Azithromycin and Diminazene Aceturate Combination Therapy in Experimental Multidrug-resistant *Trypanosoma brucei brucei* Infection in Albino Rats

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Background

- Due to extensive use and misuse over several decades and the absence of new trypanocides, resistance of trypanosomes to trypanocides has emerged with some resistant strains requiring well above the recommended doses to achieve therapeutic cure.
- Most nomads/herdsmen in Nigeria and in most sub-Saharan African countries rely on the combination of trypanocides and antibiotics for the treatment of resistant or recurring cases of animal trypanosomosis.
- Due to the weak Nigerian drug/antibiotic regulations; availability and affordability of azithromycin, combinations of trypaanocides and azithromycin enjoy widespread patronage in resistant/recurring trypanosomosis treatments.

Methodology

- ✓ Forty-five female albino rats were randomly assigned to nine groups (1 - 9) of five rats each.
- ✓ Group 1 served as the uninfected-untreated group while groups 2 - 9 were infected with 10^6 multidrug-resistant (diminazene aceturate and isometamidium chloride resistant) *Trypanosoma brucei brucei* suspended in 0.3 ml of normal saline intraperitoneally.
- ✓ Following infection and parasitaemia, group 2 was untreated while group 3 was treated once with 7 mg/kg diminazene aceturate (DA). Groups 4 - 6 were treated with 10, 20 and 30 mg/kg azithromycin (AZT) respectively for 7 days. Groups 7 - 9 were treated with combination of 7 mg/kg DA once and 10, 20 and 30 mg/kg AZT respectively for 7 days.
- ✓ Level of parasitaemia, haematological indices (packed cell volume, total erythrocyte count, total leukocyte count, haemoglobin concentration, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration), survivability, body weight and rectal temperature were used to assess the effectiveness of the combination therapy.

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Results

- ❖ A significant reduction in parasitaemia levels was observed in the DA-treated group and AZT-treated group 6 while clearance of parasitaemia was observed in the DA-AZT treated groups 7–9 for periods between 1 and 5 days post treatment.
- ❖ The haematological indices and survivability of the DA-AZT treated groups were better than the DA-treated group despite the relapse recorded in those groups.
- ❖ One rat each in the DA-AZT combination groups survived till the end of the experiment.

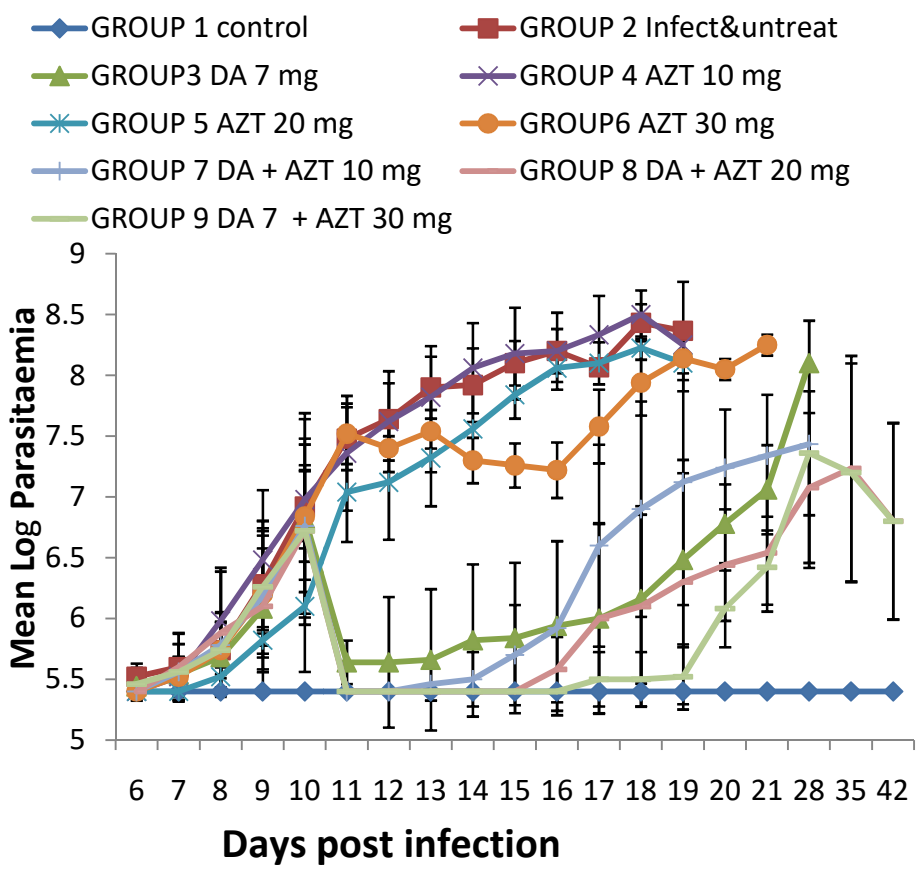

Figure 1: Mean log parasitaemia of rats infected with multidrug-resistant *Trypanosoma brucei* and treated with DA and/or AZT.

Discussion

- Molefe et al. (2019) reported the trypanocidal activity of AZT against *T. brucei* and *T. congolense* possibly by the triggering of autophagy and/or inhibition of trypanosomal protein synthesis.
- The complete clearance of the parasitaemia for some day(s), improved survivorship and reduced effect of the disease on the health status of the rats following DA-AZT combination therapy might probably be due to the synergistic effects of the drug combinations.
- AZT may have also transiently chemosensitized the multidrug-resistant *Trypanosoma brucei brucei* to diminazene aceturate and competed/interfered with their extrusion from the resistant parasites, thus allowing increased concentration, effectiveness and prolonged duration of action of diminazene aceturate.

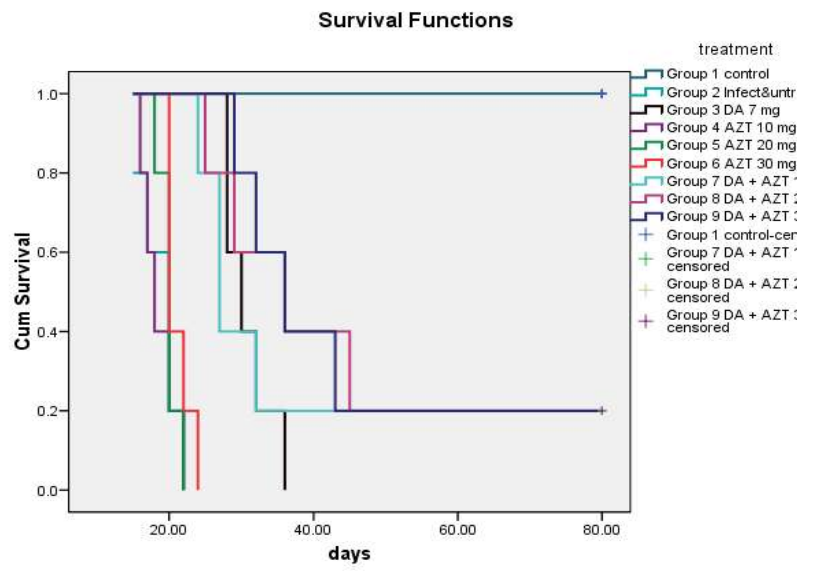

Figure 2: Kaplan-Meier survival estimates of rats infected with multidrug-resistant *Trypanosoma brucei* and treated with DA and/or AZT.

Conclusion

DA-AZT combination treatment can be used as a possible adjunct to DA in the treatment of multidrug-resistant *T. brucei brucei* infections.

REFERENCES

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