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Atypical human infections by animal trypanosomes: evaluation of human and animal trypanocidal drugs against *Trypanosoma lewisi* in Wistar rats

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Abstract

Trypanosomosis is a disease of medical and veterinary importance, mainly distributed in tropical areas of Africa, Latin America and Asia. Some *Trypanosoma* species are typically pathogenic for animals, such as *Trypanosoma vivax, T. congolense*, *T. evansi* etc, and others are zoonotic, such as the agents of sleeping sickness in Africa (*Trypanosoma brucei ssp.*), or Chagas disease in Latin America (*T. cruzi*). Beside these 2 "typical" human trypanosomes, there is a growing number of reported "atypical" human infections due to *Trypanosoma evansi*, a livestock parasite, or *Trypanosoma lewisi*, a rat commensal, especially in Asia. Drugs available for the treatment of *T. brucei* ssp in humans are obviously of choice for the control of *T. evansi* because it is derived from *T. brucei* lineage; indeed, in 2 recent cases of human infection by *T. evansi*, successful treatments were obtained using suramine. However, concerning *T. lewisi*, there is a need to determine the efficacy of trypanocidal drugs for the treatment in humans. In a recent study, pentamidine and fexinidazole were shown to have the best efficacy against one stock of *T. lewisi* in rats, they have thus been explored amongst others.

In order to explore efficient trypanocidal drugs, attempts were made to treat groups of 3 rats experimentally infected by *T. lewisi*, using low and high doses of the available human and veterinary trypanocidal drugs: diminazen aceturate (DA; 14 and 28 mg/kg), isometamidium chloride (IMC: 2 and 4 mg/kg), quinapyramine sulfate and chloride (QSC; 8.3 and 16.6 mg/kg), cymelarsan (Cym; 0.5 and 1 mg/kg), suramine (20 and 40 mg/kg), pentamidine diisetionate (Pt: 8 and 16 mg/kg), eflornitine hydrochloride (Efl; 800 and 16000 mg/kg), nifurtimox (Nt; 30 and 60mg/kg), benznidazole (Bz; 20 and 40 mg/kg) and fexinidazole (Fex; 200 mg/kg). At the exception of Nt, Bz and Fex which were administered perorale route, all drugs were intramuscularly injected. All treatments at all doses failed to clear parasites from rat's blood.

To confirm the potential efficacy of fexinidazole, a mixed infection protocol was set up in cyclophosphamide immunosuppressed rats. Animals were infected successively by *T. lewisi* and *T. evansi*, and received 10 daily peroral administrations of 200 mg/kg fexinidazole or 0.5 mg/kg Cym. *T. evansi* was cleared from the rat's blood within 24 to 48 hours; however, the treatment did not affect *T. lewisi* which remained in high number in the blood until the end of the experiment. Results are discussed and further studies suggested. Because of its potential as an emerging parasite in humans, identifying efficient trypanocides against *T. lewisi* is required.

Key words: *Trypanosoma lewisi*, trypanocidal drugs, fexinidazole, melarsomine hydrochloride, rats, *Trypanosoma evansi*.