

THE PROLONGED USE OF NICLOSAMIDE AS A MOLLUSCIDICIDE FOR THE CONTROL OF *Schistosoma mansoni*.

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SUMMARY

Applications of niclosamide at three-monthly intervals were undertaken for 14 years in foci of *Biomphalaria glabrata* in the water sources of Peri-Peri (Capim Branco, MG). All the residents of the area were submitted to an annual fecal examination (Kato/Katz) and those individuals eliminating *Schistosoma mansoni* eggs were treated with oxamniquine. A malacological survey was undertaken at three-monthly intervals by means of ten scoops with a perforated ladle each ten metres along the two banks of the ditches and streams of the region. Where snails were found, molluscicide was applied by means of dripping or aspersion using a 3 ppm aqueous suspension of niclosamide. Initially, a mean of 14.3% of snails in the region were found to be eliminating cercariae. Following the first four applications of molluscicide, this was reduced to 0.0% and maintained at about 1.5% throughout the program. Thus, there was a continued possibility of schistosomiasis transmission in the area and it was observed that the population of snails reestablished itself within three months of molluscicide application. The results obtained in this study do not encourage the continual use of niclosamide as the only method of control of schistosomiasis.

KEY WORDS: Schistosomiasis; Control; Molluscicide.

INTRODUCTION

According to the mathematical model of MacDONALD¹⁴, snail control has an essential role in the control of the transmission of schistosomiasis. Since sanitary engineering and biological control do not provide definitive solutions, chemical methods are used in areas where their application is possible^{6,13}.

Before 1950, when schistosomicidal drugs with high cure rate and low toxicity were still not available for large scale use, combating the mollusk intermediate hosts of *Schistosoma mansoni* was considered to be the principal means of controlling of schistosomiasis.

Various molluscicides were investigated⁶. Among these, niclosamide (Bayluscide®), experiments with which demonstrated that, if applied regularly and with care, it controlled the snails of the genus *Biomphalaria*, enabling the transmission of schistosomiasis to be reduced. The product

kills the majority of freshwater flora and fauna, causing serious ecological impact, although it is considered by the World Health Organization to have low toxicity for mammals²⁴. Its production within Brazil appears to be perfectly viable in view of that of salicylic acid and 1,2-dichloro-4-nitrobenzene, its principal active components. Furthermore, the team of FARMANGUINHOS-FIOCRUZ achieved the synthesis of niclosamide, making it the best choice available.

In this study, the infection of snails by *S. mansoni* in the water system of Peri-Peri, MG, is evaluated where niclosamide was used in association with specific treatment during 14 years of schistosomiasis control.

MATERIALS AND METHODS

Peri-Peri is a suburb of 650 inhabitants of the town of Capim-Branco situated 60 km from Belo Horizonte, MG. It is bordered by the Ribeirão da Mata river which is the source of a stream that

provides water for horticultural irrigation ditches, bathing, leisure activities and domestic use. Apart from a textile factory that has absorbed 35% of the active work force, the region is made up of small holdings (1 to 5 hectares), where the monoculture of garlic predominates.

The area was initially completely mapped, the buildings numbered and the complete natural water system within the urban area defined. Twenty five locations within the water system were identified as points for the malacological survey.

Standardized snail surveys were carried out at three monthly intervals at these points, ten scoops with a perforated ladle were made per ten metres of the two banks of the streams and rivers⁷. The snails were collected and sent to the laboratory where they were classified and squashed between glass plates and examined by means of a stereo microscope in order to determine whether or not the glandular region was infected²⁰.

The applications of niclosamide were made by the group of the Centro de Pesquisas "René Rachou" (CPqRR-FIOCRUZ) from 1974 to

1983 and by resident volunteers in the area from 1984 to 1987.

The techniques of dripping or aspersion of an aqueous suspension of 3 ppm of niclosamide were used.

The analysis of the data was undertaken using simple regression analysis²³. The level of statistical significance was taken as 95%.

RESULTS

During the 14 years of this longitudinal survey *B. glabrata*, and *B. straminea* were captured in the area. Only *B. glabrata* was found to be naturally infected with *S. mansoni*.

The level of infection of the snails in the area, at the beginning of the program, was 14.3% and was reduced to 0.0% after four molluscicide applications. The variation of between 0.2 and 4.7% that was observed up until the termination of the program, was found not to be statistically significant. The regression curve of annual mean numbers of snails infected with *S. mansoni* during the program showed a significant fall ($b = -0.25 \pm 0.17$, Table 1).

Table 1
Malacological survey and molluscicide applications in the water courses of Peri-Peri, MG from 1974 to 1987

Year	<i>B. glabrata</i> <i>B. straminea</i>			Nº of surveys	Mean (snails/survey)	Niclosamide applied/ Nº of application	
	collected	c/e*	%			(Kg/application)**	
1974	469	12/84	14.3	4	117	2.0/2	(1.0)
1975	125	0/108	0.0	5	25	12.1/6	(2.0)
1976	33	0/32	0.0	5	7	6.9/5	(1.4)
1977	798	11/231	4.7	8	100	16.4/7	(2.3)
1978	168	0/97	0.0	4	42	6/4	(1.5)
1979	3007	7/201	0.2	10	300	10.4/7	(1.5)
1980	454	5/419	1.7	7	65	9.3/6	(1.6)
1981	175	0/175	0.0	7	25	5.5/6	(0.9)
1982***	564	1/550	0.2	8	71	9.3/6	(1.6)
1983	465	1/445	0.2	7	66	4.8/3	(1.6)
1984	143	0/136	0.0	4	36	4.0/3	(1.3)
1985	99	3/87	3.4	4	25	5.0/4	(1.3)
1986	67	0/67	0.0	4	17	3.3/8	(0.4)
1987	345	7/275	1.8	4	69	2.5/7	(0.4)

The regression analysis showed the following inclinations:

$b = -0.25 \pm 0.17$ -0.01 ± 0.07 -0.27 ± 0.12

$p = 0.0393$ 0.4932 0.0186

* cercariae eliminated/examination

** mean in 14 years = 1.30 Kg/year

*** 48 snails were classified as *B. straminea* species

Although the number of infected snails was significantly reduced following the first four applications of niclosamide, the snail population in the area did not vary during the program showing that the snail population recovered within three months of the niclosamide application ($b = -0.01 \pm 0.07$, Table 1).

The quantity of niclosamide applied in the area was greater during the first years, and was significantly reduced towards the end of the program ($b = -0.27 \pm 0.12$, Table 1). In order to achieve a significant reduction in the number of infected snails in the area throughout the program, it was necessary to use 97.2 kg of niclosamide in 74 applications with an average of 1.3 kg of niclosamide per application in an area of 10 km².

In later years, the quantity of niclosamide applied was reduced and the number of applications increased as the resident volunteers changed to molluscicide application in small isolated foci rather than throughout the water course as was undertaken previously.

During the last three years of the program, the applications were undertaken by volunteers from the community. The numbers of infected snails in the area in this period (0.0 to 3.4%) were not statis-

tically different from those in previous years (0.0 to 0.47%, Table 1).

The annual cost per capita of the applications in US\$ was 0.79 (Table 2).

DISCUSSION AND CONCLUSIONS

A longitudinal survey was undertaken for 12 years in São Lourenço da Mata, PE. The only measure used for the control of schistosomiasis was niclosamide to combat *B. straminea*. At the end of the study, the prevalence was found to have fallen from 50.0 to 25.0% and the incidence from 30 to 8.0% both in control and experimental areas^{1,2}. Similar results were obtained in other studies^{3,5,8,19} undertaken for shorter periods and in different endemic areas.

When the application of molluscicide is combined with other measures the chances of controlling schistosomiasis are higher. For example, in Pontezinha, PE, BARBOSA et al.³, used specific treatment of infected individuals, the application of molluscicides in the water sources, basic sanitation and health education, achieving a reduction of prevalence from 30.0 to 3.8% after 7 years.

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Table 2

Cost of molluscicide applications in the schistosomiasis control program in Peri-Peri, MG from 1974 to 1987

Parameters	(units)	N
Water usage	-	irrigation
Rain fall	(cm)	75
Area controlled	(Km ²)	10
Population	-	650
Volume of surface water	(m ³ /Km ²)	1.000
Density of population	(person/Km ²)	65
Volume of water per person	(m ³)	13
Intermediate host	-	B. glabrata
Annual volume of water treated	(m ³)	40.000
Molluscicide used	-	Bayluscide ^(R)
Period of controlled	(years)	14
Total cost	(US\$)	6.673
Annual cost/100 m ³	(US\$)	1.192
Annual cost/person	(US\$)	0.79
Breakdown of cost (%)		
• Laboratory expenses and labour		39
• Molluscicide		36
• Transport		25

area⁵, the number of infected *B. glabrata* was reduced at points of application of niclosamide, together with a reduction from 5.5 to 0.8 in the average number of worms per exposed mouse, following two years of applications every two months. The fall in these levels, however, were not evaluated in terms of the reduction of the transmission of the infection in the area.

In Peri-Peri, following four three-monthly applications, the number of infected *B. glabrata* was significantly reduced from 14.3 to 0.0% and was thereafter approximately 1.5%. In contrast to the results obtained by BARRETO & PRATA⁵, there was no variation in the number snails at the collecting points in the water system during the 14 years of the program. Similar results were obtained by GILLES et al.¹⁰ and PAULINI & DIAS¹⁹ in the areas that they studied. The survival of snails following molluscicide application was attributed to a few specimens remaining hidden in the mud of the river bed where they were unaffected by the molluscicide^{12,16,17,18,22} and the flow of water during the period of action of the molluscicide¹².

The annual per capita cost of US\$ 0.79 for the applications of niclosamide in Peri-Peri was close to that observed in irrigation areas in Zimbabwe, Puerto Rico, Brazil and Iran; US\$ 1.08, 1.00, 0.70 and 0.94 respectively. In areas with a greater volume of water in Puerto Rico, St. Lucia and Brazil, the annual cost per capita was US\$ 1.50, 4.00 and 7.40 respectively^{8,11,15}.

The benefits obtained in the reduction of transmission in the area where the molluscicides were applied are questionable, both in irrigation areas and in large bodies of water^{1,2,5,9,15,21}. More encouraging results are obtained when molluscicides are applied to small foci^{4,6,13,15}.

These data do not encourage the continual use of niclosamide as the only control measure for schistosomiasis, as it does not permanently diminish the snail population or prevent the possibility of transmission of the disease.

RESUMO

Uso prolongado da niclosamida como moluscicida para o controle do *Schistosoma mansoni*.

Aplicações trimestrais de niclosamida foram

realizadas catorze anos em focos de *Biomphalaria glabrata* nas coleções hídricas de Peri-Peri, (Capim Branco, MG). Anualmente, os residentes da área eram submetidos a um exame coproscópico (Kato-Katz) e os que eliminavam ovos de *Schistosoma mansoni* nas fezes eram tratados com oxamniquine. O levantamento malacológico trimestral foi realizado através de dez conchadas a cada dez metros nas duas margens das valas e córregos da região. Onde eram encontrados caramujos aplicava-se o moluscicida pela técnica de gotejamento ou aspersão de suspensão aquosa da niclosamida a 3 ppm. O índice médio de caramujos eliminando cercárias na região era de 14,3%. Após as quatro primeiras aplicações, foi reduzido a 0,0% e mantido em torno de 1,5% durante o programa. Portanto, a possibilidade de transmissão da esquistossomose na área continuou, e a população de caramujos se refazia em até três meses após aplicação do moluscicida. Os resultados obtidos neste estudo não encorajam o uso contínuo de niclosamida como medida única de controle da esquistossomose, por não diminuir permanentemente a população de planorbídeos e por não interromper a possibilidade de transmissão da endemia.

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