The Egyptian Journal of Hospital Medicine (October 2022) Vol. 89 (2), Page 7680- 7683

Updated Treatment Modalities of Trichinellosis: Review Article

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ABSTRACT

Background: Trichinellosis is a food borne widespread zoonotic pathogen distributed all over the world, Trichnella spiralis (T. spiralis) is the most popular species to cause the disease. Medications such as anthelmintics (mebendazole or albendazole) and glucocorticosteroids are used to treat the condition.

Objective: This review article aimed to assess the updated treatment modalities of trichinellosis.

Methods: We searched PubMed, Google Scholar, and Science Direct for information on Trichinellosis with treatment. However, only the most current or comprehensive study from May 2006 to May 2022 was considered. The authors also assessed references from pertinent literature. Documents in languages other than English have been disregarded since there aren't enough resources for translation. Unpublished manuscripts, oral presentations, conference abstracts, and dissertations were examples of papers that weren't considered to be serious scientific research.

Conclusion: Trichinellosis treatment presents a number of challenges. During the time of intestinal invasion, anthelmintics are required (i.e., less than 1 week after infection). Treatment is typically initiated at the earliest stages of larval development in muscle cells, but this is rarely attainable. Efforts to improve Trichinellosis treatments by the use of pharmaceuticals are the target. Mebendazole and albendazole are the most often used medications for treating trichinellosis. Pyrantel is safe for usage by pregnant women and children. The bacterium Streptomyces avermitilis is responsible for producing ivermectin, which is then classified as a macrocyclic lactone.

Keywords: Trichinellosis, Treatment guidelines.

INTRODUCTION

Trichinellosis (formerly known as "trichinosis") is a zoonosis caused by parasitic nematodes of the genus Trichinella and is spread through the consumption of contaminated food products. The most common species responsible for the disease is Trichnella spiralis (T. spiralis). Although most Trichinella species are found in mammals, there is one species that is known to infect birds, and a new genotype has been recently reported in crocodiles in Africa, making this an infection with a global distribution [(1)].

Globally, trichinellosis is still a major health issue. In particular, it has been estimated that 10 million peoples throughout the world are infected, and during the past decade, an uptick in the prevalence of infection has been documented among domestic pigs and wildlife, with a subsequent increase among humans [(1)].

Trichinellosis is considered a rare disease in countries where the Muslim religion is predominantly practiced, but outbreaks in isolated cases who eat pork occur. Considering that the vast majority of people in Algeria and Senegal are Muslims, trichinellosis has only ever been reported there among Europeans [(2)].

The rate of occurrence decreased to 1.7% in the year 2000. High prevalence rates of infection (up to 13.3%) have been reported in synanthropic rats of Alexandria abattoirs. Two strays, as well as farmed pigs, have tested positive for T. spiralis. Larvae of the Trichinella species have also been found in Sinai wolves. Epidemiological evidence suggests both a domestic and sylvatic cycle are at play in Egypt [(3)].

Treatment Guidelines:

1) Anthelmintic drugs:

a) Albendazole as well as mebendazole:

Primary medications for treating trichinellosis. Intestinal worm medications work best when administered within the first week after an infection (less than 7 days post infection; PI), when the adult worms are still in the gut and can be killed before they lay their eggs in the NBL. Drug treatment is typically initiated once NBL have been released and settled in muscle, but it is not known how long the adult worms will be viable after this. Everyone infected with trichinellosis should take these medications for at least 4 to 6 weeks after being sick [(4)].

Action mechanism:

Microtubule polymerization inhibition by binding exclusively to parasite-tubulin while having minimal effect on binding host mammalian tubulin [(5)].

The recommended dosage of albendazole is 400 mg bid for 8 to 14 days, whereas the dosage recommendation for mebendazole is 200 to 400 mg tds for 3 days, followed by 400 to 500 mg tds for 10 days. Both treatment plans can be used on both adults and children, though they shouldn't be administered to anyone younger than two [(4)].

Received: 17/7/2022
Accepted: 19/9/2022

Administering albendazole or mebendazole early in the infection's progression yields the best results [4].

b) Pyrantel (Combantrin ®):

Pyrantel is safe for usage by pregnant women and children. The helminth's neuromuscular depolarization, spasm, and paralysis result from its method of action, which is the suppression of cholinesterase. The helminth therefore can no longer adhere to the intestinal wall and must be removed. Typically, a single dose of pyrantel (10-20 mg/kg body weight) is administered every 2–3 days. It kills intestinal worms but has little effect on NBL or muscle larva [6].

c) Ivermectin:

Streptomyces avermitilis is the source of the macrocyclic lactones known as ivermectin. Ivermectin's effect is due to the drug's ability to boost inhibitory neurotransmission, which in turn disrupts neuronal system and muscle performance. The medication increases the permeability of membranes to chloride ions by binding to glutamate-gated chloride channels (GluCls) in invertebrate nerve and muscle cells, leading to cellular hyper-polarization, paralysis, and death [7].

Side effects:

Depression and ataxia in the central nervous system are possible side effects of ivermectin due to the drug's neurotoxicity, which can increase the strength of inhibitory gamma-aminobutyric acid (GABA)-ergic synapses [7].

Levamisole:

It shows antiparasitic effect against intestinal adults with no effect on NBL nor the muscle larvae, it is given in single dose 0.1 mg\kg [8].

d) Immunomodulating drugs:

They involve thymus factor-X which is extracted from calf thymuses, levamisole and L-tetramisole HCL; these drugs potentiate the therapy of trichinellosis in patients with severe disease showing immunosuppression signs [9].

e) Myrrh:

Mice treated with myrrh on day 0 post infection and again on day 5 had an efficacy of 80.7% and 51.5%, respectively. Myrrh was effective in reducing the number of encysted larvae by 76.6% and 35.0% at 15 and 35 days after infection, respectively [10].

f) Artemesia species:

As anthelmintics, they have a long history of application. Multiple plant and animal nematocidal substances have been reported, including artemisinin from Artemesia annua. Pure ethereal oils extracted from two grown A. populations of A. absinthium had significant anti-infectious ML of T Spiralis ex vivo action, with a 72%-100% decrease in infectivity at 0.5-1 mg/ml and no damage to mammalian cells. To what extent do these oils fight off T. Spiralis reduced adult flora in the intestine by 66% [11].

g) Probiotics:

When taken in sufficient doses, probiotics are beneficial to the health of the host organism. There has been a lot of research and development into the use of probiotics in the recent decade for the prevention and treatment of enteric diseases. The gut environment, the immune system, and the production of active molecules are all processes that probiotics use to ward off enteric illnesses. New, harmless probiotic strains, Lactobacillus plantarum P164 and Lactobacillus acidophilus P110, have been reported to be protective against experimental trichinellosis. When compared to T. spiralis, L. plantarum P164 showed greater parasitologic and histopathologic improvement [12].

2) Glucocorticosteroids:

Trichinellosis is treated with anthelmintic therapy, however the symptomatic period can be reduced by administering prednisone beforehand to prevent symptoms from getting worse. Prednisolone is the most widely used glucocorticosteroid; it comes in 1 mg and 5 mg tablets and is often given at a dosage of 30 mg to 60 mg per day, split up into many doses, for 10-14 days. Within a matter of days of beginning glucocorticoid therapy, pulmonary diseases show remarkable improvement [13].

Overview the problems of the treatment:

Trichinellosis treatment has various obstacles. When parasites invade the intestines, anthelmintics are necessary (i.e. less than 1 week after infection). Unfortunately, this is rarely the case, and instead, treatment is typically initiated during the earliest stages of larval development in muscle cells. Muscle larvae, once developed, are protected from anthelmintics by a capsule that covers the larva and prevents it from being directly exposed to the drug [14].

Drugs with poor aqueous solubility have trouble dissolving in the GIT, resulting in low bioavailability; chemical and enzymatic barriers in the GIT reduce the efficacy of oral drug delivery; the epithelial cell monolayer in the GIT contributes to poor permeability for numerous drugs; and some drugs undergo first-pass metabolism in the liver; all of these factors have prompted the study of potential neoanthelmintic drugs [14].

The anthelmintic benbendazole is widely used to treat trichinellosis. Unfortunately, its action is low and its bioavailability is low, making it ineffective against encapsulated larvae. It's not very effective in getting into the bloodstream. That means it can't reach the muscle larvae deep within the tissues [15].

Moreover, in recent years, there has been a surge of activity surrounding the testing of other medications as potential anthelmintics for the treatment of Trichinellosis [16].

New anti-infective medications targeting carbonic anhydrases (CAs) as acetazolamide have recently been developed and utilised against Trichinellosis [17].

Atorvastatin is a member of the statin family of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) re-ductase inhibitors, which are commonly used to reduce the angiogenic response of the heart muscle after chronic ischemia. Because angiogenesis is crucial to the life of Trichnella spiralis, the medication played a significant role in the successful elimination of trichinellosis [(14)].

However, it was demonstrated that whereas benzimidazole compounds are quite efficient against the human intestinal stages of Trichinella spiralis, they are only somewhat effective against the tissue-dwelling larval stages. As a re-emerging zoonosis, trichinellosis necessitates a more all-encompassing strategy for treating the muscular phase, when most patients seek medical attention. Specifically, the encapsulated-Nurse cell may be the primary focus of treatment for the muscular phase of Trichinillosis. To do this, antifibrotic medicines could be used to either stop collagen synthesis in nurse cells or break down existing collagen strands. Adjuvant therapy, in which additional antifibrotic drugs are introduced alongside the primary treatment, has been the subject of extensive research in recent years (Colchicine**)** [(14)].

3) Acetazolamide (Carbonic anhydrases (CAs)):

In order to improve outcomes, it is crucial to administer effective anthelmintic medications during the intestinal invasion stage. The condition is typically treated with anthelmintics like mebendazole and albendazole, although these medicines are ineffective against either the encysted or newly born larvae of T. spiralis. The testing of alternative medications has increased in recent years due to a growing interest in discovering innovative anthelmintics for the treatment of trichinellosis [(16)].

4) Atorvastatin:

Statins, or inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) re-ductase, are commonly used to treat high cholesterol and cardiovascular disease. Statins have been gaining popularity and new uses in recent years. Atorvastatin has been shown to reduce the cardiac angiogenic response to prolonged ischemia and to inhibit angiogenesis [(18)].

Mechanism of action:

- Cholesterol metabolism is disrupted through inhibition of 3-hydroxy-3- methylglutaryl-coenzyme A (HMG-CoA) reductase by preventing the enzyme from accessing its substrate [(18)].
- Evidence for pleiotropic effects on inflammatory cytokine and mediator production, including reactive oxygen species. Statins decrease angiogenesis by preventing the production of vascular endothelial growth factor (VEGF), the primary factor responsible for the process. This is accomplished by inducing death in endothelial cells [(18)].

5) Nanoparticles (NPs):

Synthesis and development of diverse nanomaterials fall under the umbrella term of nanotechnology, which is a relatively new scientific discipline. Objects between 1 and 100 nm in size are considered nanoparticles, and they may have unique properties compared to the bulk material. Copper, zinc, titanium, magnesium, gold, alginate, and silver are just some of the metals now being utilized in the creation of these nanostructures [(19)].

Nanoparticles, because of their extraordinary qualities, have recently gained attention in numerous industries. The ability of nanoparticle technologies to transform physiologically active chemicals that are poorly soluble, poorly absorbed, and easily degraded into viable deliverable substances is extremely promising [(19)].

Disadvantages of Silver NPs:

Toxicity is the principal drawback of Silver NPs, and it is not quite clear whether this is caused by the particles themselves or by the ions, or by both. The formation of oxidative stress, and in particular the production of reactive oxygen species (ROS), is a general paradigm for explaining the in vitro toxicity of nanoparticles. This reactive oxygen species (ROS) could be produced by a variety of processes. To begin with, nanoparticles' reactive surfaces could accelerate redox processes, ultimately leading to the production of reactive oxygen species (ROS). Direct contact with mitochondria is another mechanism that could make silver especially important. Since many membrane proteins in mitochondria have sulfur-containing amino acids, silver may interact with these amino acids directly, leading to an increase in ROS generation [(19)].

CONCLUSION

Trichinellosis treatment presents a number of challenges. During the time of intestinal invasion, anthelmintics are required (i.e., less than 1 week after infection). Treatment is typically initiated at the earliest stages of larval development in muscle cells, but this is rarely attainable. The research and improvement of pharmacological treatment options for trichinellosis, the anthelmintics mebendazole (Vermox®, Janssen Pharmaceuticals) and albendazole (Zentel®, GlaxoSmithKline) are the most common choices for treating trichinellosis. Because of its negative consequences, thiabendazole is no longer employed. Flubendazole has been utilised in several countries, and pyrantel (Combantrin®, Pfizer) has been suggested for use in children and pregnant women. In any case, the reliability of these two items is questionable.

Financial support and sponsorship: Nil.
Conflict of interest: Nil.

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