High Efficacy of Praziquantel in Schistosoma haematobium-Infected Children in Taraba State, Northeast Nigeria

A follow-up study

Robert S. Houmsou, Binga E. Wama, Hemen Agere, John A. Uniga, Elizabeth U. Amuta, Santaya L. Kela

ABSTRACT: Objectives: This study aimed to assess the efficacy of praziquantel in reducing urinary schistosomiasis prevalence, parasite burden and morbidity rates among a previously reported sample of Schistosoma haematobium-infected children. In addition, predisposing factors for re-infection one year post-treatment were also determined.

Methods: This prospective follow-up study was conducted between March 2014 and February 2015 among 675 previously reported children with urinary schistosomiasis in the Murbai and Surbai communities of Ardo Kola, Taraba State, Nigeria. A single dose of 40 mg/kg of praziquantel was administered to each infected child, with a second dose administered one month later if necessary. The number of S. haematobium eggs in urine samples was calculated at baseline and post-treatment. Results: At four weeks post-treatment, the overall cure rate was 98.1%. Among children with low and heavy parasite burdens at baseline, egg reduction rates (ERRs) were 100% and 96.5%, respectively. The vast majority of children with microhaematuria (98.7%) and proteinuria (98.6%) at baseline were cured at follow-up. Following a second dose, the ERR, overall and morbidity cure rates increased to 100%. At one year post-treatment, 272 infected children (40.3%) were re-assessed; of these, 51 children (18.3%) were reinfected. Close proximity to bodies of water (odds ratio [OR] = 1.23, 95% confidence interval [CI]: 0.998–1.530; P = 0.05) and fishing (OR = 2.23, 95% CI: 0.828–6.040; P = 0.01) were significant factors that predisposed children to reinfection.

Conclusion: A moderate rate of reinfection was noted. Governmental and nongovernmental organizations in Nigeria should collaborate on mass treatment and health education campaigns to reduce the incidence of urinary schistosomiasis reinfections.

Keywords: Urinary Schistosomiasis; Praziquantel; Treatment Outcome; Follow-Up Study; Nigeria.

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S. haematobium has been reported in endemic areas.\textsuperscript{12–15} In sub-Saharan Africa, Nigeria carries the highest burden of the disease, with an estimated 103.9 million people at risk of infection and 29 million individuals infected.\textsuperscript{2} In Nigeria, the disease is predominantly caused by two species of schistosomes—\textit{Schistosoma haematobium} and \textit{S. mansoni}—which overlap in most endemic areas, although \textit{S. intercalatum} has also been reported.\textsuperscript{3,4} For the most part, people living in rural areas of Nigeria are most often infected with \textit{S. haematobium}.\textsuperscript{5,6} The disease is known to cause haematuria, proteinuria, leukocyturia, dysuria and painful urination; it has also been reported to have significant adverse effects on child development and to affect productivity in infected adults.\textsuperscript{1,7–9}

In schistosomiasis-endemic areas, the World Health Organization (WHO) recommends the administration of a single dose of praziquantel to affected individuals during mass deworming campaigns.\textsuperscript{10} Previous studies have also shown that this drug remains the safest and most effective treatment for all forms of schistosomiasis.\textsuperscript{11,12} While poor cure rates with a single dose of praziquantel have been reported in \textit{S. mansoni}-endemic areas, better cure and egg reduction rates (ERRs) have been reported in \textit{S. haematobium}-endemic areas.\textsuperscript{12–15} However, in spite of the dramatic increase in the availability and distribution of praziquantel over the last decade, less than 40 million out of 260 million infected individuals worldwide in 2013 received treatment.\textsuperscript{15} Moreover, in Nigeria, little has been done to reduce the prevalence and intensity of urinary schistosomiasis infections in endemic communities. Although a national schistosomiasis map was created to promote interventions and strategies to combat the disease, only 4% of those in need of the drug have been treated so far.\textsuperscript{16,17} In Nigeria, previous studies have reported schistosomiasis to be endemic in Taraba State, with specific prevalence rates varying between communities.\textsuperscript{15,18} Despite this, to the best of the authors’ knowledge, there has been no mass distribution of praziquantel to date in this region.\textsuperscript{18} The Murbai and Surbai villages of the Ardo Kola Local Government Area (LGA) of Taraba State are hyper-endemic for \textit{S. haematobium}.\textsuperscript{18} Most residents are subsistence farmers who also engage in fishing and trading. The area has a tropical climate and a mixture of savannah vegetation.\textsuperscript{14} Ponds, streams and rivers traverse both communities, with the majority of inhabitants dependent on these bodies of water for their daily activities. Previously, an epidemiological study was conducted among 1,153 children in the Murbai and Surbai communities, of which 675 (58.5%) were found to be infected with \textit{S. haematobium}; fishing, rice farming and dry season farming using irrigation were identified as significant risk factors for infection.\textsuperscript{14} However, only baseline prevalence and parasite burden was determined during the course of the initial study. Therefore, the current follow-up study aimed to assess the efficacy of a single dose of praziquantel in reducing prevalence, parasite burden and morbidity rates among the same sample of infected children. In addition, factors predisposing children to reinfection one year after treatment were evaluated.

### Methods

This prospective follow-up study was conducted between March 2014 and February 2015 and included a previously reported sample of 675 children with urinary schistosomiasis infections in the Murbai and Surbai communities.\textsuperscript{18} All infected children were treated with a single dose of 40 mg/kg of praziquantel administered by two qualified nurses according to WHO protocols.\textsuperscript{19} The treated children were followed up for four weeks, after which they were re-examined to ascertain the presence of \textit{S. haematobium} eggs in their urine. Those children who still excreted \textit{S. haematobium} eggs at this time were given a second dose of praziquantel and followed up again for two more weeks before being re-examined. After 12 months, all children who had been treated with either one or two doses of praziquantel were re-assessed for infection. Unfortunately, a number of the children’s families had left the villages during this time, frequently for agricultural purposes or so that the children could attend secondary schools in neighbouring villages. These children were therefore lost to further follow-up [Figure 1].
Urine samples of 20 mL each were collected from the children at baseline, follow-up and one year post-treatment among a sample of previously reported children with *Schistosoma haematobium* infections in Taraba State, Nigeria (N = 675).\(^{18}\)

Data were entered into an Excel spreadsheet, Version 2010 (Microsoft Inc., Redmond, Washington, USA), before being exported for analysis to the Statistical Package for the Social Sciences (SPSS), Version 23 (IBM Corp., Armonk, New York, USA). Chi-squared and t-tests were used to compare the prevalence of infection and parasite burden according to age and gender and to compare the mean number of eggs between those with low and heavy parasite burdens. A logistic regression analysis using odds ratios (ORs) and 95% confidence intervals (CIs) was used to determine the relationship between reinfection and risk factors. The statistical level of significance was set at \(P \leq 0.05\).

Ethical permission to conduct this study was obtained from the Health Department of the Ardo Kola LGA (#HD/AIK/16/003). Thereafter, the Health Department communicated with the heads of the Murbai and Surbai communities to inform children and their parents of the study protocols. The parents or guardians of all children enrolled in the study provided informed consent prior to their participation.

### Results

This follow-up study included 675 previously reported children infected with *S. haematobium* prior to praziquantel treatment. As previously described, males were significantly more likely to be infected than females (71.2% versus 43.7%; \(\chi^2 = 89.1; P < 0.01\)).\(^{18}\) Children aged 6–10 years and 11–15 years were also significantly more likely to be infected (78.7% and 73%, respectively; \(\chi^2 = 360.9; P < 0.01\)).\(^{18}\) A low parasite burden was significantly more frequent in comparison to a heavy parasite burden (62.5% versus 37.5%; \(\chi^2 = 97; P < 0.01\)).\(^{18}\)

According to gender, females more frequently had a low parasite burden than males (70.1% versus 58.6%; \(\chi^2 = 96.9; P < 0.01\)). Children aged 1–5 and 11–15 years old frequently had a low parasite burden (85.7% and 55.7%, respectively).\(^{18}\)

Table 1 presents the schistosomiasis parasite burden and morbidity rates of the children at baseline. The mean number of eggs was 31.1 ± 7.9 eggs/10 mL of urine among children with a low parasite burden and 86.5 ± 12.1 eggs/10 mL of urine among those with a heavy parasite burden. In terms of morbidities, males had a significantly higher proportion of both microhaematuria (61.5% versus 42.9%; \(\chi^2 = 157.8; P < 0.01\)) and proteinuria (49.1% versus 36.8%; \(\chi^2 = 107.9; P < 0.01\)) than their female counterparts. Children aged 6–10 and 11–15 years old frequently had a low parasite burden (85.7% and 55.7%, respectively).\(^{18}\)

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Cure rate = \[\frac{P_{\text{before treatment}} - P_{\text{after treatment}}}{P_{\text{before treatment}}} \times 100\]

\[\text{ERR} = \frac{1 - \text{MEC at baseline}}{\text{MEC at baseline}} \times 100\]
Table 2 describes the schistosomiasis prevalence, parasite burden and morbidity rates of the children four weeks after the administration of a single dose of praziquantel. The overall cure rate was 98.1%, with only 13 children (1.9%) requiring a second dose of praziquantel. Children aged 1–5 years old had a higher cure rate than older children (100% versus 98.6% and 96% for those aged 6–10 years and 11–15 years, respectively). In addition, female children had a higher cure rate than their male counterparts (99.6% versus 97.3%). At four weeks post-treatment, the ERR in children with low and heavy parasite burdens was 100% and 96.5%, respectively. At this time, 5.1% of the children who had had a heavy parasite burden at baseline had relapsed, although...
Table 3: Schistosomiasis reinfection rates and related risk factors at one year post-praziquantel treatment among *Schistosoma haematobium*-infected children in Taraba State, Nigeria (N = 272)

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
<th>OR (CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Reinfected (n = 51)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>154 (56.6)</td>
<td>30 (19.5)</td>
<td>- 0.72</td>
</tr>
<tr>
<td>Female</td>
<td>118 (43.4)</td>
<td>21 (17.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Age in years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–5</td>
<td>77 (28.3)</td>
<td>13 (16.9)</td>
<td></td>
</tr>
<tr>
<td>6–10</td>
<td>127 (46.7)</td>
<td>26 (20.5)</td>
<td></td>
</tr>
<tr>
<td>11–15</td>
<td>68 (25)</td>
<td>12 (17.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Proximity to bodies of water in m</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;500</td>
<td>166 (61)</td>
<td>39 (23.5)</td>
<td>1.23 (0.998–1.530) 0.05</td>
</tr>
<tr>
<td>&gt;500</td>
<td>106 (39)</td>
<td>12 (11.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Swimming</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>265 (97.4)</td>
<td>49 (18.5)</td>
<td>0.73 (0.130–4.200) 0.73</td>
</tr>
<tr>
<td>No</td>
<td>7 (2.6)</td>
<td>2 (28.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Fishing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>177 (65.1)</td>
<td>40 (22.6)</td>
<td>2.23 (0.828–6.040) 0.01</td>
</tr>
<tr>
<td>No</td>
<td>95 (34.9)</td>
<td>11 (11.6)</td>
<td></td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval.

Discussion

To the best of the authors’ knowledge, the current study represents the first longitudinal assessment of the efficacy of a single dose of praziquantel among a sample of previously reported *S. haematobium*-infected children in Taraba State. In total, 51 children (18.8%) were reinfected. However, reinfestation rates did not vary significantly by gender ($\chi^2 = 0.73, P = 0.72$) or age ($\chi^2 = 1.71; P = 0.13$). However, close proximity (i.e. within <500 m) to a body of water (OR = 1.23, 95% CI: 0.998–1.530; $P = 0.05$) and fishing (OR = 2.23, 95% CI: 0.828–6.040; $P = 0.01$) were significant risk factors for reinfection.

Although no significant gender or age differences were reported in schistosomiasis cure rates at four weeks post-treatment in the current study, females and 1–5-year-olds nevertheless had higher cure rates. This finding suggests that praziquantel may be more effective among younger children than older ones, likely due to increased exposure to * cercariae*-infested water among the latter group due to recreational activities or daily chores. This variation in reported cure rates could be the result of several factors, including the frequency of the children’s exposure to infested waters, the rate of drug absorption and the extent of drug resistance among the studied populations.

In the present study, none of the children who required a second dose of praziquantel excreted *S. hematobium* eggs or showed any signs of morbidity at six weeks post-treatment, suggesting that a second dose of praziquantel may be necessary following poor response to the initial dose. A study conducted in the Niger Republic reported a similar ERR and cure rate after *S. hematobium*-infected children received a second dose
of praziquantel three weeks post-treatment. However, the ERR and cure rate among children in the current study who received either a single or two doses of praziquantel was significantly higher than rates reported from Cameroon, wherein optimal results were only noted at nine weeks post-treatment, with doses of praziquantel administered at three-week intervals. Moreover, in the present study, most children with a low parasite burden were cured at follow-up, with only a few children with heavy parasite burdens at baseline relapsing at four weeks post-treatment. Similarly, previous research from Mozambique found that a single dose of praziquantel was more effective among children with a low parasite burden in comparison to those with a heavy parasite burden.

In terms of schistosomiasis-related morbidity, the vast majority of children in the present study were cured of microhaematuria and proteinuria at four weeks post-treatment. This indicates that a single dose of praziquantel can potentially reverse the adverse effects of S. haematobium infections. In addition, none of the children requiring a second dose of praziquantel were found to suffer from these morbidities at six weeks post-treatment. Previous studies from Ethiopia and the Ivory Coast have reported low cure rates for microhaematuria and proteinuria at seven and eight weeks post-treatment, respectively. Most studies evaluating the efficacy of praziquantel have assessed morbidity markers of S. haematobium over several months and not within weeks. In Kenya, cure rates of 58% and 46% were observed at 12 months post-treatment for microhaematuria and proteinuria, respectively.7

Unfortunately, a moderate rate of schistosomiasis reinfection was noted among treated children one year post-treatment in the current study. This rate was comparatively higher than reported rates among treated children in Kenya and Sudan.27,28 This finding clearly demonstrates the challenges that rural communities such as Murbai and Surbai face with regards to the complete eradication of schistosomiasis. Unfortunately, the lack of piped water in these communities often compels the inhabitants to continue exposing themselves to cercariae-infested bodies of water—for instance, in order to carry out domestic chores or activities such as washing utensils and clothes, bathing, swimming and fishing—thereby re-infecting themselves. As previously reported, close proximity to bodies of water and fishing were significant risk factors for infection. In the current follow-up study, such factors remained significantly associated with reinfection rates one year post-treatment.

Prompt action is necessary so as to avoid a schistosomiasis epidemic in Taraba State. To this end, a mass praziquantel campaign is recommended, in which all infected individuals are given at least two standard doses of 40 mg/kg of praziquantel at six-week intervals, in order to curtail the incidence of schistosomiasis reinfections in this region. Furthermore, the effects of praziquantel treatment should be monitored in weeks rather than months. There is also an urgent need to address the problem of high reinfection rates through public health education initiatives to warn local inhabitants of risk factors associated with schistosomiasis reinfections. In addition, the provision of piped water as well as the installation of new or the re-activation of old boreholes or wells within these communities could help to reduce the inhabitants’ contact with cercariae-infested water, thereby reducing the incidence of new and recurrent schistosomiasis infections.

The present study is subject to certain limitations. First, an egg viability test was not performed after the initial treatment in order to determine whether the single dose of praziquantel had completely cured the infected children. Second, only 40.3% of the treated children were still residing within the studied villages one year post-treatment, thus limiting the total number of cases re-assessed.

Conclusion

Praziquantel was highly effective in curing schistosomiasis among a previously reported sample of S. haematobium-infected children in Taraba State. At four weeks post-treatment, both the ERR and overall and morbidity cure rates were extremely high; these increased to 100% six weeks post-treatment following a second dose of praziquantel. However, there was a moderate rate of reinfection one year post-treatment. Proximity to bodies of water and fishing were significant risk factors for reinfection. The Nigerian Government and other agencies should initiate necessary strategies for treatment and public health education in the region. In particular, the provision of piped water is highly recommended in order to reduce the local inhabitants’ contact with cercariae-infested water.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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References


