

Full Length Research Paper

Prevalence of *Schistosoma mansoni* and effectiveness of Praziquantel in school children in Finchaa valley, Ethiopia

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Accepted 06 November, 2019

Schistosomiasis remains one of the most prevalent parasitic diseases in the world. Approximately 80% of the estimated 200 million people infected annually world-wide live in Sub-Saharan Africa, including Ethiopia where *Schistosoma mansoni* and *Schistosoma haematobium* are widespread. Recently, Praziquantel has been reported to show low cure rates in different parts of the world. Since it is the only drug for treatment of schistosomiasis in Ethiopia, there is a need to periodically evaluate its efficacy in different geographic settings. To determine prevalence and evaluate the effectiveness of Praziquantel against *S. mansoni*, a cross-sectional parasitological survey was conducted in Finchaa Sholoko Elementary School, followed by a non-randomized trial. Students who tested positive for intestinal schistosomiasis and fulfilling the criteria set were invited to take part in the efficacy study. Positive students were treated with 40 mg/kg of Praziquantel. Cure and egg reduction rate were evaluated four weeks after treatment through fecal egg count by two Kato-Katz assays on two consecutive days. Data were analyzed using SPSS version 16.0. Prevalence of *S. mansoni* was 67.6%. From the children who completed the study (n=204), parasitological cure rate and egg reduction rate were 80.9 and 99.51%, respectively. There was a significant association between cure rate and pre-treatment infection intensity ($P < 0.05$), but there was no significant association observed between cure rate and age groups ($P > 0.05$). Praziquantel in a single dose of 40 mg/kg body weight remains efficacious despite prolonged use of the drug. However, further studies in other endemic settings including other community groups are needed.

Key words: Schistosomiasis, *Schistosoma mansoni*, Praziquantel, cure rate, infection intensity, Kato-Katz, effectiveness.

INTRODUCTION

Schistosomiasis is one of the most prevalent parasitic diseases in the world. It is a major health problem in parts of Africa, South America and Asia. It is endemic in 76 countries and continues to be a public health concern especially in developing countries (Lien et al., 2002). Approximately 80% of the estimated 200 million people

infected world-wide live in Sub-Saharan Africa where *Schistosoma mansoni* and *Schistosoma haematobium* are widespread (Homeida et al., 1989). The disease is chronic and results in morbidity and mortality (WHO, 1998). Approximately 280,000 people die of this disease in Sub-Saharan Africa annually (Southgate et al., 2005).

S. mansoni and *S. haematobium* are common schistosomes in Ethiopia (Birrie et al., 1989; Kloos et al., 1988). *S. mansoni* is generally found at altitudes ranging from 1300 to 2000 m that favors *Biomphalaria pfeifferi* which is the major snail intermediate host. Previous

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studies showed that schistosomiasis is widely distributed in different regions of Ethiopia (Helmut, 1985; Kloos et al., 1988; Teklehaimanot and Fletcher, 1990; Birrie et al., 1997; Simonsen et al., 1990; Birrie et al., 1993).

Some control measures against schistosomiasis are aimed at eliminating snails by chemical, environmental management, biological control and possibly avoiding contact with cercariae-infested water (Southgate et al., 2005). In Ethiopia, the most common methods of schistosomiasis control are treatment of individuals with Praziquantel (PZQ) and application of chemical molluscicide (Lema toxin, locally known as Endod, which is prepared from the Ethiopian plant called *Phytolacca dodecandra*) on infected water bodies (Belli et al., 1994). However, in most epidemiological settings, the intermediate host snails cannot be controlled by cost-effective intervening interventions, and in the absence of a vaccine, schistosomiasis control largely relies on chemotherapy (Llen et al., 2002; King Dangerfield, 2008). PZQ is the most effective drug and is the mainstay for morbidity control, that is, it prevents chronic liver disease or bladder cancer (Fenwick et al., 2003). It is clinically effective against all schistosome species as well as against many other trematodes and cestodes infecting human (Savioli et al., 2002; Doenhoff and Pica-Mattoccia, 2006). The drug is safe (well-tolerated) and cheap as compared to other anti-schistosomes, that is why it has been widely used as a tool for morbidity control (Badreldin and Ali, 2006).

Effectiveness of the drug against schistosomiasis has been tested in other countries such as Senegal and showed low cure rates (Stelma et al., 1995), raising fears about the effectiveness of PZQ. Moreover, there have been reports of *S. mansoni* resistance to PZQ from studies in Egypt (Ismail et al., 1999; Botros et al., 2005) and Kenya (Melman et al., 2009). There are also few reports from Ethiopia on the efficacy of PZQ (Nega et al., 1999; Getinet et al., 2002). However, these studies are not recent and do not cover all parts of the country, leading to concern that resistance to PZQ might develop or already exists. As no other anti-schistosomal drug has been developed, there is concern about the extensive reliance on just one drug due to the possible development of drug-resistant parasites. This study aimed to determine the current prevalence and evaluate the therapeutic efficacy of PZQ against *S. mansoni* in school children in Finchaa Sholoko Elementary School.

MATERIALS AND METHODS

General study design

This study was conducted in Finchaa Valley, Horro Guduru Wollega Zone, Ethiopia from March to May, 2010. Finchaa Valley is found at about 334 km North-West of Addis Ababa. The Finchaa Valley Elementary School was selected purposively because the area is a

focus of *S. mansoni* infection. Local authorities and participating individuals and their family/guardians were informed about the study objective and they agreed to collaborate. The study was approved by the ethical review board of Jimma University. The sample size was determined assuming a confidence interval of 95% and a 60% prevalence of *S. mansoni* in the study area. A sample size of 351 was considered to be adequate, of which 324 students participated. Students were randomly selected for inclusion in the study. The age of these students ranged from 6 to 14 years. The students were grouped into two age groups (6 to 9 and 10 to 14 years); and these ranges were selected to provide two roughly comparable group size.

Parasitological survey

To screen for *S. mansoni* infection, all students selected to participate in the study (351) were asked to provide stool samples. For pre and post-treatment examination, the Kato-Katz technique (Katz et al., 1972) was done using the standard weight of 41.7 mg of stool. All of these study participants had no history of PZQ treatment for the last 6 months before the start of the study. The prevalence of *S. mansoni* was determined.

Students positive for *S. mansoni* were used for the PZQ effectiveness study. Participants vomiting within 2 h after treatment were excluded from the study. Percentage weight for height was used for screening severely malnourished study participants and this anthropometric data were compared with those of the National Center for Health Statistics reference population.

Drug administration

All positive eligible study participants were treated with a single dose of 40 mg/kg of PZQ (Distocide; EPICO Pharmaceuticals, Cairo, Egypt). Treated study participants were followed up by senior nurses to note any adverse effects of the drug. The re-examination of stool sample was conducted four weeks after treatment through examination of two slides per individual participants on two consecutive days. The efficacy of PZQ was evaluated using cure rate, and egg reduction rate.

Statistical analysis

The analysis was performed on the data from the study participants who obtained the treatment and provided two stool samples after treatment. Data were processed using Statistical Package for Social Sciences (SPSS) version 16.0 to assess the association of cure rate with intensity level and age group. The intensity of infection is expressed as the geometric mean egg count (GMEC) for each participant. Intensity was divided into three levels; (1) light infections (1 to 100 epg); (2) moderate infections (101 to 400 epg) and (3) heavy infections (>400 epg).

The geometric mean egg count was calculated as $\exp \left[\frac{\ln(c+1)}{n} \right] - 1$, where c is change in egg counts (epg) for a particular individual and n is the number of individuals. The percentage of egg count reduction induced by the treatment was calculated as $100[1 - \exp^{-D}]%$, where D is the geometric mean difference (the difference between pre and post-treatment) which was calculated for each individual. Cure rate (CR) was calculated as a ratio of the number of study participants who were negative after treatment to the number of study participants who were positive before treatment and who completed the study. Chi-squared test was done to see the association between dependent

Table 1. Infection with *S. mansoni* according to gender and age group of study participants in Fincha Valley Elementary School from March to May, 2010.

Variable	Infection with <i>S. mansoni</i> (%)		Total (%)	p-value	
	Negative	Positive			
Gender	Male	49 (29.9)	115 (70.1)	164 (100.0)	0.325
	Female	56 (35.0)	104 (65.0)		
	Total	105 (32.4)	219 (67.6)		
Age (years)	6-9	45 (34.3)	86 (65.7)	131 (100.0)	0.839
	10-14	60 (31.1)	133 (68.9)		
	Total	105 (32.4)	219 (67.6)		

Table 2. Intensity of *S. mansoni* infection among school children at Fincha Valley Elementary School according to gender and age groups from March to May, 2010.

Variable	Infection intensity (epg, %)			Total (%)	p-value	
	Light (<100)	Moderate (101-400)	Heavy (>400)			
Gender	Male	36 (32.7)	45 (40.9)	29 (26.4)	110 (100.0)	0.686
	Female	36 (38.3)	34 (36.2)	24 (25.5)		
	Total	72 (35.3)	79 (38.7)	53 (26.0)		
Age group (years)	6-9	30 (37.5)	26 (32.5)	24 (30.0)	80 (100.0)	0.314
	10-14	42 (33.9)	53 (42.7)	29 (23.4)		
	Total	72 (35.3)	79 (38.7)	53 (26.0)		

epg= Eggs per gram of feces.

and independent variables, and was taken to be statistically significant when p -value is less than 0.05.

RESULTS

Of 324 students involved in the parasitological survey, 219 were positive for *S. mansoni* by Kato-Katz techniques and wet mount, giving a prevalence of 67.6 and 37.96% (123), respectively. The prevalence of *S. mansoni* by Kato-Katz was 50.6% for male and 49.4% for female. However, there was no statistically significant difference in infection either in gender or age categories ($p > 0.05$) (Table 1). Infection intensity is not significantly different either in gender or age categories ($p > 0.05$) (Table 2).

Of the total (219) of school children infected with *S. mansoni*, more than half of them (116) were from families using the river water for home use as well as bathing, and the association between infection with *S. mansoni* and river water contact is also statistically significant ($p < 0.05$) (data not shown).

Four out of all the school children positive for *S. mansoni* did not fulfil the criteria for the efficacy study. One had a history of seizures, two of them vomited immediately

after drug administration, and one student refused the PZQ treatment at the time of treatment. The data from these students were not used for analysis, leaving 215 children who were included in the follow-up process; all of these children had no history of treatment with PZQ during the last 6 months. The anthropometric data of these study participants indicated that they were not severely malnourished. During re-examination, three of these school children did not provide both first and second stool specimens after treatment, while eight missed the second stool specimen, because they were absent from school on stool collection days. Those who did not comply with the two days of follow-up stool examination were not included in the calculation of the cure rate and egg reduction rate. Thus, 204 of the study participants completed the follow-up, with an overall compliance rate of 94.9%.

The overall parasitological cure rate determined in this study was 80.90% ($n = 165$). When determined using a single stool specimen, the cure rate was 89.7% ($n = 183$), and 8.80% increase as compared to the two stool specimen examination. There is no statistically significant difference between the age groups regarding the cure rate ($p < 0.05$) (Table 3). In contrast, the cure rate of PZQ

Table 3. Parasitological cure rate in *S. mansoni* infected school children in Fincha Valley Elementary School at different age groups and pre-treatment intensity levels, 4 weeks after treatments with Praziquantel from March to May, 2010.

Variable		Cure rate (%)		Total	p-value
		Cured	Uncured		
Age groups	6-9	65 (81.2)	15 (18.8)	80 (100.0)	0.915
	10-14	100 (80.6)	24 (19.4)	124 (100.0)	
	Total	165 (80.9)	39 (19.1)	204 (100.0)	
Infection intensity (epg)	Light	71 (98.6)	1 (1.4)	72 (100.0)	0.000
	Moderate	77 (97.5)	2 (2.5)	79 (100.0)	
	Heavy	17 (32.1)	36 (67.9)	53 (100.0)	
	Total	165 (80.9)	39 (19.1)	204 (100.0)	

epg= Eggs per gram of feces.

in relation to infection intensity did differ significantly, with a higher cure rate observed in lightly and moderately infected study participants as compared to that observed in the heavily infected study participants ($p < 0.05$).

The percentage of egg count reduction for the study participants not cured was calculated to be 99.51%. Most (61.5%) of them were those students in the older age group (10 to 14 years), while 38.5% of them were in the younger age group (6 to 9 years). The egg reduction rate was different among the two age-groups (85.2 and 96.2% in younger and older age groups, respectively).

DISCUSSION

The prevalence of intestinal schistosomiasis has been determined in many developing countries. Similarly, there are some studies regarding distribution of this parasite in Ethiopia (Kloos et al., 1988; Simonsen et al., 1990; Birre et al., 1993). The distribution of this parasite in Ethiopia is not cosmopolitan, but is restricted to foci related to water-based development schemes (Helmut, 1985; Steinmann et al., 2006). The area of investigation in this study is known to be endemic for *S. mansoni* (Birrie et al., 1993; Ismail et al., 1999; Erko et al., 2002). The prevalence of the parasite in the study area was 67.6%. This prevalence is high as compared to that found in a previous study conducted on the same population during 2009 (60%; unpublished data). This higher value may be attributed to the fact that, two stool samples were used per individual in contrast to the use of single stool samples in previous studies (Nega et al., 1999; Getinet et al., 2002). In general, there is no statistical deference in prevalence and intensity of infection between gender of the study participants (Tables 1 and 2). These findings differ from those of a previous study conducted on *S. haematobium* infection in Malawi (Kapito-Tembo et al., 2009), where dramatically higher infection rates were found in boys as

compared to girls. This difference between genders could be partly be explained by the fact that boys are usually more likely to play in the stream as compared to girls.

Infection with *S. mansoni* was significantly associated with water contact habit of the study population ($p < 0.05$). This result is in accordance with other studies conducted in Malawi (Atupele et al., 2009). This association could be due to school proximity to an open water source and weather conditions which force children to bathe and swim together due to a lack of tap water; however, duration and frequency of water contact is not studied in present study.

The efficacy of the anti-schistosomal drug (PZQ) was assessed for treatment of *S. mansoni* in this study and the overall parasitological cure rate of PZQ, administered at 40 mg/kg body weight in a single dose, in the school children was 80.90%. This is lower than previous studies conducted on school children in some parts of Ethiopia, in which cure rates of 83.2 (Nega et al., 1999) and 94.0% (Getinet et al., 2002) were found. This difference could be attributed to the number of Kato-Katz slides examined to determine cure rate. In both previous studies, the cure rate was determined based on a single Kato-Katz slide for cure evaluation. There is significant day-to-day variation in egg counts of *S. mansoni* (Dirk et al., 1996), so the method for sampling of stool specimens can have an important effect on the apparent cure rate. Moreover, it has been evident that the amount of stool used and number of slides examined would influence the estimate of prevalence of *S. mansoni* especially in low transmission areas (Enk et al., 2008). Thus, accurate egg counts could be missed using a single stool sample. For instance, when the parasitological cure rate for our data was calculated on the basis of a single stool examination, the cure rate was 89.70%, but decreased to 80.90% when two Kato-Katz slides were examined.

The cure rate determined in this study was greater than

that of previous studies in Western Cote d'Ivoire (Raso et al., 2004), Egypt (Sanaa et al., 2005) and Senegal (Stelma et al., 1995). This difference could be due to the time interval used for cure evaluation. Here, the time interval between drug administration and evaluation of cure was 4 weeks, a short period that is not sufficient for completion of the life cycle following re-infection. As a result, the cure rate for this study was expected to depend only on fecal egg count of the original infection rather than re-infection (although the presence of pre-patent infections cannot be ruled out). For the other studies, the time interval for cure evaluation after PZQ administration was 5 weeks and above. This long time interval for cure evaluation used could favor re-infection.

In this study, the cure rate was not significantly higher in the older age group than in the younger age group (Table 3). This finding differs from the studies conducted in western Cote d'Ivoire (Raso et al., 2004) and Senegal (Picquet et al., 1998), in which significantly higher cure rates were observed in older age groups. On the other hand, in this study, there was a statistically significant association between cure rate and infection intensity. The highest cure rate was found among school children with light and moderate categories of pre-treatment of *S. mansoni* egg intensity and that rate highly decreased in heavy category of infection intensity. This result is in accordance with previous findings in Cote d'Ivoire (Uttinger et al., 2000; Raso et al., 2004) and Ethiopia (Nega et al., 1999) in which cure rates are consistently higher in individuals with light infections before treatment than in those with moderate or heavy infections.

The egg reduction rate with PZQ was calculated assuming that egg counts are a logical estimate of the adult worm burden. Hence, the egg reduction rate determined was high (99.51%) and this result is comparable with the result of the study done in North-West Ethiopia (Getinet et al., 2002). Most of the study participants who were not cured had markedly heavy pre-treatment intensity of *S. mansoni* infection. This showed that PZQ is less effective in the heavily-infected group. The possible reason for this could be due to heavy pre-treatment infection or pre-patent infections. However, we did not find any increase in egg count from the pre-treatment which may indicate pre-patent infection, but more likely, a small number of residual worms surviving treatment to lay eggs. Another explanation for incomplete clearance is reduced parasite susceptibility to the drug, which has been reported in Egypt (Ismail et al., 1999) and Kenya (Melman et al., 2009).

Overall, the result of this study implies that PZQ is efficacious against *S. mansoni*. The result of this study is based on the examination of two stool specimens on different days for cure evaluation. This short time interval between drug administration and re-examination reduces the time for re-infections to complete the life cycle. However, due to budget constraints, only one diagnostic

method was used.

Conclusion

Prevalence of *S. mansoni* in Finchaa Valley Elementary School is high (67.6%) and infection with *S. mansoni* is associated with water contact. PZQ (single dose of 40 mg/kg) remains efficacious against *S. mansoni* despite prolonged use of the drug. Further studies are needed to judge treatment failures in *S. mansoni* using multiple stool examinations, or other more sensitive diagnostic techniques, as well as other community groups, for the ongoing monitoring of the efficacy of PZQ.

ACKNOWLEDGEMENTS

The authors would like to extend their gratitude to the school teachers, study participants and families/guardians of the study participants of Finchaa Valley and village authority. They also specially thank the excellent support of the data collectors and laboratory technicians. This work was supported by a grant from Jimma University, Haramaya University and VLIR-JU-IUC project of Jimma University. Lastly, they thank Professor Asrat Hailu for critically reading the manuscript and providing them with useful comments.

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