

A REVIEW ON TREATMENT AND VARIOUS ANTI TRYPANOSOMIASES DRUG

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ABSTRACT

Human African trypanosomiasis is an infectious parasitic disease which is transmitted through Flies which are found in African countries. In this review we have to study various causes, signs, symptoms, and various drugs which are used in treatment of African trypanosomiasis.

KEYWORDS: Trypanosomiasis, sleeping sickness, Anti trypanosomiasis, Fexinidazole.

Trypanosomiasis

Another name for Human African trypanosomiasis is sleeping sickness and it is the one of the most underappreciated diseases of world.^[1] It is insect born parasitic disease and the main causative agent is tsetse flies. And it is largely transmitted through Bite of tsetse flies.^[2] After the bite of tsetse flies' infection of disease get transmitted in three stages beginning from mild to moderate and its symptoms may get various at each stage of disease.^[3] In Sub Saharan African trypanosomiasis is a vector born disease with major public health and economical implementation. It is parasitic illness spread by mosquito bite and cause by flagellate protozoans.^[5] A disease is same in both Animal and Human as compared with its etiology and epidemiology.

Morphology of African trypanosomiasis

Trypanosoma is a genus of hemoflagellate protozoa that infect plant, mammals and other species of animal as obligate parasites (Fish, bird, reptiles etc.) Trypanosoma are the unicellular creatures that relay on both craniates and spineless animal host for their life cycle. In which some prevalent species are located in Africa and are responsible for African trypanosomiasis in various sectors of sub-Saharan regions of Africa, many others can also be found in all over world including topical and sub topical regions of America and sub-Parts of Canada.^[9]

There are various species of African trypanosome which are varies according to their morphological characteristics.^[9]

- T. brucei
- T. equiperdum
- T. cruzi

- T. bancrofti
- T. anguillicola
- T. granulosum
- T. aulopi

Causes of African Trypanosomiasis

African trypanosomiasis mainly divided into Two types and it may be various according to their causative agent. The disease occurs in east Africa is called as East African sleeping sickness which is mainly cause by causative agent Trypanosoma brucei Rhodesiense and the disease which occurs in west African region is called as west African sleeping sickness which mainly caused by Trypanosoma brucei Gambiense.^[3] In various regions Africa African trypanosomiasis is mainly cause by the bite of infected parasitic infection and which is spread through the saliva of flies which inter into human body after the bite of tsetse flies.^[4] Another way of transmission of disease is depend on many factors such as some time the disease is also transmitted from mother to its child if the infection of disease is also present in placenta.^[4] The transmission of disease also occurs due to some mechanical and human defects such as sharing of same needle to multiple patients and it may be 20 % chances of transmission of disease through sexual way.^[4] In several regions disease it is spread Flagellate protozoans of genus Trypanosoma. A human and animal may be affected by parasite which will directly affect on blood and central nervous system.^[5]

There are mainly three species of protozoan parasite which are responsible for development of disease these species are as follows.^[7]

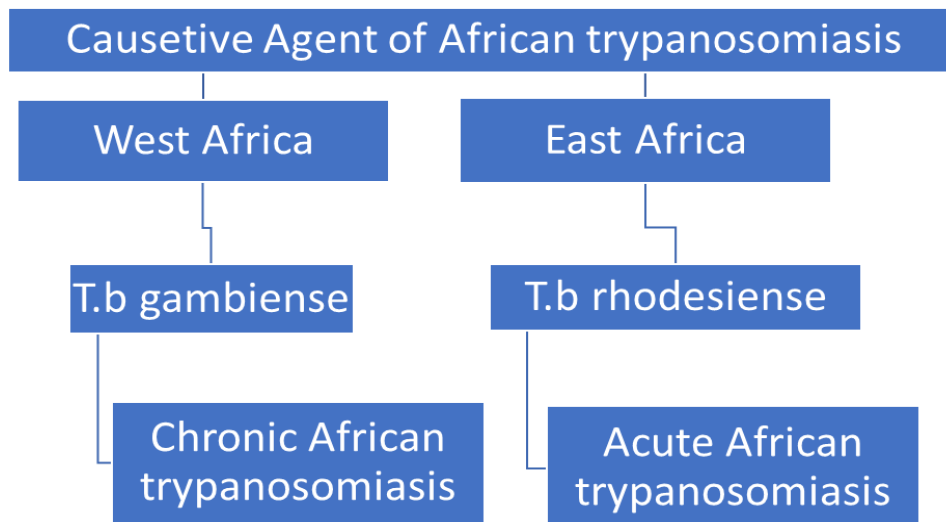
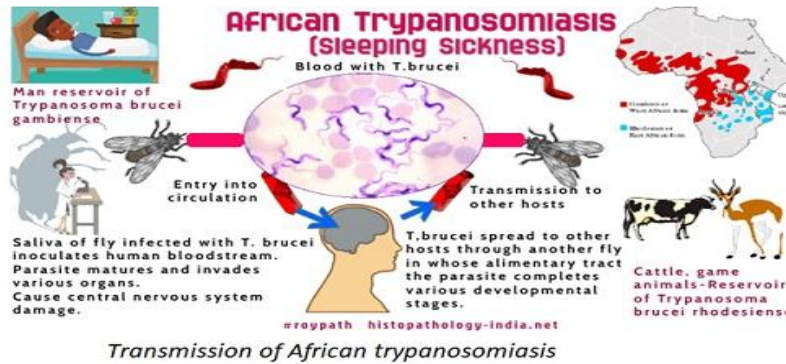
1. Trypanosoma brucei
2. Trypanosoma brucei Gambiense

3. Trypanosoma brucei rhodesiense

Other causes of transmission of African trypanosomiasis-

1. A pregnant woman can also transmit the Disease from its placenta to its fetus.^[4]
2. Another causative agent for transmission of disease is use of infected or pre used syringe or needles with other patients.^[4]

3. In some cases, sexual contact also responsible for transmission of disease.^[4]
4. Directly come in a contact with tsetse flies is a main cause of transmission of a disease.^[4]
5. The disease also causes due to single cell parasites which is known as Trypanosoma brucei.^[6]
6. There are two other different species which causes the disease are named as follows :1.T.brussi and 2.T.b, Gambiense.^[6]



Stages and symptoms of African Trypanosomiasis

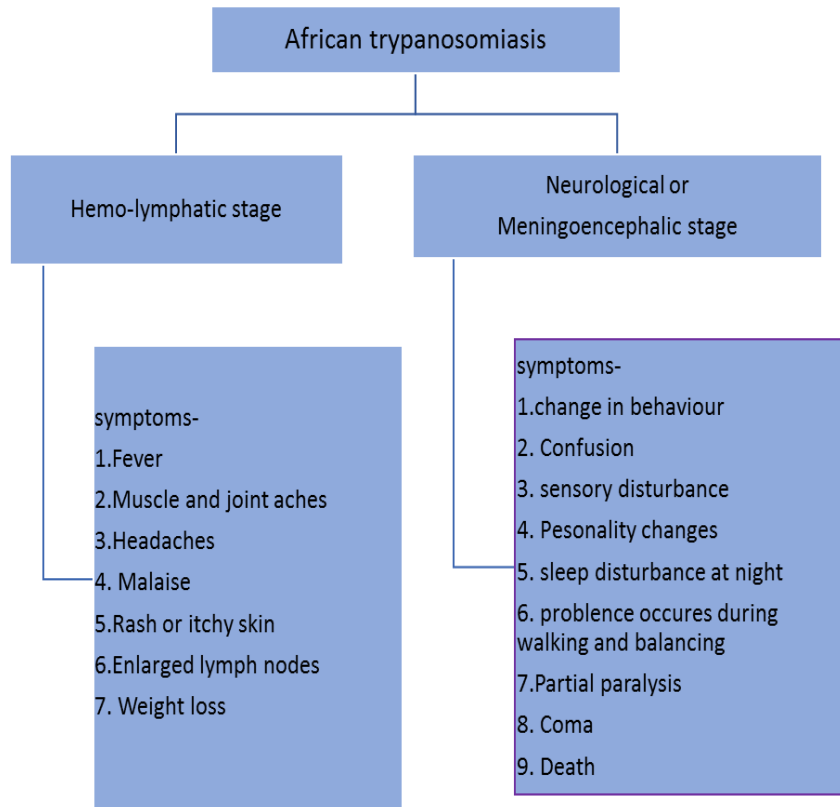
African trypanosomiasis is mainly classified into two stages it mainly includes Hemo-lymphatic stage and Neurological or Meningoencephalic stage.

1. Hemo lymphatic stage^[8]

In the initial stage, trypanosomes multiply in subcutaneous tissues, blood vessels, and lymph nodes this is also known as hemo-lymphatic stage. If a person has African trypanosomiasis, the parasite enters into the circulation and symptoms are similar to those of other infectious disorders.

2. Neurological or Meningoencephalic stage^[8]

In the initial stage, trypanosomes multiply in subcutaneous tissues, blood, and lymph. The hemo-lymphatic stage is also known as this. When a person has African trypanosomiasis, the parasite circulates in the circulation for a while, generating symptoms that are similar to those of other infectious disorders. During the first stage of sleeping sickness, the following symptoms are common.



Disease management

Treatment

In the initial phase of Disease Nifurtimox and benzimidazole these two drugs are used in treatment.

In some cases, some antifungal drugs like Posaconazole are also used in treatment due to failure in treatment of benzimidazole.^[9] Pentamidine is a second most usable drug in treatment of African trypanosomiasis because of its high efficiency against trypanosoma brucei rhodesiense. After that if pentamidine may be fail then we have to start the treatment with suramin which is high potent and highly efficient drug against African trypanosomiasis.^[11] In the initial stage of disease the patients are suffering from high fever and malaise. So it

is important to control that condition of patients so initially we have started the treatment with antipyretics and some other analgesics. If the fever and malaise is not controlled by these two drugs than we have to start the new treatment by using some higher antibiotics such as Pentamidine.^[12] In some cases, patient shows some abnormal activities which are related to CNS symptoms in this case we have treat the patient with 2nd line antitrypanosomal drugs such as eflornithine and nifurtimox. If there is no change in mental behavior the doctors treat the patient with Melarsoprol for better and quick response.^[12] In some cases, combination therapy also uses for better results in patient condition in combination therapy both drugs such as nifurtimox and Melarsoprol are given to patients.^[12]

The drug used in treatment of disease as per their dose tendency is as follows.^[13,14,15]

Drug use in treatment	Frequency and Dose of drug given to patient	Rout of Administration
Eflornithine	400mg/kg for 7 days	Oral/ Intravenous
Nifurtimox	15mg/kg per day after every 8hrs for 10 days	Oral/ Intravenous
Fexinidazole	400mg/day for 7days	Oral
Pentamidine	4 mg/day	Intravenous/intramuscular
Suramin	100-200 mg/day	Intravenous/ Intramuscular
Melarsoprol	4 mg /week	Intravenous

Chemotherapy against African trypanosomiasis^[14,16]

Pentamidine is widely used in treatment of African trypanosomiasis. And pentamidine is water drug and it is useful in earlier stage of disease but it is useless in modern and final stage of disease. In the chemotherapy we have to provide the same drug i.e., pentamidine to

infected patient for 7-8 times in an earlier stage of disease development. It results in development of nucleosides in plasma.^[14]

In recent era Hoechst developed a Therapy for bovine trypanosomiasis called nevertheless because it shows

High therapeutic activity over the minimum side effects, hence many physicians and doctors suggest this therapy for endemic regions. It destroys the species of African

trypanosomiasis ie. T.b. gambiense and T.b rhodesiense in earlier stage of therapy.^[16] Berenil has also utilized in last stage of illness in conjugation with melarsoprol.

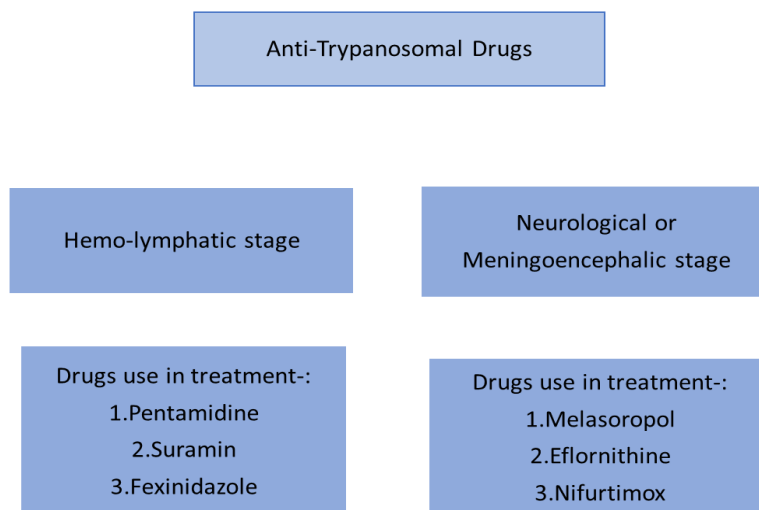
Following drugs were used in chemotherapy as per the saturation level of disease observe in patients.^[14,16]

Saturation stage of disease	Drug used in chemotherapy	Results
Earlier stage	Pentamidine	It is effective against T. b. gambiense infection in the early stages, but less effective against T. b. rhodesiense infection and ineffective against late-stage sickness.
	Suramin	
Last stage	Diminazene aceturate	Both drugs were used in last stage of disease. these are given in single dosage form as well as in combined dosage form for better and positive results.
	melarsoprol	
	Berenil + Pentamidine	These drugs are used in separately as well as in combination at a last stage of chemotherapy and it gives better recovery of patient.
	Eflornithine	It is used in critical conditions of chemotherapy with less side effects.
	Nifurtimox + DMFO	Shows great results when take it for 10 days with 94% cure rate.
Melarsoprol + nifurtimox		

Anti-trypanosomiasis^[2,14,15]

The drug which used in treatment of Sleeping sickness is commonly called as Anti-trypanosomiasis drugs.

Drug Therapy in Different stages of African trypanosomiasis with different types of species		
Stage of Disease	First line Therapy	Another /alternate Therapy
Initial stage (Trypanosoma brucei)	Suramin	Not available
Initial stage (Trypanosoma brucei Gambiense)	Pentamidine	Suramin
Final stage (T.b rhodesiense)	Melarsoprol	None
Final stage (T.b Gambiense)	Melarsoprol	Eflornithine & nifurtimox
Hemo-lymphatic stage	Fexinidazole	Pentamidine
Neurological stage	Melarsoprol	Eflornithin



Prevention & Control of Disease

1. The African trypanosomiasis is a insect born infection so the best way of prevention is protect our self by bite of Tsetse flies.^[17]
2. Use of insect repellents and some other techniques to reduce the Tsetse flies' population.
3. Use of various insecticides in contaminated and polluted places to reduce the chances of growth of Tsetse flies and other mosquitos.^[17]
4. Always wear protective clothes including full sleeves and long shirt and pants while hanging out.^[17]

5. Always check your vehicle before entering into it to avoid tsetse bite.^[17]
6. It is better to stop Tourism in endemic areas.^[18]
7. It is always protective to wear light color dresses instead of dark color dresses because dark color may lead to attract insects and Flies.^[18]
8. Always choose the dresses in khaki, Olive or other neutral colure is in area of flies.^[19]
9. The most effective control method for *T.brucei gambiense* human African trypanosomiasis is case detection and treatment which minimizes the human reservoir and hence it reduces the risk of transmission.^[21]
10. The bites of these potentially dangerous insects have been proved so it can be protected by bed nets.^[23]
11. The number of flies can be reducible through improving housing condition by cleaning and removing vegetation and it results in decrease in rate of infection.^[23]
12. Before interning into car make sure to clear the air of these flies it may be help you to prevent from getting bitten while driving.^[23]
13. Blood screening on a regular basis help you to avoid spreading of infection.^[23]

Current treatment of Human African trypanosomiasis^[27]

The current or latest treatment of African trypanosomiasis is totally base upon mainly four drugs are as follows-: Suramin, pentamidine, melarsoprol and eflornithine. These all drugs are developed in the 21st Century for treatment of savior effect of sleeping sickness. Some drugs of above mention list are not be use frequently because some of them are fail to pass all safety trials of mention standards. But due to there is no other alternative drugs are available in market so in many cases these drugs are use for treatment of disease.

There are lots of drugs were used in primary and secondary stage of disease. These drugs are use according to condition of patient and the stage of disease development. There are mainly three stages of disease initial, mild and modarent

Case study^[28]

In case study we have to discuss about the 1st case of African trypanosomiasis which was found in China. The patient was 45 years old and he was admitted to Jiangsu Province Hospital on September 15, 2014. Because he suffering from low grade fever from last 21 months. But there are no other symptoms were observed like skin irritation, skin rashes, Headache, cough or night sweating etc. but for many years the patient is continuously suffering from high body temperature, During the physical and medical examination number of tests are carried out on this patient like HIV and TB but all tests are observed negative, there is no any plasmodium was found in blood sample and the proper diagnosis was not clear so there is no any treatment was provided to patient.

After some months patient feels swelling in his lymph nodes and suffers from high level of inflammation in lymph's. The swelling of lymph is about 0.3- 5cm in diameter. Due to that he also loss his weight about 20 kg, and he feels chronic tiredness. The eating habit also change in same patient also observes some mental changes and some changes in its behavior.

The blood sample was tested for same patient the small amount of disease was observed. The patient is taking under observation for mini mental condition. So that physician tests its CSF sample to check mental condition and balance but during this test the species of *T. b. gambiense* were observed.

Medical evaluation of patient in mental condition	IgG	306 mg/L
	White cell count	60 /μL
	protein	1.39g/L
Stage of treatment	Drug	Route of administration
Final stage	Eflornithine (100mg/KG)	Intravenous

RESULT OF TREATMENT

At the end of all medical examination and the use of various drugs and a long time treatment, the patient comes in normal condition and he take a normal sleep ; normal health and normal behavior was observed in the patient.

CONCLUSION AND DISCUSSIONS

From the above review we study the signs, symptoms, causes, stages, treatment, Prevention and the various drugs use in treatment of "African-trypanosomiasis"

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