Archives of Health Science
Review Article

Prevention, Control and Treatment Strategies for Trypanosomiasis: A Review

Tinuoye, O.O.[1], Muhammad Ali[2], Muhammad S. Abdallah[3] and Lurwan Mu'azu[4]

[1]Faculty of Computing and Applied Science, Baze University Abuja, Nigeria
[2]Department of Microbiology, Federal University Gusau, Nigeria
[3]Department of Microbiology, Yobe State University Damaturu, Nigeria
[4]Department of Biological Sciences, Federal University Gusau, Nigeria

***Corresponding Author**: Muhammad Ali, Department of Microbiology, Federal University Gusau, Nigeria.

Abstract

Tryponosomiasis is a disease that afflicts populations in rural Africa, where the tsetse fly vector that transmits the causative trypanosome parasites thrives. There are two forms of Human African Trypanosomosis (HAT): one, known as gambiense HAT, is endemic in West and Central Africa and causes over 95% of current cases; the other, known as rhodesiense HAT, is endemic in East and southern Africa and accounts for the remainder of cases. The presence of parasites in the brain leads to progressive neurological breakdown. Changes to sleep–wake patterns are among the symptoms that characterize the disease, also known as "sleeping sickness". Eventually, patients fall into a coma and die if not treated. Different treatments are available against parasites present in the haemo-lymphatic system (first-stage) and those that have entered the brain (second-stage). Currently, lumbar puncture is required to select the appropriate drug. The paper was aimed to review the prevention and treatment strategies for tryponosomiasis.

Keywords: Control, Tsetse fly, Treatment, Tryponosomiasis

Introduction

Trypanosomoses refer to a group of vector-borne parasitic diseases caused by protozoa of the genus Trypanosoma. *Trypanosoma brucei brucei, T. congolense, T. vivax, T. evansi, T. simiae* are all infective to animals causing African animal trypanosomosis while *T. brucei gambiense* and *T. brucei rhodesiense* are the only species pathogenic to man in Africa. Trypanosomiasis in humans has been poorly reported over the years, despite affecting an alarming number of persons. There are over 60 million people in endemic areas all over the world [1]. Disease surveillance and reporting of cases of Human African trypanosomiasis is still in the rudimentary stage in the sub-sahara regions of the world especially Nigeria [2]. Several trypanosome species cause important animal diseases; however, significant human diseases are caused by 2 species of trypanosome. In Nigeria, as in some other western African regions, *Trypanosoma brucei gambiense is* the etiology of sleeping sickness or Human African trypanosomiasis [3]. The second stage (meningoencephalitic stage) of the infection is usually severe, affecting the cerebrospinal fluids of humans unlike the first stage (hemolymphatic stage) which is usually less severe [1]. Some of the clinical presentations include; dullness, intermittent somnolence and apparent confusion. Also, intention tremor in all limbs and myoclonic jerks are often seen [3]. Trypanosomes possess Variant Surface Glycoprotein (VSG) which constitutes a characteristic molecular interface between the protozoan and the human host immune system, thereby evading lysis by

complement alternative pathway [4]. There is usually a high level of serum IgM due to sensitization of polyclonal B-cells in the blood. Human African Trypanosomosis has been attributed as the deadliest diseases in the world by the World Health Organization [5]. The treatment of this menace has since been a burden because of the adverse drug reactions that most drugs present when administered to patients [6]. Sporadic transmission of trypanosomes can occur when there is a contact between *Glossina* species and humans from tse-tse flies that normally enjoy a blood meal on cattle, especially in Northern part of Nigeria. Human African Trypanosomosis (HAT) and Animal African Trypanosomosis (AAT) or Nagana occur in 37 sub-Saharan countries covering more than 9 million km2, an area which corresponds approximately to one-third of the Africa's total land area [7].

Epidemiology of Tryponosomiasis

According to Siqueira *et al*. [8], WHO ranked trypanosomiasis among the list of 17 neglected tropical diseases amidst leprosy, leishmaniasis, malaria, and tuberculosis. The disease is most predominant in low-income populations and therefore do not attract the interest of pharmaceutical companies. For this reason, advancement in therapies is seriously hampered [9]. Human schistosomiasis is a great concern in public health taking its bang on over 200 million people in more than 70 countries. More than 800 million people stand at risk of being contaminated with the parasite illness. Even though death rates are difficult to ascertain, the disease has been predicted to cause 280,000 per annum and is likely to constitute more harm to the host [10]. The early 20th century witnessed a distressing outbreak of HAT in Uganda, the Democratic Republic of the Congo, Cameroon, and other western African countries probably due to environmental disturbances and compulsory movement of populace embraced by colonialism. Transitions in land use and climate extremely diminished parasite vector in areas thought to be endemic [11]. *T. cruzi*, the vector for Chagas disease [12] is first released via the countryside to the metropolitan areas of Latin America and to other areas of the world. I8 million individuals suffer from Chagas disease in Mexico, Central America and Latin America. Majorly, awareness of this ailment is poor among the victim predisposed populations; however, if the disease condition is untreated, infection perseveres for a long time and can inevitably pose a serious threat to the victim's survival [13].

Tsetse Flies as Vectors of Human-Infective Trypanosomes

Tsetse flies can be grouped into three main subgroups depending on the environment they inhabit: thus, riverine (*palpalis*), savannah (*morsitans*), or forest-dwelling tsetse (*fusca*). All tsetse species are capable of transmitting human-infective trypanosomes. However, the major species involved in HAT transmission are the *palpalis* group tsetse, specifically *G. palpalis spp* and *G. fuscipes spp*. Sleeping sickness occurs in geographically delineated zones referred to as "foci" [14]. Such foci are often infested by sympatric species, whereby one species is the predominant one [15,16]. Flies pick up bloodstream parasites from their hosts: livestock, wildlife, and humans. Vectorial capacity describes the innate ability of a specific fly species to acquire, mature, and transmit trypanosomes. Different tsetse species co-infesting the same habitat often have varying vectorial capacities for human-infective trypanosomes [17,18]. For this reason, it is important to determine the infection prevalence in sympatric tsetse species so as to identify which species are keys in disease transmission. Such data can then be used to inform decisions on control interventions. In addition, infection prevalence data helps scientists to better understand transmission dynamics and detect spatiotemporal trends, both of which have important implications for disease control [19].

Prevention Strategies for Trypanosomiasis

Generally, HAT can be prevented by reducing stings from tsetse flies, carrying out earlier diagnosis and immediate treatment for patients diagnosed with the disease. Individuals can also protect selves although bites may penetrate clothing that is not heavy enough. Insect repellants are not quite common in endemic areas. At the

neighborhood level, vector control can be achieved by screen and treatment plans, this has to do with the identification of human cases.

Another way by which control of tsetse fly populations can be accomplished is via successive mid-air insect repellent spraying to target adult vector. This should be done during the developmental stage of tsetse flies from pupal stages in the ground, the use of insecticides as traps may be of immense help when treating cattle [20].

Monitoring systems that take surveillance should present discovery, investigation and disruption of subsequent transmission as a major drive and purpose of its existence alongside with disease prevention of tsetse bites. Having an effective management system will help disease managers to pinpoint risky areas, prevalent population and pattern of infection in animals and human that needs intervention and control measures where essential. For instance, monitoring of Schistosoma in Japan has been continuous, meanwhile animal to human disease transmission persisted extensively even when the disease was declared to have been eradicated in humans in Japan in the year 1996 [12]. This can be achieved using chemicals such as tablets and liquids preparations. Baits such as metaldehyde and methiocarb tablets, granular, and liquid preparations could be applied. Ingestion of m etaldehyde baits is poisonous resulting in desiccation and the consequent demise of organisms. Similarly, carbamate, methiocarb disrupts the central nervous system, preventing acetylcholinesterase, instigating of animal death [21]. Since the neglected tropical disease is a public health problem bringing about several deaths, WHO recommends the use of chemicals for prevention as well as improved access to uninfected drinking water, hygienic environment education [10].

Treatment for Tryponosomiasis

Treatment is still suboptimal, but substantial achievements have been made during the past decade, and the treatment recommendations require urgent revision. In the 1980s, an antineoplastic drug, eflornithine, received attention for its antitrypanosomal activity [22], and the compound was eventually registered by the United States Food and Drug Administration for this indication in 1990 [23]. Because its administration is highly complex, however, requiring sophisticated logistics and nursing care, and because of its high price, its use was limited for a long time to emergency interventions by a few nongovernmental organizations. In addition, eflornithine is not active against *T. b. rhodesiense* [24], which restricts the treatment options for the second-stage of this form of HAT to melarsoprol. At the same time as eflornithine was introduced, nifurtimox, which had been developed against Chagas disease, was used experimentally mainly to treat cases refractory to melarsoprol. The compound had only limited activity when used alone and it caused significant adverse reactions [22].

In the mid-1990s the pharmacokinetics of melarsoprol was finally elucidated [25], which allowed the proposal of an abridged regimen for treatment of second-stage sleeping sickness with melarsoprol instead of the variety of empirically derived, complex, lengthy schedules. The abridged schedule was recommended by the 27th International Scientific Council for Trypanosomiasis Research and Control in 2003 [26] as standard treatment for second-stage gambiense HAT. Treatment could be shortened from 25–36 to 10 days, which was a major socioeconomic advantage because of shorter hospitalizations and drug savings. A programme for improved application of melarsoprol (IMPAMEL) included the first large-scale clinical trial on treatment of HAT conducted according to good clinical practice. This trial demonstrated the feasibility of conducting modern clinical trials in resource-limited conditions in sub-Saharan Africa and paved the way for future clinical research in such settings. Nevertheless, the abridged melarsoprol regimen could not be regarded as a breakthrough, as the frequency of the major adverse drug reaction remained stable: encephalopathic syndromes continued to occur in 5–10% of patients treated with melarsoprol and resulted in the death of 10–50% of those in whom encephalopathy developed. The first exploratory comparison of different

treatments, including a drug combination, was carried out in 1998. The standard national schedule for melarsoprol (three series of doses of 3.6 mg/kg for 3 days with 7-day breaks), an adapted form of the abridged 10-day schedule (incremental doses of 0.6 and 1.2 mg/kg followed by 8 x 1.8 mg/kg); nifurtimox alone for 14 days (5 mg/kg orally three times a day); and consecutive 10-day melarsoprol–nifurtimox combination therapy (0.6 mg/kg melarsoprol on day 1, 1.2 mg/kg on day 2 and 1.2 mg/kg/day intravenously, combined with oral 7.5 mg/kg nifurtimox twice a day on days 3–10) were compared for safety and efficacy. The frequency of adverse drug reactions was similar in the four arms; however, the drug combination appeared to be considerably more effective: no relapses were reported, and more patients were considered to be cured (randomized patients minus deaths, relapses and unknown outcome) after 24 months of follow-up [27]. Hence, by the end of the past century, moderate progress had been made, but the treatment of sleeping sickness was in peril. The availability of the drugs was threatened by increasing price (pentamidine), halted production (eflornithine) or planned cessation of production (nifurtimox, suramin and melarsoprol) [22]; in addition, an increasing number of cases in certain foci were refractory to melarsoprol [25,28]. In 1999, WHO created the "HAT treatment monitoring and drug resistance network" to ensure the availability and affordability of anti-trypanosomal drugs. The exercise resulted, in 2001, in a contract with two manufacturers of these drugs, which will be continued until at least 2017. In the agreement, the companies have committed themselves to ensure continued manufacture and donation of the essential drugs to treat HAT through WHO and funds to support control of the disease [29]. The contract boosted the activities launched in the mid-1990s to control the disease by WHO and several nongovernmental organizations, and it allowed gradual replacement of melarsoprol with eflornithine. The abridged schedule was recommended by the 27th International Scientific Council for Trypanosomiasis Research and Control in 2003 [26] as standard treatment for second-stage gambiense HAT. Treatment could be shortened from 25–36 to 10 days, which was a major socioeconomic advantage because of shorter hospitalizations and drug savings.

A programme for improved application of melarsoprol (IMPAMEL) included the first large-scale clinical trial on treatment of HAT conducted according to good clinical practice. This trial demonstrated the feasibility of conducting modern clinical trials in resource-limited conditions in sub-Saharan Africa and paved the way for future clinical research in such settings. Nevertheless, the abridged melarsoprol regimen could not be regarded as a breakthrough, as the frequency of the major adverse drug reaction remained stable: encephalopathic syndromes continued to occur in 5–10% of patients treated with melarsoprol and resulted in the death of 10–50% of those in whom encephalopathy developed [27].

The first exploratory comparison of different treatments, including a drug combination, was carried out in 1998. The standard national schedule for melarsoprol (three series of doses of 3.6 mg/kg for 3 days with 7-day breaks), an adapted form of the abridged 10-day schedule (incremental doses of 0.6 and 1.2mg/kg followed by 8 x 1.8 mg/kg); nifurtimox alone for 14 days (5 mg/kg orally three times a day); and consecutive 10-day melarsoprol–nifurtimox combination therapy (0.6 mg/kg melarsoprol on day 1, 1.2 mg/kg on day 2 and 1.2 mg/kg/day intravenously, combined with oral 7.5 mg/kg nifurtimox twice a day on days 3–10) were compared for safety and efficacy. The frequency of adverse drug reactions was similar in the four arms; however, the drug combination appeared to be considerably more effective: no relapses were reported, and more patients were considered to be cured (randomized patients minus deaths, relapses and unknown outcome) after 24 months of follow-up [27]. Hence, by the end of the past century, moderate progress had been made, but the treatment of sleeping sickness was in peril. The availability of the drugs was threatened by increasing price (pentamidine), halted production (eflornithine) or planned cessation of production (nifurtimox, suramin and

melarsoprol) (van Nieuwenhove); in addition, an increasing number of cases in certain foci were refractory to melarsoprol [28,30].

In 1999, WHO created the "HAT treatment monitoring and drug resistance network" to ensure the availability and affordability of anti-trypanosomal drugs. The exercise resulted, in 2001, in a contract with two manufacturers of these drugs, which will be continued until at least 2017. In the agreement, the companies have committed themselves to ensure continued manufacture and donation of the essential drugs to treat HAT through WHO and funds to support control of the disease [29]. The contract boosted the activities launched in the mid-1990s to control the disease by WHO and several nongovernmental organizations, and it allowed gradual replacement of melarsoprol with eflornithine. The use of eflornithine remained below 20% until 2006, however, when a standardized kit was developed by WHO, simplifying the logistics and leading to a usage rate of 64% in 2009 [31]. The agreement between industry and WHO, not only significantly improved the access of patients to treatment but also triggered a new era of research. In the 1990s, the arrival of newer compounds against HAT raised the interest of scientists in the possibilities of combination therapy. Large series of combinations of registered and experimental compounds were tested in animals [32], and several trials of combinations of eflornithine, melarsoprol and nifurtimox were conducted. In all the trials, the combinations were more effective than any of the drugs alone; however, all the combinations containing melarsoprol caused high frequencies of severe adverse reactions [27,33] and were rapidly abandoned. Eventually, in a multi-centre trial, NECT was compared with standard eflornithine therapy in the Republic of the Congo and the Democratic Republic of the Congo [34]. NECT reduces the required number of eflornithine infusions from 56 to 14, shortens hospitalization by one third and reduces the total amount of eflornithine required by half [33]. In view of its favourable results, NECT was included for treatment of second-stage gambiense HAT into WHO's Essential Medicines List in May 2009 [35]. One year later, the rate of use of NECT was about 88% and that of melarsoprol only 12% for administration in exceptional situations, e.g. areas in which training had not yet been conducted [31,36]. Today, there is no place for melarsoprol in the treatment of gambiense HAT, apart from the treatment of relapses. NECT is a landmark improvement, but the complexity of its application still restricts its use to facilities with specially trained personnel and to second stage disease. Lumbar puncture for diagnostic staging and long hospitalization are still required, and the targeted integration of HAT treatment into public health structures is still limited. The situation of treatment of rhodesiense HAT remains far more constrained. The only substantial progress made in the past 60 years was recommendation of the abridged treatment regimen with melarsoprol by the International Scientific Council for Trypanosomiasis Research and Control in 2009 on the basis of the last trial of the IMPAMEL programme [37,38]. The number of compounds under research and development is limited, although there are more promising substances in the pipeline than ever before.

Future Prospects

After more than 100 years of tsetse fly and trypanosomiasis research, the prognosis of the disease remains ambiguous. There is a prominent idea that vector eradication may be impossible to achieve, even with sustained integrated approaches but these may be enough to maintain high levels of suppression [39]. In addition, it is thought that elimination of *T. brucei rhodesiense* is unlikely due to its extensive zoonotic distribution, given that, future research towards disease control should focus on improvement of vector control methods, cost-effective disease surveillance, early case detection and treatment 40]. However, some outlooks are generally more positive. The WHO, by including HAT in its roadmap for "Eradication, Elimination, and Control of Neglected Tropical Diseases" has set a target to eliminate HAT as a public health problem by 2020, when fewer than one new case/10,000 inhabitants in at least 90% of endemic foci is expected [41]. It is argued that transfer of all the accumulated scientific knowledge on tsetse and HAT

from the bench to the field will lead to effective diagnosis, treatment and vector control interventions [42]. In particular, the elimination of *g*HAT is considered feasible because of "the epidemiological vulnerability of the disease, the current state of control, the availability of strategies and tools, and international commitment and political will" [43].

Conclusion

Trypanosomiasis is a neglected tropical disease according to the World Health Organization. Socio-economically deprived communities observed in Sub-Saharan Africa and other parts of the world are at-risk populations. Man is the major target of trypanosomiasis, although tsetse fly serves as an intermediary host. Though the clinical signs of trypanosomiasis are unclear, the disease can be diagnosed and as well treated. Drugs such as suramin, pentamidine, praziquantel, eflornithine etc., have been used in the treatment of trypanosomiasis. Novel drug research has been geared towards developing inhibitors for novel targets recognized to be crucial to the parasite survival in the host organism.

References

[1] Karshima SN, Ajogi I and Mohammed G. (2016) Eco-epidemiology of porcine trypanosomosis in Karim Lamido, Nigeria: prevalence, seasonal distribution, tsetse density and infection rates. Parasites & Vectors (2016) 9:448 DOI 10.1186/s13071-016-1732-x

[2] Onyebiguwa, P., Nworsi, G., Isaac, C., Igho Igbinosa, B., Umukoro, D.O and Aitaiikuru D.P. Human African trypanosomiasis in endemic focus of Abraka, Nigeria: Asian Pacific Journal of Tropical Medicine, 2010; 448-450

[3] Kalu, A.U., Uzoukwu, M., Ikeme, M.M. and Magaji, Y. Trypanosomiasis in Nigeria. High prevalence among ruminants in Gboko Local Government Area.Bull. Anim. Hlth. Prod. Afr. 1991; 39: 3-8

[4] Kuintel, A., Lowe, L. and Cooper, A. Case of Nigeria-acquired Human African Trypanosomiasis in United Kingdom, 2016: Emerging Infectious Diseases, 2017; Vol. 23 1225-1228.

[5] Musa, D., Fajinmi, A.O., Abdullahi, R., Tese, T., Irhue, A.E. Immunology and Immunopathology of African Trypanosomiasis. Global Advance Research Journal of Medicine and Medical Science, 2015; Vol. 4(5) pp.218-230

[6] World Health Organization. *Control and surveillance of African trypanosomiasis.* Geneva: WHO; 1998. [WHO technical report Series 881.]

[7] Ugoji, C.U., Andrew, A., Bock-Oruma, Duncan Umukoro, Geraldine U. Ndukwu. Human African Trypanosomiasis successfully treated with Melarsoprol in Pregnancy in a Niger Delta Rural Hospital. Case Reports in Clinical Medicine, 2014, 3, 353-356.

[8] Edeghere, H., Elhassan, E., Abenga, J., Osue, H.O. Lawani, F.A.G and Falope, O. Effects of infection with *Trypanosoma brucei* on different trimesters of pregnancy in ewes. Vet. Parasitol.43: 203-209, 1992.

[9] Gambino, D. and Otero, L. Design of prospective antiparasitic metal-based compounds including selected organometallic cores. Inorganica Chimica Acta 2018; 472: 58-75

[10] Büscher, P., Cecchi, G., Jamonneau, V., Priotto, G. Human African trypanosomiasis. The Lancet 2017; 390: 2397-2409

[11] Siqueira, L.D.P., Fontes, D.A.F., Aguilera, C.S.B., Timoteo, T.R.R., Angelos, M.A. et al. Schistosomiasis: Drugs used and treatment strategies. Acta Trop 2017; 176: 179-187

[12] Tomiotto-Pellissier, F., Miranda-Sapla, M.M., Machado, L.F., Bortoleti, B., Sahd, C.S. et al. Nanotechnology as a potential therapeutic alternative for schistosomiasis. Acta Trop 2017;174: 64-71

[13] Gorchakov, R., Trosclair, L.P., Wozniak, E.J., Feria, P.T., Garcia, M.N. et al. Trypanosoma cruzi infection prevalence and blood meal analysis in triatomine vectors of Chagas disease from rural peridomestic locations in Texas, 2013– 2014. J Med Entomol 2016;53: 911-918

[14] Nass, J. and Efferth, T. The activity of Artemisia spp. and their constituents against Trypanosomiasis. Phytomedicine 2018;47: 184-191

[15] Cattand, P., Jannin, J and Lucas, P. Sleeping sickness surveillance: an essential step towards elimination, *Tropical Medicine and International Health*, 2001;vol. 6, no. 5, pp. 348–361

[16] Farikou, O., Njiokou, F., Simo, G., Asonganyi, T., Cuny, G and Geiger, A. Tsetse fly blood meal modification and trypanosome identification in two sleeping sickness foci in the forest of southern Cameroon, *Acta Tropica*, 2010;vol. 116, no. 1, pp. 81–88.

[17] Mwanakasale, V., Songolo, P. and Daka, V. Challenges in the control of Human African

Trypanosomiasis in the Mpika district of Zambia, *BMC Research Notes*,2013;vol. 6, article 180

[18] Dennis, J.W., Durkin, S.M., Horsley, Downie, J.E., Hamill, L.C., Anderson, N.E. and Macleod, E.T. Sodalis glossinidius prevalence and trypanosome presence in tsetse from Luambe National Park, Zambia, *Parasites and Vectors*, 2014;vol. 7, article 378

[19] Kohagne, T.L., M'eyi, M.P., Mimpfoundi, R. and Louis, J.F. Entomological patterns in the human African trypanosomiasis focus of Komo Mondah, Gabon, *African Health Sciences*, 2010;vol. 10, no. 4, pp. 341–348

[20] Auty, H.K., Picozzi, K., Malele, I., Torr, S.J., Cleaveland, S. and Welburn, S. Using molecular data for epidemiological inference: assessing the prevalence of *Trypanosoma brucei rhodesiense* in tsetse in Serengeti, Tanzania, *PLoS Neglected Tropical Diseases*, 2012;vol. 6, no. 1, Article ID e1501

[21] Welburn, S.C., Molyneux, D.H., Maudlin, I. Beyond Tsetse--Implications for Research and Control of Human African Trypanosomiasis Epidemics. Trends Parasitol 2016;32: 230-241.

[22] Useh, M.F. Control of Shistosomiasis. Rokni MB. Shistosomiasis. Croatia: Rijeka 2012; 73-102.

[23] Van Nieuwenhove, S. Advances in sleeping sickness therapy. Annales de la Société Belge de Médécine Tropicale, 1992;72 (Suppl 1):39–51.

[24] Nightingale, S. Drug for sleeping sickness approved. Journal of the American Medical Association, 1991; 265(10):1229

[25] Iten, M. et al. Innate lack of susceptibility of Ugandan Trypanosoma brucei rhodesiense to DL-alpha-difluoromethylornithine (DFMO). Tropical Medicine and Parasitology, 1995; 46(3):190–194.

[26] Burri, C. et al. Pharmacokinetic properties of the trypanocidal drug melarsoprol. Chemotherapy, 1993; 39(4):225–234.

[27] Schmid, C. et al. Effectiveness of a 10-day melarsoprol schedule for the treatment of late-stage human African trypanosomiasis: confirmation from a multinational study (IMPAMEL II). Journal of Infectious Diseases, 2005; 191(11):1922–1931.

[28] Bisser, S. et al. Equivalence trial of melarsoprol and nifurtimox monotherapy and combination therapy for the treatment of second-stage Trypanosoma brucei gambiense sleeping sickness. Journal of Infectious Diseases, 2007;195:322–329.

[29] Legros, D. et al. Therapeutic effects of melarsoprol among patients treated for late-stage T. b. gambiense human African trypanosomiasis in Uganda. Bulletin de la Société de Pathologie Exotique, 1999; 92 (3):171–172.

[30] Anonymous. Killer coma: the evolving story of sleeping sickness treatment. Lancet, 2010, 375:93.

[31] Burri C, Keiser J. Pharmacokinetic investigations on patients from northern Angola refractory to melarsoprol treatment. Tropical Medicine and International Health, 2001;6(5):412–420.

[32] Simarro, P.P. et al. Update on field use of the available drugs for the chemotherapy of human African trypanosomiasis. Parasitology, 2012;6:1–5.

[33] Jennings FW. Future prospects for the chemotherapy of human trypanosomiasis. [2. Combination chemotherapy and African trypanosomiasis]. Transactions of the Royal Society of Tropical Medicine and Hygiene, 1990; 84(5):618–621.

[34] Priotto G et al. Three drug combinations for late-stage Trypanosoma brucei gambiense sleeping sickness: A randomized clinical trial in Uganda. PLoS Clinical Trials, 2006;1(8):e39:1–8.

[35] Chappuis, F. Melarsoprol-free drug combinations for second-stage Gambian sleeping sickness: the way to go. Clinical Infectious Diseases, 2007;45(11):1443–1445.

[36] WHO includes combination of eflornithine and nifurtimox in its Essential List of Medicines for the treatment of human African trypanosomiasis. Geneva, World Health Organization, 2009 (http://www.who.int/neglected_diseases/disease_management/drug combination/en/; accessed 4 January 2013).

[37] Yun, O. et al. NECT is next: implementing the new drug combination therapy for *Trypanosoma brucei gambiense* sleeping sickness. PLoS Neglected Tropical Diseases, 2010;4(5):e720.

[38] International Scientific Council for Trypanosomiasis Research and Control. Reports and recommendations. 30th Meeting of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC), 2009, Kampala, Uganda. Nairobi

[39] Kuepfer, I. et al. Safety and efficacy of the 10-day melarsoprol schedule for the treatment of second stage rhodesiense sleeping sickness. PLoS Neglected Tropical Diseases, 2012; 6(8):e1695.

[40] Adam, Y., Cecchi, G., Kgori, P. M. et al., "The sequential aerosol technique: a major

component in an integrated strategy of intervention against riverine tsetse in Ghana," PLoS Neglected Tropical Diseases, 2013;vol. 7, no. 3,Article ID e2135

[41] Kotlyar, S, Recommendations for control of East African sleeping sickness in Uganda," Journal of Global Infectious Diseases, 2010;vol. 2, no. 1, pp. 43–48

[42] WHO, Control and Surveillance of Human African Trypanosomiasis: Report of a WHO Expert Committee, WHO Technical Report Series, WHO, Rome, Italy, 2013

[43] Aksoy, S. Sleeping sickness elimination in sight: time to celebrate and reflect, but not relax," PLoS Neglected Tropical Diseases, 2011;vol. 5, no. 2,Article ID e1008

[44] Franco, J.R., Simarro, P.P.,Diarra, A. and Jannin, G.J. Epidemiology of human African trypanosomiasis," Clinical Epidemiology, 2014;vol. 6, no. 1, pp. 257–275

Citation: Tinuoye, O.O. et. al, (2020), "Prevention, Control and Treatment Strategies for Trypanosomiasis: A Review", Arch Health Sci; 4(1): 1-8.

DOI: 10.31829/2641-7456/ahs2020-4(1)-146