

Efficacy of Praziquantel on *Schistosoma Haematobium* Infection After 12 Weeks of a Single Dose Intervention Among School-Age Children in Makurdi, Nigeria

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Abstract: The study was conducted to ascertain the efficacy of praziquantel (PZQ) against urogenital schistosomiasis after 12 weeks post-treatment period. A total of 1600 school age children, 400 each from Agbo (GB), Agwan Jukun (AJ), Agwan Reke (AR) and Ijaha (JH) communities were enrolled at baseline. Urine samples were collected between the hours of 10am and 2 pm following standard procedures and analysed using the filtration technique to check for the presence of *S. haematobium*. 379 (23.69%) tested positive to *S. haematobium* infection and were treated with PZQ using appropriate dosages and screened for urogenital schistosomiasis at 12 weeks post-treatment. Data generated was analysed using chi-square and simple percentages. Infection prevalence declined from 379 (23.69%) to 40 (10.55%). Also cure rates was significantly associated with sex ($P=0.020$) and age ($P=0.000$) of study participants as well as sampled locations ($P=0.000$), respectively. The intensity of infection declined from 281 (74.14%) and 98(25.86%) for light and heavy infection at baseline to 31 (77.50%) and 9(22.50%) at 12 weeks post-treatment ($P<0.05$). the Arithmetic mean of *S. haematobium* eggs declined from 208.85 to 96.22 yielding a cumulative Egg Reduction rate (ERR) of 53.93%. ERR was highest in AR (76.13%), followed by JH (70.75%), GB (55.00%) then AJ (53.48%) ($P=0.001$). The study outcome shows that PZQ is not wholly effective against urogenital schistosomiasis at 12 weeks post-treatment. This calls for concerted efforts of public health sector as well as researchers to carry out expanded studies involving repeated doses of PZQ to ascertain the right dose and duration that connotes PZQ efficacy.

Keywords: Praziquantel efficacy, *Schistosoma haematobium*, School children, Makurdi, Nigeria.

1. Introduction

Urogenital schistosomiasis remains a public health concern and about 85% of the estimated 240 million people infected across 78 countries globally occur in Africa (Ndukwe *et al.*, 2019). Five species of Schistosomes infect humans however, *Schistosoma haematobium* and *Schistosoma mansoni* are the most prevalent in Sub-Saharan Africa including Nigeria, where

they are incriminated for urogenital and intestinal schistosomiasis respectively (Meslo *et al.*, 2022). Mass Drug Administration (MDA) with praziquantel (PZQ) targeted at School Age Children (SAC) has been the mainstay of control efforts at National and State levels, since inception. Research evidence indicates that the mode of action of PZQ is by obstructing calcium channels and antigen exposure, rendering the parasite susceptible to elimination by antibodies (Darko *et al.*, 2020).

Studies on schistosomiasis in Nigeria, including Benue State has focused mostly on its prevalence and associated epidemiological and risk factors in endemic areas (Yauba *et al.*, 2018; Onah *et al.*, 2017; Iboyi *et al.*, 2018; Chikwendu *et al.*, 2019; Ndukwe *et al.*, 2019; Okezie *et al.*, 2020; Obisike *et al.*, 2021; Odoya *et al.*, 2021; Opara *et al.*, 2021). As a result, there is paucity of information on the effect of PZQ on urogenital schistosomiasis and no published data on the subject matter exist in Benue State. In addition, there is growing concern regarding the low cure rate and drug resistance as evidenced by the reduced therapeutic efficacy of PZQ documented in different endemic location (Darko *et al.*, 2020; Meslo *et al.*, 2022).

In as much as control efforts for the disease continues to gain momentum in Nigeria owing to concerted efforts of the Government, Non-governmental Organizations (NGOs) and pharmaceutical companies, constant monitoring of PZQ efficacy in endemic regions will be an added advantage to the fight against schistosomiasis. In that context, the current study sought to ascertain the reinfection, cure and egg reduction rates of a single dose of PZQ against *S. haematobium* after 12 weeks of treatment in Makurdi, Benue State.

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2. Materials and Methods

A. Study Area

The study was conducted among School age children from four communities: Agbo (latitude 7.7301361; longitude 8.4865667), Angwan Reke (latitude 7.74510; longitude 8.512580), Angwan Jukun (latitude 7.733977; longitude 8.54291) and Ijaha (latitude 7.7408604; longitude 8.4992064) all located in Makurdi, Benue State, Nigeria. The study span between May to November 2021. Benue State is geographically located on latitude 7.74° North and longitude 8.51° East and has 104m elevation above sea level. The mean monthly rainfall ranges from 150 mm to 180 mm, and the mean monthly temperature ranges from 27 °C to 38 °C. Makurdi, the state capital is located along the bank of the Benue River which serves as the predominant water source for anthropogenic activities of its inhabitants. It is characterized a typical high tropical climate with two clearly marked seasons: rainy season which is prolonged and starts from the month of April to October and the dry season that begins in late October and ends in March. Makurdi inhabitants are mostly civil servants and locals who engage in activities such as regular and irrigation farming, fishing, trading and rustling of ruminant animals.

B. Ethical Consideration and Consent

The study procedure was reviewed and approved by the Ethical Review Board of Benue state Ministry of Health, Makurdi. Prior to the commencement of the study, oral and written consent was sought from the community and school heads as well as the parents/guardians of the study participants. The objectives of the study were adequately explained to the concerned parties. Only participants between the ages of 5 years and above whose parents/guardians gave consent and were willing to take part in the study were enrolled.

C. Sample Size

The sample size was calculated using formula for public health studies as described by Pourhoseingholi *et al.* (2013). A urinary schistosomiasis prevalence rate of 44.1% as reported by Onah *et al.* (2017) for Benue State was considered. The error margin was set at 0.05 and a total sample size of 1600 subjects consisting of 400 from each sampled location was used for the study.

D. Collection of Urine Samples

The subjects were selected at random. A structures questionnaire was used to document the demographic data of the participants as well other information relevant to the study. Urine samples were collected at baseline and 12 weeks after treatment with PZQ, following aseptic techniques into wide-mouthed plastic containers that were labelled with identification codes. Samples were collected between 10.00am to 2.00pm, the period when peak excretion of eggs is expected (Mduluzza *et al.*, 2020) and transported in black polythene bags, placed on ice packs to the zoology laboratory of Benue State University for analysis.

E. Parasitological Analysis of Urine samples

The filtration technique using polycarbonate (PCTE) membrane filters (12.0 micron, 13mm, 100/pk) by sterlitech corporation and procedure as described by Iboyi *et al.* (2018) was used to screen for the presence of *S. haematobium* eggs in the urine samples. Samples with one or more oval eggs with terminal spine characteristic of the parasite were classified as positive (Plate I-III).

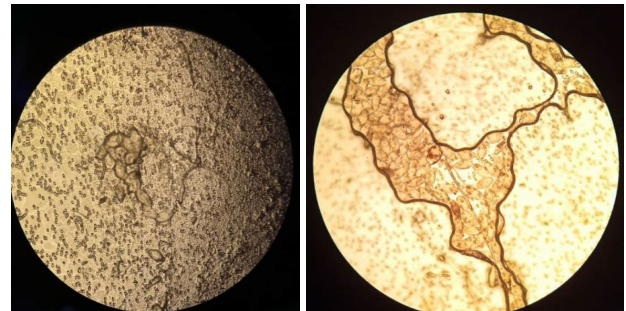


Fig. 1. Plate I: positive slides showing light infection with *S. haematobium* eggs



Fig. 2. Plate II: Heavy intensity with *S. haematobium* eggs with visible haematuria

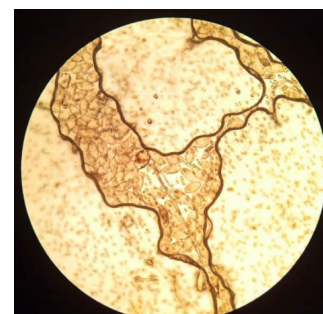


Fig. 3. Plate III: heavy intensity with *S. haematobium* eggs without visible haematuria

F. Primary Drug Administration

Out of the 1600 SAC involved in the screening at baseline, 379 were found excreting *S. haematobium* eggs and were treated with PZQ at the standard dose of 40mg/kg body weight as recommended by WHO (Kabuyaya *et al.*, 2017). Drug administration was carried out by the health Staff of Benue State Epidemiological Unit, Makurdi, Nigeria. To ensure adherence, every child took the tablets in front of the research team members after it was confirmed that the child had eaten.

G. Post-treatment Evaluation

12 weeks after treatment with PZQ, the treated participants were re-screened for the presence of eggs of *S. haematobium* using the same diagnostic procedure employed at baseline.

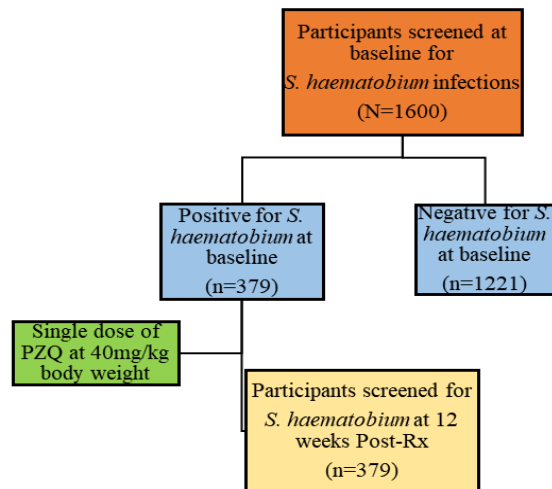


Fig. 4. Study design showing the number of infected participants at baseline and 12 weeks after treatment with PZQ in makurdi, Nigeria

3. Data Analysis

Study data was subjected to Chi-square to determine associations between schistosomiasis prevalence and study variables. Infection prevalence was defined as the number of infected subjects with *S. haematobium* over the total number of screened participants. Infection intensity was classified as “light” for >50 eggs/10mls of urine (Plate I and II) and “heavy” for <50eggs/10mls of urine (Plates III and IV) (Kabuyaya et al., 2017). Efficacy of PZQ was defined as the absence of parasite egg(s) in the specimen at 12 weeks post treatments in subjects who tested positive at baseline. To determine PZQ efficacy, cure rate (CR) and egg reduction rate (ERR), the following formulae used by Kabuyaya et al. (2017) were employed.

$$CR (\%) = \frac{\text{Number of negative individuals after treatment who were positive at baseline}}{\text{Number of positive individuals at baseline}} \times 100$$

$$ERR (\%) = \frac{1 - (\text{Arithmetic mean egg count per 10mls after treatment})}{\text{Arithmetic mean egg count in infected people at baseline}} \times 100$$

4. Results

Association of Cure rates of PZQ for S. haematobium at 12-week Post-intervention with Sex and Age of school aged children and Sampled Locations in Makurdi, Nigeria

The study documented an overall cure rate 89.44% for schistosomiasis, 12 weeks post exposure to praziquantel. Cure rates was significantly associated with the sex of the study participants with 92.95% and 87.34% in females and males respectively, $P=0.020$. This is as shown in table 1.

Cure rates of PZQ at 12-week post-treatment was highly associated with the age of the participants studied. Infection decline was documented across various age groups as follows: 17.23% to 9.09% in age 5-10years (CR = 90.90%), 24.77 to 10.42% in 11-15years (CR = 89.58%), 29.38% to 11.93% in 16 to 20 years (CR = 88.07%) and 16.90% to 8.33% in 20 years and above (CR = 91.67%), $P=0.000$.

Also, the association between cure rates for schistosomiasis at 12 weeks post exposure to PZQ versus sampled locations was highly significant, ($P=0.000$) as shown in Table 1. The highest cure rates were documented in Angwan Reke (92.56%), followed closely by Ijaha (91.93%), Angwan Jukun (89.23%) with Agbo (79.71%) being the least.

Intensity of S. haematobium at baseline and 12 weeks Post-intervention with PZQ in Makurdi, Nigeria

Urogenital schistosomiasis intensity varied across the sampled locations both at baseline and 12 weeks after treatment with PZQ. At baseline, 281(74.14% had light infection while 8(25.86%) had heavy infection $P=0.016$.

Also, 31 (77.50%) and 9(22.50%) prevalence of heavy and light infection with *S.haematobium* eggs was documented 12 weeks post exposure to PZQ, $P=0.007$. there was a general decline in the prevalence of urogenital schistosomiasis at baseline and afterwards. Infection reduced from 23.69% to 10.55%. This is as presented in table 2.

S. haematobium Egg Reduction Rate (ERR) across the locations sampled in Makurdi, Nigeria

Table 3 shows a significant association between ERR for *S.*

Table 1
Association of cure rates of PZQ for *S. haematobium* at 12-week post-intervention with sex and age of school aged children and sampled locations in Makurdi, Nigeria

Variables	Baseline prevalence		Post-Rx prevalence		Cure Rate (%)	P value
	NE	NI (%)	NE	NI (%)		
SEX						
Male	912	237 (29.93)	237	30 (12.66)	87.34	0.020*
Female	688	142 (20.64)	142	10 (7.04)	92.95	
Total	1600	379 (23.69)	379	40 (10.55)	89.44	
AGE (yrs)						
5 – 10	383	66 (17.23)	66	6 (9.09)	90.90	0.000*
11 – 15	775	192 (24.77)	192	20 (10.42)	89.58	
16 – 20	371	109 (29.38)	109	13 (11.93)	88.07	
>20	71	12 (16.90)	12	1 (8.33)	91.67	
Total	1600	379 (23.69)	379	40 (10.55)	89.44	
LOCATION						
AJ	400	65 (16.25)	65	7 (10.77)	89.23	0.000*
AR	400	121 (20.25)	121	9 (7.44)	92.56	
GB	400	69 (17.25)	69	14 (20.29)	79.71	
JH	400	124 (31.00)	124	10 (8.06)	91.93	
Total	1600	379 (23.69)	379	40 (10.55)	89.44	

Table 2
Intensity of *S. haematobium* at baseline and 12 weeks Post-intervention with PZQ in Makurdi, Nigeria

Study time/ Location	Prevalence		Infection Intensity/10mls of urine		P value
	NE	NI (%)	LIGHT (%)	HEAVY (%)	
Baseline AJ	400	65 (16.25)	60 (92.31)	5 (7.69)	0.016*
AR	400	121 (20.25)	80 (66.12)	41 (33.88)	
GB	400	69 (17.25)	62 (89.86)	7 (10.14)	
JH	400	124 (31.00)	79 (63.71)	45 (36.29)	
Total	1600	379 (23.69)	281 (74.14)	98 (25.86)	
Post-intervention					
AJ	65	7 (10.77)	7 (100.00)	0 (0.00)	0.007*
AR	121	9 (7.44)	8 (88.89)	1 (11.11)	
GB	69	14 (20.29)	10 (71.43)	4 (28.57)	
JH	124	10 (8.06)	6 (60.00)	4 (40.00)	
Total	379	40 (10.55)	31 (77.50)	9 (22.50)	

Table 3
ERR of *S. haematobium* across various sampled locations in Makurdi, Nigeria

Location	AR of eggs at baseline	AR of eggs post-Rx	ERR (%)	P value
AJ	13.2	6.14	53.48	0.001*
AR	74.30	17.73	76.13	
GB	19.1	42.45	55.00	
JH	102.25	29.90	70.75	
Total	208.85	96.22	53.93	

haematobium and the various locations sampled. The overall ERR was 53.93%. The ERR was highest in AR (76.13%), followed by JH (70.75%), GB (55.00%) and AJ (53.48%) had the least, P= 0.001.

The Arithmetic Mean (AR) of eggs declined from 208.85 at baseline to 96.22 at 12 weeks post exposure to PZQ prophylaxis.

5. Discussion

An overall cure rate (CR) of 89.44% and Egg Reduction Rate (ERR) of 53.93% was documented in the study. A relatively lower CR of 78.0% was observed among pupils between the ages of 2-16 years in Adim, Cross River State (Ben and Useh 2017). Various cure rates and ERR of schistosomiasis following PZQ administration have been reported from different locations in Africa. Data from Ethiopia include CR (91.7%); ERR (86.8%) from Kemisse town (Meslo *et al.*, 2022) and CR (88.99% - 93.44%) from Tamuga (Dejenie *et al.*, 2010). Also, CR of 71.6% and 79.9% have been documented in studies from Cote D'Ivoire (2021), CR (51.7%-55.2%); ERR (58.8&-60.2%) in Western Niger (2013). A cure rate of 84.62% which is comparable with that of the study was reported from Kwazuzlu Natal in South Africa after four weeks post exposure to PZQ in school children (Kabuyaya *et al.*, 2017). Factors such as infection intensity at baseline, geographical location, brand of praziquantel used for treatment as well as post-treatment duration have been suggested to affect CR and ERR of PZQ against schistosomiasis.

Schistosoma haematobium infection significantly declined across various age groups with ages 20 years and above having the highest cure rate (91.67%). A similar cure rate of 92.4% in ages 10-14 years was reported among primary school children in Northeast Ethiopia (Meslo *et al.*, 2022). Contrasting findings have been highlighted by different researchers. Ben and Useh (2017) reported a 100% CR in ages 2-4 years, 1 month after treatment. Nazareth *et al.* (2022) documented the least mean egg count of 47.8 which translates to a higher cure rate among

ages 13-15 years at 6-month post treatment. Also, Mazigo *et al.* (2022) recorded no age group difference in mean egg intensities and hitherto cure rate after 15 years of repeated mass drug administration in Tanzanian school age and pre-school age children. Higher cure rates as compared to the study have also been observed in 11-year-old children in South Africa (Kabuyaya *et al.*, 2017).

Data on cure rates based on the sex of study participants varied from 87.34% in males to 92.95% in females. Similarly, a higher geometric mean egg count was reported among males than females after 15 years of MDA with PZQ in Northwest Tanzania (Mazigo *et al.*, 2022). In addition, Meslo *et al.* (2022) recorded higher cure rate in girls than boys at 4 weeks post treatment with PZQ for *S. mansoni* in Northeast Ethiopia. An outcome which differs from the current study was documented in South African children, where males had higher cure rates compared to females (Kabuyaya *et al.*, 2017). The disparity in cure rates with respect to sex could be attributed to an interplay of gender and socio-cultural roles across Africa. Activities related to water contact may be attributed to males mostly in some countries and the reverse case in other countries thereby predisposing the affected persons to being re-infected with schistosomiasis after treatment.

There was a decline in schistosomiasis prevalence from 23.96% at baseline to 10.55 % at 12 weeks after treatment with praziquantel. Lower post-treatment prevalence has been put forward by different studies. Mazigo *et al.* (2022) observed 7.40% among Preschool and SAC in Northwestern Tanzania after 15 years of repeated MDA. Also, reinfection rates of 8.03% and 8.00% have been recorded at 20- and 20-weeks post-treatment period respectively in Kwazulu-Natal, South Africa (Kabuyaya *et al.*, 2017). In a study by Griswold *et al.* (2022), there was a reduction in *S. haematobium* prevalence from 12.9% to 9.0% after 5 years of MDA. Lastly, research to test the efficacy of PZQ treatment on *S. mansoni* infection yielded a drastic reduction in infection prevalence from 52.10% at baseline to 8.33% at 4 weeks post-exposure to prophylaxis

(Meslo *et al.*, 2022). PZQ cure rates have been observed to be dependent on factors such as; the duration of treatment, availability of water, sanitation and hygiene (WASH) facilities in endemic locations, the prevailing risk factors for continual transmission of schistosomiasis in endemic areas, being in an area with high intensity of infection as well as the water-contact behavior of people in endemic regions (Kabuaya *et al.*, 2017). In the same light, ecological and seasonal factors have also been labelled to affect schistosomiasis reinfection rates (Kabuaya *et al.*, 2017) and to corroborate this, the current study span from the rainy (May 2021) to dry season (November 2021). This may create opportunities for participants who were cured at baseline to be re-infected due to water-contact activities such as irrigation farming, fishing, swimming, etc that characterize the sampled locations during the dry season.

Arithmetic Mean (AM) of eggs excreted decline from 208.85% at baseline to 96.22% 12 weeks after treatment. Kabuyaya *et al.* (2017) also observed a reduction in AM/10mls of urine at 4 weeks post-treatment with PZQ. Intensity of infection also greatly reduced in the uncured study participants. Owing to the already, mentioned factors incriminated to affect PZQ efficacy against schistosomiasis, it is inconclusive as to whether the uncured subjects were resistant to PZQ. On the flip side, since PZQ is known to offer cure for schistosomiasis in short term by mainly killing the adult stage of the schistosome species infective to man, the uncured participants may have harboured the immature stages of the parasite during treatment (Ben and Useh 2017). To support this there are the parasite ova captured microscopically as demonstrated in plate.

6. Conclusion and Recommendation

In as much as the study noted a significant reduction in infection prevalence and a high cure rate of schistosomiasis, the Egg Reduction rate was relatively low. This is indicative of the low efficacy of PZQ at 12 weeks post-treatment in Makurdi, Benue State which is endemic for urogenital schistosomiasis. Expanded studies including other locations within Benue State should be considered and control programmes should also consider the use of concurrent standard doses of PZQ in high-risk areas to reduce infection level and consequently transmission.

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