Short Report

# The efficacy of praziquantel against *Schistosoma mansoni* infection in Ndombo, northern Senegal

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## Introduction

Since low efficacy of praziquantel has recently been observed in Senegal and Egypt (FALLON *et al.*, 1995; STELMA *et al.*, 1995; ISMAIL *et al.*, 1996), the possible existence of praziquantel-resistant strains of schistosomes has been the subject of debate, concern and 'panic' (alarming comments). Praziquantel is the drug of choice for the treatment of schistosomiasis, and is commonly used as the principal tool for its control in endemic countries. The development of resistance to praziquantel has been strongly suspected in northern Senegal, a recent and very intense focus of *Schistosoma mansoni*, where unusually low cure rates of 18–35% have been observed in humans (STELMA, 1997). Several explanations have been considered to explain these low cure rates: (i) extremely high intensity of infections in this focus, so that, even if treatment was 99% effective, a sufficient number of schistosome pairs would survive and continue laying eggs; (ii) intense transmission and high reinfection rates, so that many individuals would harbour immature schistosomes, which are not susceptible to praziquantel, at the time of treatment (SHAW, 1990); (iii) repeated infection in the interval between treatment and parasitological assessment; (iv) immaturity of the human's anti-schistosome immune response in this recently established focus; it has been proposed that praziquantel acts synergistically with the immune response of the host (SABAH *et al.*, 1985); and (v) possible resistance/tolerance of the northern Senegalese strain of *S. mansoni* to praziquantel.

## Methods

To investigate the hypothetical existence of a possibly drug-resistant *S. mansoni* strain, and to further our understanding of praziquantel efficacy, field investigations were carried out in Ndombo in June–August 1997. Cure rates and reduction of infection intensity following 2 treatments with praziquantel 40 mg/kg, with an interval of 4 weeks, were assessed. Initially, 88 subjects were selected from 'low cure rate' individuals (STELMA *et al.*, 1995), who had been treated at least twice but who were still excreting schistosome eggs. They were invited to participate in the study, and were registered only after explanation and full approval. A first survey was conducted in June 1997, when 76 individuals provided a stool sample. All were then treated with 40 mg/kg praziquantel. Stool samples were examined using duplicate 25 mg thick smears examined by 2 microscopists, using a 25 mg Kato–Katz template. The second and third surveys, with repeated parasitological examination and treatment, were conducted at intervals of 4 weeks thereafter.

Of the 88 subjects initially identified for the study, 57 (24 males and 33 females) participated in all 3 surveys, and only these were considered in the present analysis, which examined cure rates after 1 and 2 treatments. The mean egg counts of infected individuals were calculated; geometric mean (GM) values of positive samples only were used to assess egg counts. Individuals excreting *S. mansoni* eggs before the first treatment were subdivided into 3 infection intensity classes (group 1: 20–400 eggs/g, group 2: 401–1000 eggs/g, and group 3: > 1000 eggs/g). These 3 groups were then followed throughout the study. Parasitological cure rates were calculated as the proportion of those excreting eggs at the first survey before treatment who were not excreting eggs in their stools (i) 4 weeks after the first treatment, and (ii) 4 weeks after the second treatment. The reduction in egg counts in individuals excreting eggs before the first treatment was also calculated after (i) the first and (ii) the second treatments, as [1 – (GM eggs/g after treatment/GM eggs/g before treatment)] × 100.

## Results

Before the first treatment, only 43 of the 57 people examined (75%) were infected with *S. mansoni*. The 14 subjects who were not obviously infected at the first survey were excluded from analysis, since cure rate cannot be determined when initial egg counts are zero. Mean egg counts, parasitological cure rates and reductions in the intensity of infection are summarized in the Table. The GM egg count of infected persons was 459 eggs/g before treatment, 180 eggs/g after the first treatment, and 201 eggs/g after the second treatment. The cure rate after the first treatment was 58·1%, and it remained unchanged after the second treatment; the intensity reduction rates were 60·8% and 56·2%, respectively.

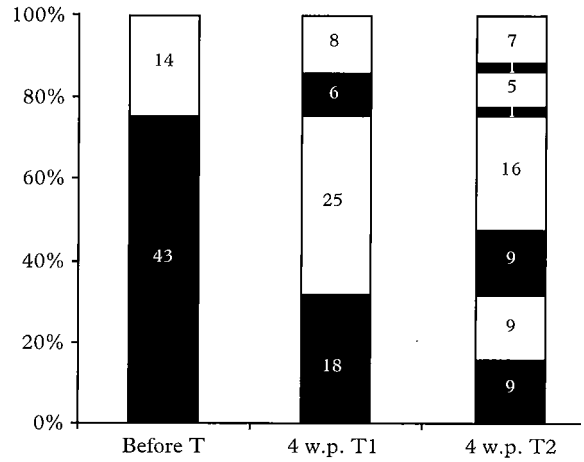


Figure. The survey-to-survey status changing, from positive to negative (solid bars) and vice versa (open bars), before and after treatment with praziquantel of people infected with *Schistosoma mansoni* in Ndombo, northern Senegal. The numbers of individuals per category are reported in the corresponding bars. Before T: before treatment; 4 w.p. T1: 4 weeks after the first treatment; 4 w.p. T2: 4 weeks after the second treatment.

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**Table. Parasitological cure rates, geometric mean egg counts of positive individuals, and intensity reduction rates of persons infected with *Schistosoma mansoni* after one and two treatments with praziquantel 40 mg/kg in Ndombo, northern Senegal**

| | Before treatment | | After one treatment | | | | After two treatments | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Intensity class (eggs/g) | No. | Eggs/g[a] | No. subjects infected | Cure rate (%) | Eggs/g[a] | Intensity reduction rate (%)[b] | No. subjects infected | Cure rate (%) | Eggs/g[a] | Intensity reduction rate (%)[b] |
| 20–400 | 20 | 118 | 6 | 70 | 67 | 43·2 | 6 | 70 | 61 | 48·3 |
| 401–1000 | 9 | 559 | 5 | 44·4 | 173 | 69·1 | 6 | 33·3 | 448 | 19·9 |
| > 1000 | 14 | 2814 | 7 | 50 | 431 | 84·7 | 6 | 57·1 | 297 | 89·4 |
| All classes | 43 | 459 | 18 | 58·1 | 180 | 60·8 | 18 | 58·1 | 201 | 56·2 |

[a]Geometric mean egg count.
[b]See text for method of calculation.

## Discussion

Though cure rates were somewhat higher than those (< 40%) obtained by STELMA (1997), our results confirmed the low parasitological cure rates in this intense transmission focus of *S. mansoni*. Comparable cure rates were observed, after one treatment, by PICQUET *et al.* (1998) in a similar investigation in Nder, a village 25 km south of Ndombo. However, in contrast to Ndombo, cure rates and intensity reduction rates in Nder improved considerably following a second treatment 40 d after the first, particularly in those individuals initially heavily infected. A possible explanation for this may be different transmission intensity levels at the time of the surveys, since the study in Ndombo was conducted in the high transmission season whereas that in Nder was in the low transmission season. Reinfections would probably be greater in the high transmission period, leading to many more immature worms at the time of treatment. POLDERMAN *et al.* (1988) also observed relatively poor cure rates (47%) after one treatment with praziquantel 40mg/kg in children in a highly intense focus in the Democratic Republic of Congo (former Zaire).

Interestingly, there were some switches of infection status between surveys with conversion from positive to negative and vice versa (Figure). This probably reflects high transmission in this focus and suggests that reinfection may play an important role in the poor cure rates observed with praziquantel. This emphasizes the difficulty of assessing drug efficacy in such intense transmission foci. Another confounding factor may be egg count fluctuations. Increasing the praziquantel dose from 40 mg/kg to 60 mg/kg (2 doses of 30 mg/kg) did not significantly improve the response (GUISSÉ *et al.*, 1997). However, the issue remained puzzling as oxamniquine at 20 mg/kg gave the expected high cure rates (79%) (STELMA *et al.*, 1997). This has been addressed by the European Commission, which supported 'Concerted Action on Praziquantel' which proposed a protocol to examine the evidence for drug resistance in high intensity foci (RENGANATHAN & CIOLI, 1998).

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