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Susceptibility of a rodent-adapted strain of *Trypanosoma vivax* to Berenil, Samorin and Novidium

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Summary

The susceptibility of a rodent-adapted strain of *Trypanosoma vivax* (Leeflang strain Y58) to Berenil, Samorin and Novidium was tested in mice. When infected mice were treated on the second day of detectable parasitaemia, there was complete cure with Berenil at 10 mg/kg, Novidium at 4 mg/kg and Samorin at 0.2 mg/kg body weight respectively. Berenil and Novidium at lower doses rendered the mice aparasitaemic for a few days followed by heavy parasitaemia (relapses) and death. Lower doses of Samorin, on the other hand, were curative for none or only some of the mice but without relapses. These observations are related to the accepted modes of action of these drugs and their use in the field.

Introduction

Until recently it was difficult to work with *Trypanosoma vivax* in laboratory rodents because of its inherent inability to produce persistent infection in rats or mice. In 1974, Leeflang established two mouse-adapted strains of *T. vivax* (Y58 and Y486 Zaria) which remained pathogenic to ruminants and transmissible by tsetse flies (Leeflang et al., 1976; de Gee et al, 1976). Earlier, Isoun (1975) had shown that the Y58 strain produced an acute infection in mice with heavy parasitaemia and death within 4–8 days.

Berenil (diminazene aceturate)[1], Samorin (isometamidium chloride)[2] and Novidium (homidium chloride)[2] are among the most commonly used drugs against animal trypanosomiasis in Tropical Africa. In Nigeria, Berenil at 3.5–7.0 mg/kg body weight and Novidium at 1.0 mg/kg body weight are used to

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[2] May and Baker Ltd., Lagos

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treat clinical cases caused mainly by *T. vivax* and *T. congolense*, whereas Samorin at 0.5 mg/kg is recommended for chemoprophylaxis (Na' Isa, 1970). Recently there have been renewed studies on the mechanisms of action of these and other drugs against trypanosomes in vitro (Williamson and Macadam, 1975; Williamson, 1976).

As part of on-going studies aimed at enhancing the prophylaxis of trypanocides used in animals, we first of all decided to investigate the susceptibility in mice to commonly used trypanocides, of the Y58 strain of *T. vivax* which is pathogenic to livestock.

Materials and methods

One hundred and twenty young adult male Wister mice were used for this study. The Y58 strain of *T. vivax* has been previously described (Isoun, 1975). After several passages in mice, a stabilate was prepared in capillary tubes and stored at $-70°$ C. Before the mice of this experiment were inoculated, the strain was rapidly passaged five times in mice. Heparinised cardiac blood was collected from a heavily infected mouse and appropriately diluted with ice-cold sterile phosphate-buffered saline, pH 7.8. Each test mouse was inoculated intraperitoneally with 8.7×10^5 trypanosomes in 0.1 ml of the diluted blood and the mice were placed in groups A, B, C, D each with 15–50 mice (Table 1). Two to three days after inoculation and when parasitaemia was of the order of 1–2 per microscope field, mice in groups A, B, and C were treated with varying doses of Berenil, Samorin and Novidium respectively using 5 mice per dose administered by deep intramuscular injection (Table 1). Group D animals were left as untreated controls. Tail blood of the mice was examined daily by wet mount for two weeks and the number of parasites per fifty fields under the microscope was determined using $\times$ 40 objective. Mice were regarded as cured if after treatment they became aparasitaemic for the duration of the experiment. Relapsed cases were those that were aparasitaemic soon after treatment, and subsequently developed parasitaemia without further inoculation.

Results

The results are summarized in Table 1. Berenil at 3.5 mg/kg body weight (the recommended field dose for livestock) caused transient aparasitaemia with relapses leading to death in all 5 mice. Even at twice the recommended field dose, 3 out of 5 mice died during the period of examination. Complete cure was obtained at 10.0 mg/kg and above. Similarly, Novidium at 2.0 mg/kg (twice the recommended field dose) did not result in any cure; this was achieved at 4.0 mg/kg and above. On the other hand, Samorin at 0.2 mg/kg (less than half the recommended field dose) resulted in complete cure of 5 out of 5 mice. Even at 0.05 mg/kg one out of 5 mice was cured without relapsing. All control mice had heavy parasitaemia and died within the period.

Discussion

This study has shown that the Y58 rodent-adapted strain of *T. vivax* is susceptible in mice to Berenil, Samorin and Novidium at doses which are different from the recommended field doses for livestock. Whereas greater than

Table 1. Susceptibility of a rodent-adapted strain (Y58) of *T. vivax* in mice to Berenil, Samorin and Novidium

Group	Dosage mg/kg b.w.	No. of mice treated	No. aparasitaemic (within 48 h)	No. of relapses	No. cured	No. of death	Remarks
A (Berenil)	3.5	5	5	5	0	5	Deaths following massive parasitaemia
	5.0	5	5	5	0	3	
	7.0	5	5	5	0	3	
	10.0	5	5	0	5	0	
	12.0	5	5	0	5	0	
B (Samorin)	0.01	5	0	0	0	5	dito
	0.025	5	0	0	0	5	
	0.05	5	1	0	1	4	
	0.1	5	3	0	3	2	
	0.2	5	5	0	5	0	
	0.3	5	5	0	5	0	
	0.4	5	5	0	5	0	
	0.5	5	5	0	5	0	
	1.0	5	5	0	5	0	
	2.0	5	5	0	5	0	
C (Novidium)	1.0	5	5	5	0	4	dito
	2.0	5	5	5	0	2	One accidental death
	3.0	5	4	0	3	2	
	4.0	5	5	0	5	0	
	6.0	5	5	0	5	0	
	8.0	5	5	0	5	0	
D (Control)	–	15	0	–	0	15	Deaths following massive parasitaemia

twice the recommended field dose of either Berenil or Novidium was required to cure infected mice, less than half the usual dose of Samorin was effective. The strain thus appeared to be more susceptible to Samorin than to Berenil or Novidium.

The relapses observed with subcurative doses of Berenil and Novidium could be due to the drugs reducing the number of circulating parasites and inhibiting multiplication up to the point where the parasites were not detectable in the blood for a while by microscopic examination. Subsequent multiplication of the few survivors as the effect of the drugs wore out would result in a relapse, since Berenil and Novidium have minimal residual effects in tissues, as compared to Samorin (van Hoeve and Cunningham, 1964). It is possible, however, that we might be dealing with a strain of *T. vivax* which is relatively resistant to Berenil and Novidium, as has been reported for Berenil in cattle in Northern Nigeria (Na' Isa, 1968) and East Africa (Staak, 1976).

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