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Chagas Disease: A Neglected Disease

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Abstract

Chagas disease or American trypanosomiasis is a neglected disease caused by *Trypanosoma cruzi* and spread by insects 'triatomine' or 'kissing bugs'. Once, this disease was completely confined to the region of Latin America, but has now spread to different regions of the world due to immigration. Around 6 to 7 million people across the world are affected with this infection. This disease presents itself in two phases: acute and chronic, each with its own characteristic features. Various diagnostic techniques are available to confirm this infection. Benznidazole and nifurtimox are clinically used to relive the infected patients. Both these have 100% efficacy, if given soon after infection at the onset of acute phase. However, both of them are associated with some limitations, thereby necessitating the need for novel and safe agents.

Keywords: Chagas disease; Diagnosis; Treatment; Trypanosomiasis; Parasitemia

Abbreviations: *T. cruzi: Trypanosoma cruzi*; ELISA: Enzyme Linked Immunosorbent Assay

Introduction

Chagas disease, which is also known as American trypanosomiasis is an infection caused by the protozoan, *Trypanosoma cruzi* (*T. cruzi*). It is generally transmitted by feces of a triatomine insect, also known as kissing bugs belonging to family Reduviidae [1]. As per WHO report, 2017, about 6 to 7 million people are estimated to be infected with T. cruzi. This disease is not constrained to Latin America, where it is endemic in 21 countries. However, this is spreading to other areas like Europe, North America, Japan and Australia due to international immigration. It is a major contributor for deaths from parasitic disease [2]. This disease is considered as a proxy for poverty and disadvantage as it generally affects population group with low visibility and little political voice. It is generally neglected by researchers but is reported to have significant effect on morbidity and mortality [3]. Since, this disease affects majority people living in poverty in remote areas, less than 1% of the people have access to diagnosis and treatment [2].

Development of this disease can be due to different modes of transmission which can be vectorial, congenital, oral or latrogenic. Vectorial refers to the transmission by the vector 'kissing bug'. Congenital happens from mother to child. Oral mode of transmission is through the ingestion of contaminated food or drink. Latrogenic is due to contaminated blood transfusion or organ transplantation [2,4,5].

Variable clinical presentation is observed in humans. Just following the parasite infection, there is a short acute phase in which there is abundant parasitemia which is relatively easy to detect by direct blood examination. Very mild or nonspecific symptoms make recognition of the contagion difficult. Majority of the patients of this phase go unrecognized due to scarcity or absence of the clinical manifestations. Following this acute phase, the disease enters chronic phase characterized by long, asymptomatic clinical latency that lasts for 10-30 years or throughout life. In this phase, around 30% of the infected people develop one of the clinical manifestations like cardiomyopathy and/or mega gastrointestinal syndromes [6]. Progressive heart failure and sudden deaths are the main causes of deaths in these patients [7].

Life Cycle of *T. cruzi*

This disease gets transmitted when an infected triatomine insect vector takes a blood meal and releases trypomastigotes

in its feces near site of wound. These trypomastigotes enter the host through wound or intact mucosal membranes. Upon invasion of cells near the site of inoculation they get differentiated into intracellular amastigotes. Amastigotes multiply by binary fission and differentiate into trypomastigotes and then are released into circulation as bloodstream. These forms then infect cells from a variety of and get transformed into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle. Kissing bugs become infected by feeding on human or animal blood that contains circulating parasites. These ingested trypomastigotes get transformed into epimastigotes in the vector's midgut. These parasites multiply and get differentiated into infective metacyclic trypomastigotes in the hindgut [8,9]. Life cycle of the parasite is shown in Figure 1.

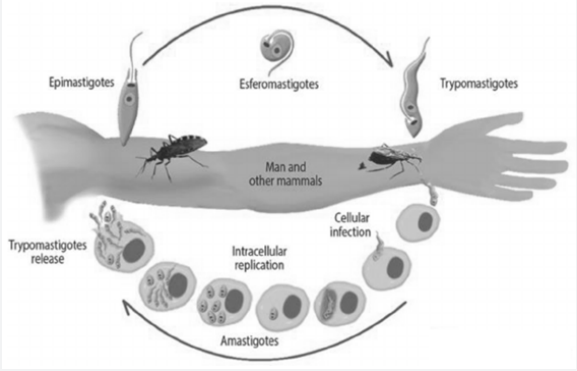

Figure 1: Lifecycle of *T. cruzi*.

Diagnosis and Treatment

Diagnosis of this fatal disease can be done by both direct and indirect parasitological methods, molecular method. Direct parsitological methods for detection of acute phase include examination of fresh samples, blood smear, micro-strout test and strout concentration method. Xenodiagnosis and blood culture are a part of indirect methods. Polymerase chain reaction can also be employed for determination of acute phase of the disease [10]. Chronic phase can be detected by serological methods by enzyme linked immunsorbent assay (ELISA), indirect immunofluorescence, indirect haemagglutination and Western blot [11,12].

Since 1960s, the only drugs available for the treatment of this infection have been benznidazole and nifurtimox (Figure 2) [13]. These two have been the mainstay of parasiticidal treatment for the past 50 years, despite the fact that their efficacy and safety profile is far from ideal conditions. Nifurtimox was the first drug used. This is administered orally in three to four doses for a period of 60-90 days. Anorexia, weight loss, neurological disorders, digestive malfunctions like nausea, vomiting and occasionally fever and rash are the frequent side effects associated with the use of nifurtimox [14,15].

Benznidazole is however preferred over the use of nifurtimox due to its better tolerability profile, tissue penetration and efficacy. It is administered orally in two or three doses usually for a period of 60 days. Common side effects of its use are hypersensitivity, digestive intolerance, headache and sleeping disorders. Neuropathy and depression of bone marrow are very rare [16,17]. Researchers are actively involved in the development of novel agents. However, the major obstacle associated is poor translation of in vivo data to human disease. Animal models available bear a drawback of limited predictive value [18-23].

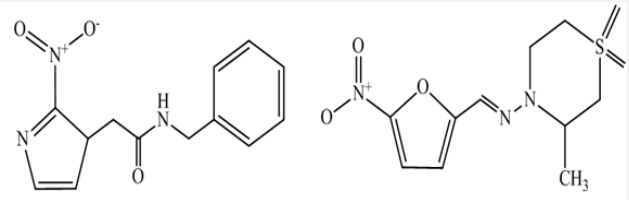

Figure 2: Structure of Benzimidazole and Nifurtimox.

Conclusion

Chagas disease is one of the neglected tropical diseases. Benzidazole and nifurtimox have been the mainstay for treatment of this infection since long. However, there are many shortfalls associated with these drugs which necessitate the need for development of newer agents with better safety and efficacy profile.

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