RESEARCH NOTE

Activity of Oxamniquine at Skin, Pulmonary and Sexual Maturation Phases, on a *Schistosoma mansoni* Strain (R1) Previously Reported as Resistant at the Adult Phase

Paulo Marcos Z Coelho*//+, Fábio Ribeiro*, Rômulo T Mello, Francisco C Lima e Silva**, José Augusto Nogueira-Machado****

Departamento de Análises Clínicas e Toxicológicas, Faculdade de Farmácia *Departamento de Parasitologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Caixa Postal 486, 30l6l-970 Belo Horizonte, MG, Brasil **Santa Casa de Misericórdia, Belo Horizonte, MG, Brasil

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The R1 strain of *Schistosoma mansoni* was isolated from a patient previosuly submitted to treatment with oxamniquine and praziquantel, and considered not cured. The chemotherapeutic tests carried out with that strain, using oxamniquine (250 mg/kg) in outbred mice, 50 days after infection, showed a significant resistance to the drug (PMZ Coelho et al. 1977 *Rev Inst Med Trop S Paulo 39*: 101-106). The present work aims at verifying the activity of oxamniquine against the R1 strain at the skin (1 day), pulmonary (5 days), and sexual maturity (25 days) phases. Thus, outbred albino mice were infected with 65 (non-resistant, standard LE strain) and 30 (R1 strain) cercariae, by transcutaneous route. All the infected animals related to each strain were subdivided into groups, and were given 200 mg/kg oxamniquine, by oral route, on days 1, 5 and 25 after infection. Sixty days after each treatment, all groups were sacrificed and perfused (J Pellegrino & AF Siqueira 1956 *Rev Bras Malariol Doenças Trop 8*: 589-597) for worms, the control group (infected and untreated) being perfused on day 50 after infection.

Statistical analysis of the data obtained was performed by means of Kruskal-Wallis' non-parametric test. The results showed that the activity of oxamniquine on 1 and 5-day-old schistosomula was found to be partial for both strains. There were no statistically significant differences either between the two strains or between males and females, as well as in relation to the total amount of worms. However, when treatment occurred on day 25 after infection, females of R1 strain showed an absolute resistance to oxamniquine, whereas a decrease in male numbers was statistically significant in the controls (although reduction rate was low (17.7%), when compared with the LE strain) (decrease in male numbers of 69.2%). On the other hand, the LE strain showed a significant decrease of male and female worms, and no reduction differences between both sexes could be seen (Table).

Resistant human strains against the activity of schistosomicide drugs have been reported by several authors (N Katz et al. 1973 *Rev Soc Bras Med Trop 6*: 381-387, R Campos et al. 1976 *Trans R Soc Trop Med Hyg 70*: 261-262, LCS Dias et al. 1978 *Rev Saúde Publ S Paulo 12*: 110, 1982 *Trans R Soc Trop Med Hyg 76*: 652-659, 1988 *Rev Inst Med Trop S Paulo 30*: 81-85, RX Guimarães et al. 1979 *Rev Ass Méd Bras 25*: 48-50, N Araújo et al. 1980 *Amer J Trop Med Hyg 29*: 890-894, RJ Pedro et al. 1980 *Rev Inst Med Trop S Paulo 22*: 32-36, GC Coles et al. 1987 *Trans R Soc Trop Med Hyg 81*: 782-785, D Cioli et al. 1993 *Parasitol Today 9*: 162-166, 1995 *Pharmacol Therap 68*: 35-85, PG Fallon et al. 1995 *Amer J Trop Med Hyg 53*: 61-62, FF Stelma et al. 1995 *Am J Trop Med Hyg 53*: 167-170).

Nevertheless, isolation and characterization of a resistant strain to drugs are not easy. In this way, N Araújo et al. (1995 p. 51, Abstracts V International Symposium on Schistosomiasis) carrying on researches with mice, using ten strains isolated from patients treated with oxamniquine and praziquantel and not cured, were not able to demonstrate resistance or tolerance to those drugs. The majority of the papers that appears in the literature shows that resistance of *S. mansoni* strains to drugs is detected at the adult phase of worms. Thus, Coelho et al. (1997 *loc. cit.*) verified that resistance of R1 strain to oxamniquine occurred in mature infection, and it was more pronounced in relation to male worms.

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+Corresponding author. Fax: +55-31-499.2829.
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In the present study, when oxamniquine was given at the dose of 200 mg/kg, it was shown that resistance recorded by those authors could not be detected in schistosomules at skin and pulmonary phases, but occurred in an absolute manner in females, at sexual maturation phase (25 days after infection).

The present findings show the importance of drug-resistance studies taking into account the evolutive stages of *S. mansoni* in the definitive host.

TABLE

Mean ± standard deviation and reduction in the number of male and female worms recovered from mice infected with 65 (LE strain) and 30 (R1 strain) cercariae, and treated with oxamniquine (200 mg/kg) on days 1, 5 and 25 after infection (15 mice per group)

	LE strain						R1 strain					
	Males		Females		Total		Males		Females		Total	
Days	MD±SD (n)	Red (%)	MD±SD (n)	Red (%)	MD±SD (n)	Red (%)	MD±SD (n)	Red (%)	MD±SD (n)	Red (%)	MD±SD (n)	Red (%)
1	2.23±2.59 (13)	80.2	1.38±1.61	86.2	3.61±2.47	87.4	0.69±0.85 (13)	87.4	0.46±0.66	88.4	1.15±0.81	87.8
5	3.57±2.56 (14)	68.3	2.43±1.83	75.7	6.00±2.38	71.8	1.67±1.99 (15)	75.5	0.73±0.96	81.5	2.40±1.31	74.5
25	3.47±2.29 (15)	69.2	2.67±2.53	73.3	6.14±2.71	71.1	4.50±3.08 (16)	17.7	4.94±2.59	25.1	9.44±3.17	0
C	11.25±2.79 (20)	-	10.0±3.23	-	21.25±3.56	-	5.47±2.59 (19)	-	3.95±1.87	-	9.42±2.44	-

MD±SD: mean ± standard deviation; (n): number of animals; Red: reduction of worm numbers; C: control group (infected and untreated); Total: males + females.