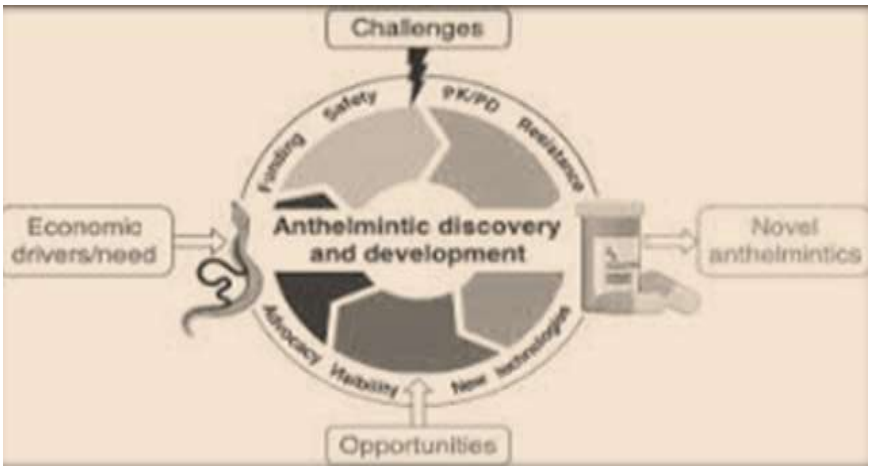

Figure: 1

Ascaris lumbricoides

Ascaris lumbricoides is the most common infectious intestinal worm known worldwide. Some estimates put the infection globally at over 1 billion people annually. The high prevalence of infections may be due in part to the pervasiveness of the organism and the ability of the female to lay up to 200 000 eggs per day. The Adult worms appear pink in color with tapered ends, and infection typically occurs by the ingestion of the eggs from soiled hands, food products, or other fomites. The Eggs hatch in the intestine within about 1 to 2 days after ingestion, molt into the second stage larvae, and travel through the blood to the liver and lungs. Once in the lungs the larvae penetrate the respiratory structure named alveoli and gain access to the capillary beds at which point they again molt, this time tothe third stage larvae. The larvae ascend the endobronchial tree, are mainly swallowed, and return to the intestine. The mature females begin synthesizing eggs 2 to 3 months after the initial infection (Richards et al.,1989).

The Symptoms can be seen 5 to 6 days after the initial ingestion. After the larvae travel to the lungs 14 days after the ingestion, the patient may experience wheezing, dyspnea, cough, and fever lasting 10 days or more (the Loeffler's syndrome). Infiltrates in the lungs can be observed on X-ray image, and the patient may have an increase in eosinophils. This is seen in much more severe infections, whereas mild to moderate infections may be asymptomatic. The Other common symptoms are abdominal pain, nausea, anorexia, diarrhea, and/or constipation. Heavy infection or the chronic disease may rarely cause intestinal or biliary obstruction, appendicitis, and the intestinal perforation necessitating surgical intervention. Diagnosis is made through the identification of the eggs, larvae, or adult worms (Mishra et al.,2008).

Several anthelmintics can be availed for treatment of *A lumbricoides* infection. In the absence of mebendazole, albendazole is the treatment of choice. A meta-analysis of the 10 placebo controlled trials or the dummy trials of albendazole found egg reduction rates of 86.5% to 100% and a cure rate of 88% compared to the placebo. There are varying dynamics of disease (Dr. S. Sreeremya,2024a). Placebo is an effective way of treatment (S. Sreeremya,2022). The advancement in pharmacology (Dr. S. Sreeremya, 2024b) and biotechnology paved the way to understand in detail about the drugs and diseases (Dr. S. Sreeremya,2024c).

In contrast, cure rates for mebendazole in the same meta-analysis were 95% with the egg reduction rates of 96.1% to 99% (Bryan et al.,1991). Ivermectin, nitazoxanide, and the pyrantel pamoate are alternative agents available in the United States. A randomized, double-blind study and analysis of ivermectin compared to albendazole for the treatment of the intestinal nematode infections was conducted in China. The study evaluated 818 patients infected with nematode infections. The cure rates for *Ascaris* were similar, with the ivermectin (100%) and albendazole (99%) demonstrating the efficacy of ivermectin against this nematode. The Nitazoxanide has been evaluated in a study of 70 children with the *Ascaris* who were randomized to treatment with either albendazole or nitazoxanide. The Nitazoxanide produced a cure rate of 89% and an egg reduction rate of 99.9% while albendazole had similar cure rate of 92% and an identical egg reduction rate (Pilotte et al.,2016). Pyrantel pamoate has been evaluated in a meta-analysis of 3 randomized placebo-controlled trials that included 132 patients. The mean cure rate was 89%, and 1 of the 3 trials reported an egg reduction rate of 87.9%.

Pinworm

The *Enterobius vermicularis*, or pinworm, is a white threadlike worm primarily infecting the cecum and adjacent bowel. The Worldwide estimates of infection are nearly 30%, while prevalence rates may be as high as 100%.Humans are believed to be the only known carriers or vectors; however, common household pets may transfer eggs on their fur(Chatterjee,2009).

Drugs like Vermox

Do not use the Vermox suspension if:

- Patients are allergic to anything in Vermox suspension (listed in section 6 below)
- Patients is pregnant Do not use this medicine if any of the above applies to you. If Patient is not sure, talk to your doctor or pharmacist before using Vermox suspension. Warnings and precautions
- The Vermox suspension should not be given to children under 2 years of age (Dent et al.,1972)
- The Vermox should only be given to younger children if your doctor has specifically prescribed it. Your doctor will decide whether Vermox is suitable for your child. One must follow the doctor’s instructions carefully.
- Convulsions (seizures) have been reported, encompassing in infants. Vermox should only

be given to children under 2 year of age if the doctor has specifically prescribed it. Taking other medicines Please tell the doctor or pharmacist if you are taking or have recently taken any other medicines. This encompassess medicine that you buy without a prescription, herbal medicines, dietary supplements or the vitamins.

In particular, tell your doctor or pharmacist if you are taking:

- **The Metronidazole**- for certain infections
- **Cimetidine**- for excess stomach acidity talk to the doctor before using Vermox suspension if you are taking any of these medicines.

Pregnancy and the breast-feeding

- Do not take Vermox suspension if you are pregnant, think one may be pregnant or might become pregnant
- Ask your doctor or pharmacist for advice if one is breast-feeding Driving and using machines this medicine is not likely to affect one being able to drive or use any tools or machines.

Important information about some of the ingredients of the Vermox suspension Vermox suspension contains

- **Sucrose.** If the doctor has told you that you are intolerant of some sugars, contact them before taking this medicine
- The Methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216). This may cause severe allergic reaction. This reaction may happen some time after one have taken Vermox suspension
- This medicine contains less than 1 mmol sodium (23 mg) per mL, that is to say essentially the 'sodium-free (Thein-Hlaing et al.,1990).

Lymphatic Filariasis (LF)

The Lymphatic filariasis (LF) is a parasitic disease, commonly known as elephantiasis. It is caused by the thread like worms known as filarial parasite. The adult worms (male and female) settle in the lymph nodes and the female worm gives birth to millions of young ones known as microfilariae (mf).

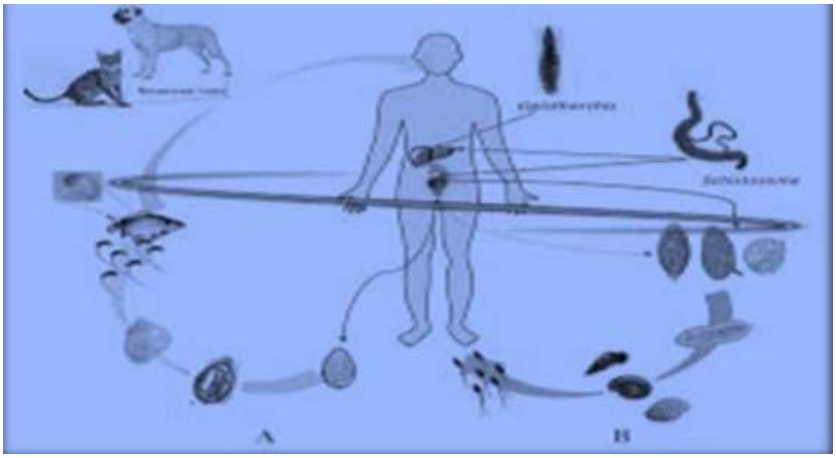

Figure: 2

The Mode of LF transmission

The Filarial parasite species in India lives only in man. The adult worm produces microfilaria which mainly circulates in the peripheral blood system of the infected people. When the mosquito feeds on the infected person, it mainly ingests the microfilaria. 2 The ingested microfilaria grows and within 12 days, it reaches the stage when it can infect another human being. When the mosquito with the infective stage larva bites another person, the parasite enters and reaches the lymphatic systems. How to prevent infection? Administration of single dose of antifilarial drugs to the entire community (the mass drug administration), yearly once for 5-6 years. Diethylcarbamazine (DEC) and albendazole are the drugs used for mass drug administration Protection from the mosquito bites

Dec and Albendazole Tablets During Mass Drug Administration (MDA)

People living in filaria endemic areas, who look healthy, may be carrying the mf in their blood without any recognizable symptoms at the very initial stage (Jardim-Botelho et al.,2008). Finding the infected persons at this crucial stage and giving them alone treatment is tedious. Both DEC and albendazole are safe drugs and even non-infected can take the drugs. DEC kills mf and albendazole normally clears the intestinal worms, which is an added benefit. When both the drugs are given to-gether, it has synergestic effect on adult worm and therefore the parasites will be destroyed preventing the infected persons from developing disease When every individual in the community takes the drugs under MDA, microfilaria will be cleared and not present in the blood for the mosquitoes to mainly transmit. MDA repeated annually over 5-6 years may interrupt transmission. This eventually paving to future generation being free of this infection (Albonico et al.,2008).

DRUGS USED

1. Albendazole

Albendazole is a member of the drug class benzimidazoles, it has wide classification. It acts by compromising the cytoskeleton, impairing the locomotion and reproduction. It also has ovicidal and larvicidal effects. It is availed for the treatment of pinworm and hookworm infections, ascariasis, trichuriasis and the strongyloidiasis. It has systemic activity also, and is the drug of choice for treating cysticercosis and the hydatid disease. Its ovicidal activity is better than that of mebendazole(Savioli et al.,2000).

2. Mebendazole

This is a synthetic benzimidazole anthelmintic drug and has the twin advantages of wide spectrum and safety. The drug has poor absorption when given orally and hence is availed for intestinal parasites. It blocks the uptake of the glucose by worms, thus reducing survival and reproduction. It also kills eggs of hookworms, ascaris, and the trichuris.

Mebendazole is recommended for the treatment of the ascaris, the hookworms, pinworm and trichuris. The drug can be taken before or after meals, but tablets should be orally chewed

3. Pyrantel pamoate

This drug is a nicotinic receptor agonist. It mainly causes spastic muscular paralysis of the worms, which lose their grip in the intestines and are mainly expelled by normal peristalsis. Pyrantel pamoate is effective against hookworms,the pinworms, and ascaris, but not against trichuris and the strongyloides. Since the drug is poorly absorbed, it is mainly useful against intestinal worms. For pinworms, a single dose is much effective, but should be repeated after two weeks to take care of reinfection (Horton,2003).

4. Tetramisole and levamisole

These drugs cause a much prolonged activation of the excitatory nicotinic acetylcholine receptors in worms, paving to spastic paralysis. The paralysed worms are then expelled from the body by peristalsis. Levamisole is the more active isomer and can be availed for the treatment of hookworms and ascariasis.

Levamisole dose: age less than 12 years: 2.5 mg/kg. Age 12–18 years: 150 mg.

5. Ivermectin

This is one of the newest anthelmintics, introduced in the year 1980s. It is a semi-synthetic derivative of avermectin. Other similar drugs are moxidectin, the doramectin, milbemycin oxime, eprinomectin, abomectin, and selamectin.

Ivermectin causes a paralysis of the pharyngeal and body wall musculature of nematodes. It is the drug of choice for strongyloides and onchocerciasis (river blindness). Against strongyloidiasis, the drug ivermectin has a cure rate approaching 100% (Gonzalez-Moreno et al.,2011).

6. Niclosamide

Niclosamide is a derivative of the salicylamide. It is used as a second line drug for the treatment of tapeworm infections. It kills the adult worms rapidly by inhibition of oxidative phosphorylation. It does not kill ova.The tablets should be orally chewed. Oral absorption is minimal, and this drug is availed for intestinal parasites. The cure rates against *Taenia saginata* and *Taenia solium* are about 95.2%. Against the *Diphyllobothrium latum*, it is somewhat less effective, with a success rate of 85.4% (Stephenson et al.,2000).

7. Piperazine

This is a drug availed for ascariasis and pinworms. Against ascariasis, the cure rate is 90%. It causes paralysis of the worms, which are then expelled along with the faeces.

The Adverse effects are nausea, vomiting, abdominal pain, diarrhea, and headache. Rarely, some patients may have much of an allergic reactions or neurotoxicity. Piperazine should be avoided in pregnancy, people with the reduced hepatic and renal function, and in those with a history of epilepsy or chronic neurological disease (Greenland et al.,2015).

8. Praziquantel

Praziquantel is a synthetic isoquinolone–pyrazine derivative. Among the intestinal parasites, it has activity against the tape worms. It is well absorbed, and is mainly availed for systemic parasites such as the schistosomes.

Praziquantel is the drug of choice against *H. nana*. It is also effective against the species *T.*

solium, *T. saginata*, and *D. latum*, in a single dose. Against the species *T. saginata*, its cure rate is 100%.Common adverse effects are headache, dizziness, the state of drowsiness, lassitude, loose stools, abdominal pain(Kattula et al.,2014).

CONCLUSION

There are much serious diseases caused by several pathogenic nematodes. The drugs mainly used for preventing and remediatiing these disease are niclosamide, mebendazole, albemndazole, ivermectin, praziquantel, diethylcarbamzine(DEC)etc.The life cycle and features of nematodes and their site of action and their broad pharmacological implicaations are discussed vividly.

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