## Original article

# Praziquantel in the control of Schistosoma mansoni infection in Jiga, Northwestern Ethiopia

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**Abstract:** The curative efficacy and side effects of praziquantel were observed in patients with intestinal schistosomiasis in Jiga town, Northwestern Ethiopia. A total survey of the inhabitants (4861) was done and all those positive for S. man.soni and with no serious contraindications (1248) were treated with praziquantel, single oral dose of 40 mg per kg body weight. The drug has a cure rate of 89% , with a significant reduction in prevalence (P <0.001, OR: 3.58, CI:2. 77, 4.64) and a marked decrease in average intensity of infection (from 187 to 111 EPG). The most frequent (64.4% )' side effects were headache and dizziness, directly related to intensity of infection, and most often did not last more than 48 hours. Therefore, it is concluded that praziquantel is a safe and effective therapy for schistosomiasis and can be used as a key component in the control of the disease. [Ethiop. I. Health Dev. 1996;10(2):105-110]

### Introduction

The importance of population-based chemotherapy in the reduction of morbidity and prevalence of schistosomiasis has been emphasized, WHO (1). The criteria for drug choice are efficacy, few major side effects and acceptable cost. Praziquantel is recognized as the drug of choice for treatment of schistosol!;es pathogenic to man (1, 2, 3). Massoud et al (3) have indicated that there is a direct association between drug dose and cure rate. It has also been observed that the apparent efficacy of schistosomicidal drugs can vary between trials within the same area (4), and between different geographical areas (5).

Wi1kens et al (6) have shown that side effects of praziquantel are mild and transient; others (2, 7) claim that it is well tolerated and .as few side effects. However, Polderman (8), in his study in Zde has indicated that side effects of praziquantel could be intense though short lived, and differences in side effects can occur among various communities within the same country .The variation in side effects, was attributed to variation in egg 1oa High eeg excretors have intense intestinal side effects such as bloody diarrhea. The relationship between egg load and drug side effects has been well demonstrated during morbidity studies due to S. man.soni in Machakos, Kenya (9).

Information on the role of chemotherapy, particularly praziquantel, in the control of schistosomiasis in Ethiopia is quite fragmentary .Woldemichael et al (10) studied the efficacy and side effects of this drug in the
treatment of urinary Schistosomiasis in Ethiopia. They reported that out of 199 patients with urinary schistosomiasis who were treated with praziquantel 30 developed swelling of extremities, periorbital and scrotal areas; fever and generalized malaise. Taddesse et al (11), in their study of state farm workers in Central Ethiopia, have found that the cure rate for praziquantel was 93% , and the side effects were mild and transient. Simonsen et al (12) have shown that the cure rate in Ethiopian labour village children (Wonji Sugar Estate) was 69%; they did not report on side effects. Fletcher and Teklehaimanot (13) found a 94% prevalence of side effects in 354 persons

checked 24 hours after treatment with pra;:iquantel, in a new settlement area, in Metekel, Northwestern Ethiopia.

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The purpose of our: study was to evaluate the effectiveness and "side effects of praziquantel in the treatment of S. mansoni in a setting different from the studies referred to above, a mixture of semiurban and peasant
populations. This was part of a multidisciplinary schistosomiasis control activity including snail control, water supply, environmental sanitation and health education.

**Methods**

*Population*. To determine overall prevalence and intensity of infection as well as to treat positive cases, all residents of Jiga town, 4861 at the time of this study in August 1987, were summoned for stool examination. It was possible to screen 88.3% (4294/4861) of the residents, the rest being either too young or away on business.

*Clinical investigation.* About 10% (113/1080) of the households were selected by systematic random sampling, using the total number of households (1080) as the sampling frame. All members (467 persons) in the selected households were subjected to medical history and physical examination. The purpose of this investigation was to determine the occurrence of signs and symptoms suggestive of intestinal schistosomiasis such as hepatosplenomegaly, ascites and bloody diarrhea. The following were also looked for: pregnancy, lactation, severe acute or chronic illness, age below five years which would then be used as criteria for excluding from treatment with praziquantel. This blind assessment of signs and symptoms was made by a physician prior to laboratory investigation.

*Laboratory investigation.* Stool was processed for microscopic examination by the Kato thick smear method (14), and two slides were prepared for each stool specimen collected from all 4294 individuals. They were then checked in a temporary laboratory at Jiga Health Station by experienced laboratory technicians from the Institute of Pathobiology, Addis Ababa University.

*Treatment.* Those individuals positive for s. mansoni infection were referred back to the physician for treatment. Lactating and pregnant mothers, children below five years of age, and debilitated patients (those with acute or chronic severe illness) were not given the drug. Individuals with no contraindications were then treated. Praziquantel (Bayer-R) 40 mg per kg body weight was dispensed as a single oral dose and swallowed on a full stomach, under supervision.

*Side effects.* Among the 467 persons who underwent clinical investigation and had stool examination, 38% (178/467) were found to have intestinal schistosomiasis. Treatment was given to 170 of these, eight being excluded because of contraindications. Then 101 of the 170 patients

were randomly selected, using simple lottery method, to check for side effects of praziquantel. The patients were told to come back 24 hours after treatment, at which time they were investigated for signs and symptoms resulting from treatment. In addition to these 101 persons, all patients were advised to come to the clinic if they experienced any major discomfort following treatment. Checking for side effects consisted of responding to a questionnaire with both open and closedended questions and physical examination. The informal part of the observation continued for a few more days, during which time patients were encouraged to come if they had any complaints.

*Assessment of effectiveness*. Two months after treatment, the effectiveness of praziquantel was evaluated using parasitological parameters in 54% (670/1248) of individuals who were selected randomly from all those treated. A simple lottery method was employed to pick out subjects. Statistical analysis. Calculation of simple proportions and odds ratios were made as well as chisquare and Fisher's exact tests employed using Epi Info version 5 statistical computer soft ware.

## Results

Out of 4861 residents, 88.3% (4294) were examined, and 30.8% (1322) were positive for S. mansoni. Of these, 94.4% (1248) were treated while the rest did not get treatment either due to absence or because of contraindications. There were no hepatosplenomegaly or other manifestations attributable to schistosomiasis at both the initial and follow-up examinations.

The results of drug effectiveness (Table 1 ) showed a cure rate of 89% (596/670). There was a reduction in prevalence from 30.8% to 11.0%, and intensity declined from 187 to III eggs per gram of feces (EPG) in those who were not cured. The reduction in prevalence was statistically significant ($P < 0.001$, OR 3.58, CI: 2.77, 4.64).

Table 1: Prevalence and intensity of Schistosoma mansoni infection before and after treatment, Jiga NW Ethiopia, 1987.

| Before treatment | | | | | 2 months after treatment | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Age group** | **No, Exam.** | **No.Pos** | **% Pos.** | **EPG*** | **No. Exam.** | **No.Pos** | **% Pos** | **EPG** | **% reduction EPG** |
| 5-9 | 892 | 220 | 25.6 | 198 | 102 | 11 | 10.8 | 98 | 50.1 |
| 10-14 | 862 | 289 | 33.5 | 194 | 266 | 33 | 12.4 | 123 | 36.6 |
| 15-19 | 488 | 230 | 47.1 | 266 | 58 | 6 | 10.3 | 93 | 65.0 |
| 20-24 | 300 | 103 | 34.3 | 183 | 41 | 3 | 7.3 | 93 | 49.2 |
| 25-29 | 302 | 88 | 29.1 | 149 | 39 | 4 | 10.2 | 93 | 37.6 |
| 30-34 | 311 | 97 | 31.2 | 151 | 46 | 4 | 8.7 | 138 | 8.6 |
| 35-39 | 306 | 96 | 31.4 | 151 | 45 | 7 | 15.5 | 115 | 23.8 |
| 40-44 | 211 | 51 | 24.2 | 143 | 25 | 2 | 8.0 | 87 | 39.2 |
| 45-49 | 178 | 49 | 27.5 | 113 | 15 | 1 | 6.7 | 100 | 11.5 |
| 50-54 | 163 | 36 | 22.1 | 164 | 10 | 1 | 10.0 | 100 | 39.0 |
| 55-59 | 107 | 31 | 28.9 | 125 | 10 | 1 | 10.0 | 60 | 52.0 |
| 60+ | 174 | 32 | 18.4 | 128 | 13 | 1 | 7.7 | 108 | 15.6 |

* Eggs per gram of feces (geometric means)

Table 2 shows the side effects. Out of 101 patients checked for signs and symptoms, 50.5% (51/101) were in the 10-19 year age group. It was observed that 70.3% (71/101) had one or more manifestations suggestive of
side effects of praziquantel, whereas the remaining 29.7% (30/101) had no complaints or signs at all. The most frequent symptoms were those related to the central nervous system (headache and dizziness), 64.4% (65/101), followed by abdominal pain (cramps and epigastric pain), 46.5% (47/101).

Diarrhea (14 bloody and IS watery stool) occurred in 28.7%) (29/101); nausea and vomiting in 8.9% (9/101), out of the treated patients. In most cases, the patients had more than one manifestation, while two patients in
the 40-49 year age group had all of the signs am symptoms. Two of the three patients who "were ~ years or older h4'1 only headache and dizziness No of the children under 10 years of age develop nausea, vomiting or dermatological problems.

Table 2: side effects recorded in 101 patients by age group 24 hours after treatment with praziquantel (40 mg/kg, in Jiga, NW Ethiopia, 1987.)

| | | **Patients with side effects** | | | | | | | | | | **Without side effects** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age group** | **No. Treated** | **Nausea/Vomiting** | | **Abdominal Pain** | | **Diarrhea** | | **Itching/Skin rash** | | **Headache/dizziness** | | **Other** | | | |
| | | **No.** | **%** | **No.** | **%** | **No.** | **%** | **No.** | **%** | **No.** | **%** | **No.** | **%** | **No.** | **%** |
| 5-14 | 45 | 10 | 22.2 | 17 | 37.8 | 12 | 26.7 | 2 | 4.4 | 21 | 46.7 | 3 | 6.7 | 14 | 31.1 |
| 15+ | 56 | 9 | 16.1 | 30 | 53.6 | 17 | 30.4 | 7 | 12.5 | 44 | 78.6 | 4 | 7.1 | 16 | 28.6 |
| Total % Average | 101[a] | 19 [a] | 18.8[b] | 47 [a] | 46.5 [b] | 29 [a] | 28.7 [b] | 9 [a] | 8.9 [b] | 65 [a] | 64.4 [b] | 7 [a] | 6.9 [b] | 30 [a] | 29.7 [b] |

Further analysis of the relationship of side effects of praziquantel to the intensity of infection as expressed by EPG was made. Table 3 sh.ows that 44.9% (79/176) of the side effects were observed in the very heavy egg
excretors ( > 800 EPG), followed by the heavy excretors (101-800 EPG). Tl}e fewest side effects were ,encountered in the lightly infected patients (50 or less EPG), followed by those excreting.51..100 EPG. Table 4 presents the relationship of the number of patients having side effects and .EPG. The proportion of
patients with .side effects increased directly with a rise in EPG. The association was statistically significant (chi-square=33.92, 3 df, P. < 0.000001).

Table 3: Side effects of praziquantel in relation to intensity of infection (EPG), in 101 patients Jiga, NW Ethiopia 1987.

| Eggs per gram of stool | | | | | |
|---|---|---|---|---|---|
| **Side effects** | **0-50** | **51-100** | **101-800** | **>800** | **Total** |
| Nausea/Vomiting | 1 | | 14 | 4 | 19 |
| Abdominal Pain | 3 | 5 | 17 | 22 | 47 |
| Diarrhea | 2 | 2 | 14 | 11 | 29 |
| Dermatological code. | 1 | | 4 | 4 | 9 |
| Headache/dizziness | 4 | 6 | 22 | 33 | 65 |
| Others | | 1 | 1 | 5 | 7 |
| **Total** | 11(6.3%) | 14(8.0%) | 72(40.9%) | 79(44.9%) | 176(100%) |

Table 4: Relationship of S.Mansoni egg load (EPG) with the number of patient having side effect (S/E) of praziquantel, Jiga, NW Ethiopia,1987

| **Patients** | | | | | |
|---|---|---|---|---|---|
| **EPG Class** | **Examined** | **With S/E** | | **Without S/E** | |
| | | **No.** | **(%)** | **No.** | **(%)** |
| <50 | 26 | 10 | (38.5) | 16 | (61.6) |
| 51-100 | 24 | 12 | (38.5) | 12 | (50.0) |
| 101-800 | 27 | 25 | (92.6) | 2 | (7.0) |
| >800 | 24 | 24 | (100.0) | - | - |
| Total | 101 | 71 | (70.3) | 30 | (29.7) |

The time of onset of side effects was also looked at following treatment with / praziquantel. Nearly 45% (21/47) of patients with abdominal cramps and epigastric pain developed these symptoms within the first half an hour of ingesting praziquantel, and 55% (26/47), later than this. Dizziness occurred within 30 minutes.in: 37% (17/46) and 63% (29/46) had the onset within 30 minutes; 38% (11/29) after the first hour; and the rest
occurred between these times. Among those who complained of nausea and/or vomiting, 36.8% (8/19) had the onset within the first 30 minutes, while it took 60 minutes or more in the remaining 63.3% (12/19). Of 19 patients who had headache, 26.3% (5/19) developed it between 30 and 60 minutes, while the rest, 73.7% (14.19), had none during the first hour post treatment. All nine cases of dermatological manifestations, which included itching, urticaria and miscellaneous skin rashes, had onset beyond one hour following treatment. Almost all of the patients were free of the side effects before 48 hours.

## Discussion

This study attempted to evaluate the effectiveness and side effects of praziquantel at the community level. The drug was shown to have a high cure rate of 89% when checked two months after treatment. The reduction in prevalence and intensity of infection observed in this study is mainly due to praziquantel. These results are similar to those observed in Egypt (3), Zambia (1S) and Nigeria (16), showing that the drug is as effective in Ethiopia as in those countries. Whether this means for similar strains of S. mansoni or not in these countries needs further investigation. The

cure rate observed in a labour village children in Ethiopia by Simonsen et al (12) was lower than that of this study, most probably because they ..did the follow-up examination one month earlier, by which time excretion of viable or nonviable eggs would continue. On the other hand, the results of Taddesse et al (11) are quite similar to this study.

The present findings also agree with the WHO report (1), indicating that praziquantel is well tolerated, the main side effects being abdominal discomfort, diarrhea and dizziness. Although nearly 70% (71/101) of the patients had complaints after treatment with praziquantel, generally speaking the tolerability of the drug was acceptable. As in the study of Taddesse et al (11), this study also found that the side effects of praziquantel were mild and transient. In fact, none of the patients had complaints which lasted more than 48 hours. The prevalence of side effects in the patients (70%) was lower when compared to 94% .observed by Fletcher and Teklehaimanot (13) who studied a newly settled population. This could mean either parasite strain variation or host factors.

Swelling of the extremities, periorbital and scrotal areas observed in 30 patients by Woldemichael et al (10) following treatment with praziquantel was not encountered in the study. Since their study was on patients with S. hematobium, the difference could be explained by the difference in parasite species and the location of schistosomes and their eggs. Besides, they studied hospitalized patients who might have been admitted due to serious illness resulting from the infection.

The results of this study related to abdominal pain and diarrhea are in conformity with the findings of Polderman (8); His suggestion that the intensity of symptoms varied directly with egg load was also supported by the findings of this study. It is also shown that the number of patients presenting with one or more side effects of praziquantel varied directly with egg load.

The limitations of this study which was launched as part of a multidisciplinary control measure, and is essentially of a descriptive nature, with no rigorous sampling procedures applied, except for clinical assessment are admitted. However, we believe we have shown the effectiveness of praziquantel since more than 54 % of the patients were rechecked with a fair representation of EPG groups. The absence of serious and long lasting side effects in this setting needs to be noted. Therefore, praziquantel can be safely used in population- based mass chemotherapy for comprehensive schistosomiasis control programs in the area studied. However, this would be more lasting if a multidisciplinary approach is employed in terms of safe water supply and environmental sanitation. This multidisciplinary approach had been initiate4 in the study area, and it Would be of importance to assess the status at present.

It is also recommend that at least pilot studies on praziquantel be conducted in other areas with endemic schistosomiasis, to screen for its efficacy and side effects, since there could be differences in PI1'88ite strains add also among communities. It should be noted, however, that the cost of praziquantel is rather expensive currently (about US$O.75 per 600 mg tablet). Hence, there is need for a substantial investment when considering mass chemotherapy.

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**References**

1. WHO/TRS. The control of schistosomiasis. 1985;728.
2. Davies A, Wagner DHG. Multicenter trials of praziquantel in human schistosomiasis: design and technique. Bull WHO. 1979;57:767-771.
3. Massoud AAE, Elkholy AM, Wagner WA Assessment of praziquantel against Schistosoma mansoni infection. J Trop Med Hyg 1984;87:119-121.
4. McMahon JE. A note on drug trials in Schistosomiasis. Trans R Soc Trop Med Hyg 1981;75:597-598.
5. Davis A. Management of patients with Schistosomiasis. In Schistosomiasis, Epidemiology, Treatment and Control. ed. Jordan, P. and Webbe, G.) Heinmann, London. 1982:84.
6. Wilkens HA, Moore PJ. Comparative trials of regimes for the treatment of urinary schistosomiasis in the Gambia. J Trop Med Hyg 1987;90:83-92.
7. Homeida MM, el Tom IA, Sulaiman SM, Daffalla AA, Bennet JL. Efficacy and tolerance of praziquantel in patients with Schistosoma mansoni infection and symmer's fibrosis: a field study in the Sudan. Am J Trop Med Hyg 1988;38(3):496-8.
8. Polderman AM, Gryseels B, Gera:Id JL, Mpamila K, Mashande JP. Side effects of praziquantel in the treatment of Schistosoma mansoni in Maniema, Zaire. Trans R Soc 'irop Med Myg 1984;78:752-754.
9. Arap Siongok, TK, Mahmo-ud AAF, Ouma JM, Warren KS, Muller AS, Manda and Mouser MB. Morbidity in Schistosomiasis mansoni in relation to intensity of infection: study of a community in Machakos, Kenya. Am J Trop Med Myg 1976;27:273-284.
10. Woldemichael T, Wondimagegnehu T. Schistosomiasis hematobium treatment with praziquantel: Preliminary cliDical observations. Ethiop Med J 1986;24:155.
11. Taddesse K, Zein ZA. Comparison between the efficacy of oxamniquine and praziquantel in the treatment of Schistosomq mansoni infections on a sugar estate in Ethiopia. Ann Trop Med Parasitol 1988;82(2): 175-80.
12. Simonsen PE, Nega A, Furu P. Intestinal schistosomiasis among children in a labour village of Wonji Sugar Estate, Ethiopia. East Afr Med J 1990;67(8):532-8.
13. Fletcher M, Teklehaimanot A. Schistosoma mansoni infection in a new settlement in Metekel district, North Western Ethiopia: morbidity and side effects of treatment with praziquantel in relation to intensity of infection. Trans R Soc Trop Med Myg 1989;83:793-7.
14. Peters MA, Alamy MA, Warren KS, Mahmoud AAF. Quick Kato smear for field quantification of Schistosoma mansoni eggs. Am J Trop Med Myg 1980;29:217-219.

15 .Sukwa TY , Bulsara MK, Wurapa FK Reduction in prevalence, intensity of infection and morbidity due to Schistosoma mansoni infection in a community following treatment with praziquantel. J Trop Med Hyg 1987;90:205-211.

16. Chuks Ejezie G, Oeke GCEChemotherapy in the control of schistosomiasis in Nigeria. J Trop Med Hyg 1987;90:149-151. .