Schistosomiasis and HIV in Rural Zimbabwe: Efficacy of Treatment of Schistosomiasis in Individuals with HIV Coinfection

Per Kallestrup, Rutendo Zinyama, Exnevia Gomo, Anthony E. Butterworth, Govert J. van Dam, Jan Gerstoft, Christian Erikstrup, and Henrik Ullum

Departments of Infectious Diseases and Clinical Immunology, Rigshospitalet, and Cluster of International Health, University of Copenhagen, Copenhagen, Denmark; National Institute of Health Research, Department of Immunology, College of Health Sciences, and Department of Medical Microbiology, University of Zimbabwe, and Biomedical Research and Training Institute, Harare, Zimbabwe; London School of Hygiene and Tropical Medicine, London, United Kingdom; and Department of Parasitology, Leiden University Medical Center, Leiden, The Netherlands

Background. There is evidence from experimental models that the praziquantel-induced clearance of schistosomiasis is dependent on the host’s immune response. Consequently, human immunodeficiency virus (HIV)—related immunodeficiency may impair the effect of praziquantel treatment.

Methods. In a prospective cohort study, schistosome-infected subjects who were or were not coinfected with HIV were treated with praziquantel and followed up 3, 6, and 12 months after treatment. Quantitative measures of intensity of schistosomiasis (egg counts and levels of circulating anodic antigen in serum) and immunodeficiency (CD4+ cell counts and viral loads) were collected.

Results. Cure rates based on egg counts 3 months after treatment were satisfactory and were similar for HIV-positive individuals (cure rate, 86%) and HIV-negative individuals (cure rate, 85%); the magnitude of decrease in egg count was equal. Cure rates based on circulating anodic antigen levels were much lower than cure rates based on egg counts, with HIV-positive individuals experiencing significantly less clearance of schistosomiasis (cure rate, 31%) than HIV-negative individuals (cure rate, 52%), whereas the magnitude of decrease in circulating anodic antigen was also lower among HIV-positive individuals (P<.01).

Conclusion. The effect of praziquantel may be limited to affecting the fecundity of adult schistosomes in the immunocompromised host, thus reducing egg excretion while leaving schistosomes metabolically active, as shown by the fact that levels of antigen production are maintained. Special guidelines for treatment of schistosomiasis in HIV-coinfected individuals may need to be developed.

For the past decade, praziquantel has been the main drug of choice for treatment of all species of schistosomes because of its efficacy, ease of administration, safety, and cost [1]. A single dose of 40 mg/kg has been widely accepted as the standard dosage, resulting in cure rates of 60%–95% [2].

Experimental studies have demonstrated reduced efficacy of praziquantel against schistosome infections in immunodeficient animals [3] but have shown that restoration of efficacy could be achieved by passive transfer of immune serum from immunocompetent animals [4–6], indicating that a functional immune response is necessary for drug efficacy [7]. Praziquantel induces a spastic paralysis of the worm musculature by a rapid influx of Ca2+ into the tegument of the schistosome [8], which instigates morphological alterations at the parasite surface and allows the exposure of target antigens for specific humoral antibody recognition, necessary for worm elimination [6, 9]. Whether the dynamics in the human host are similar can only be speculated, but because praziquantel requires the synergy of an intact immune response in experimental animals, it may be less effective against schistosome infections in immunocompromised humans.

In contrast to the data from animal studies, Karanja and colleagues [10–12] found, in a study of 15 individuals coinfected with HIV and Schistosoma mansoni and 32 individuals infected with S. mansoni alone in...
Kisumu, Kenya, that both groups responded equally well to standard-regimen praziquantel therapy and that, in the HIV-positive group, there was no relation between treatment response and CD4+ cell percentages. Similarly, in a prospective cohort study involving 73 individuals coinfected with Schistosoma haematobium and HIV in Zambia, Mwanakasale et al. [13] demonstrated praziquantel to be effective in curing schistosomiasis, as diagnosed by egg counts, despite the concurrent HIV infection.

In the past decade, the HIV epidemic has emerged in full scale, in particular in the sub-Saharan region of Africa [14]. Because high prevalences of schistosomiasis and HIV infection are geographically concurrent, and because praziquantel remains the recommended drug of choice for the global efforts to control schistosomiasis, the ability of praziquantel to clear schistosomiasis in the face of concurrent HIV infection deserves to be evaluated in a large study that includes complementary measures of schistosomiasis intensity and HIV-induced immunodeficiency. This article presents the results of such an evaluation, conducted with a large cohort of individuals coinfected with schistosomiasis and HIV-1 in rural Zimbabwe.

**MATERIALS AND METHODS**

**The Mupfure Schistosomiasis and HIV Cohort.** The study was conducted from October 2001 through June 2003, and the study population comprised adults residing in the Mupfure and adjacent areas in Shamva District, Mashonaland Central Province, Zimbabwe, as described elsewhere [15]. A total of 1545 individuals were screened by tests for HIV and microscopic examination of urine and stool samples [15]. Microscopic examination of fixed-volume urine samples collected on 3 consecutive days and filtered on Nytrel filters (VesterGaard Frandsen) was used to identify and quantify eggs of *S. haematobium* [16]. The quantitative modified formol-ether concentration technique was used for 1 stool sample from each participant to detect and quantify eggs of *S. mansoni* and other helminth ova [17]. Schistosomiasis status was thus defined according to egg detection, and treatment decisions were made on this basis.

After the screening procedure, 154 coinfected participants were consecutively included in a prospectively followed cohort. Simultaneously, 133 HIV-uninfected but schistosomiasis-infected control subjects were randomly included in the study. The schistosomiasis-infected participants were randomized to receive treatment either immediately or after a delay of 3 months with a single oral dose of praziquantel (40 mg/kg) [15, 18]. Of 287 participants who received a diagnosis of schistosomiasis at inclusion, 81 were censored from the evaluation of treatment response; these included 15 participants with insufficient urine or stool samples, 40 participants (from the delayed treatment group) whose urine or stool samples were free of eggs at the time of treatment initiation (as the result of either spontaneous clearance or inaccurate diagnostic findings because of low infection intensity), and 26 participants (from the delayed treatment group) who did not present for treatment.

Exclusion criteria were applied to participants presenting with clinical signs and symptoms of tuberculosis, terminal stages of schistosomiasis, or severe anaemia. Pregnant women were excluded from the study but received a diagnosis and were offered praziquantel as treatment for schistosomiasis after delivery and termination of breastfeeding.

CD4+ cell counts and full blood counts were measured at the Department of Haematology of Parirenyatwa Hospital (Harare, Zimbabwe) (FacsCalibur [Becton-Dickinson] and Haematology Analyser SF 3000 [Sysmex]). Levels of circulating anodic antigen (CAA), which originates from the parasite gut and is a unique marker of an active schistosome infection, were measured in serum by means of an ELISA, in accordance with previously described techniques [19–21]. CAA levels of $\geq 40$ pg/mL were considered to be positive. This cutoff point was chosen from a receiver operating characteristic curve to give a specificity of at least 98%. HIV RNA level was measured using Roche Ampliprimer (F. Hoffmann-La Roche).

**Treatment and follow-up.** All participants were followed up with scheduled examinations 3, 6, and 12 months after treatment. At the end of follow-up, all participants who had initially been negative for HIV infection were retested for HIV antibodies to detect possible seroconversion during the study period; 2 participants were found to have experienced seroconversion and were excluded from analysis. There was no public system of antiretroviral treatment in Zimbabwe at the time of the study, and it can be assumed that all participants were antiretroviral naive during the study. HIV-positive participants were clinically assessed at each visit in accordance with Centers for Disease Control and Prevention (CDC) clinical staging criteria [22].

**Ethical considerations.** Informed written consent was obtained from all participants in this study. Ethical approval was granted by the Medical Research Council of Zimbabwe (MRCZ/A/918) and by the Central Medical Scientific Ethics Committee of Denmark (624-01-0031). In addition, permission was given by the Provincial Medical Director of Mashonaland Central Province and the District Medical Officer of Shamva District, by the village headmen, and at village meetings.

**Statistical analyses.** All statistical analyses were made using SAS software, version 8.2 (SAS Institute). Egg counts, CAA levels, and viral load were log$_{10}$ transformed to approximate normal distribution.

Cure rates for schistosomiasis, as measured by the absence of eggs from urine and stool samples 3 months after treatment, were compared between HIV strata (HIV-infected participants with a CD4+ cell count <200 cells/$\mu$L, HIV-infected participants with a CD4+ cell count $\geq 200$ cells/$\mu$L, and HIV-uninfected
participants) by Fisher’s exact test. The test was supplemented with the equivalent logistic regression, allowing for age and sex adjustments. Effects of CD4+ cell count, viral load, and hematological test results at baseline were evaluated and added to the model one by one. Similar statistical tests were performed using CAA as the diagnostic criterion. Results are presented as \( P \) values and ORs with 95% CIs.

Student’s \( t \) test was used to compare the baseline value and \( \Delta \) value (the value determined at 3 months minus the baseline value) of egg counts between HIV strata. The result was appraised with an analysis of covariance (ANCOVA) using egg count 3 months after treatment as the dependent parameter and baseline egg count, baseline CAA level, age, sex, and HIV status as predictors. Thereafter, CD4+ cell count, viral load, and hematological test results were added to the model one by one. An analysis of variance (ANOVA) was performed to compare \( \Delta \) values of egg counts between participants stratified to 3 groups according to HIV status and CD4+ cell count. Similar statistical tests were performed using CAA level as the dependent parameter.

Normality and independence of residuals were checked graphically. Regarding the ANCOVA, slopes did not differ between groups. Values of \( P < .05 \) were considered to be statistically significant. All confidence intervals reported are 95% CIs.

## RESULTS

Selected baseline characteristics of the participants with schistosomiasis, as verified by either egg count or CAA level, are presented in table 1. Of 206 participants (111 of whom were HIV positive, and 95 of whom were HIV negative) with test results for 3 urine samples and 1 stool sample at baseline, only those participants who were followed up with at least 2 urine samples and 1 stool sample at 3 months were included in the analysis of cure rates based on egg counts (142 participants, including 80 HIV-positive participants and 62 HIV-negative participants). In 69 (86%) of the HIV-positive participants and 53 (85%) of the HIV-negative participants, no eggs were detected in either urine or stool samples 3 months after treatment, and Fisher’s exact test revealed no difference in clearance rate according to HIV status (\( P = .57 \)). The same cure rates were found when the cohort was stratified into 3 groups: HIV-positive participants with a CD4+ cell count <200 cells/\( \mu L \), HIV-positive participants with a CD4+ cell count \( \geq 200 \) cells/\( \mu L \), and HIV-negative participants (figure 1A).

A logistic regression analysis adjusted for age and sex showed a similar relative risk for remaining positive for schistosomiasis 3 months after treatment between HIV-positive and HIV-negative groups (OR, 1.3; 95% CI, 0.5–3.6; \( P = .66 \)), with an effect of age (OR per 10-year increase in age, 0.5; 95% CI, 0.3–1.0; \( P < .05 \)) but not of sex (OR for female vs. male sex, 1.6; 95% CI, 0.4–5.6; \( P = .56 \)). When adding baseline values for CD4+ cell count, plasma HIV RNA load, total WBC count, neutrophil count, monocyte count, basophil count, eosinophil count, lymphocyte count, platelet count, and hemoglobin level one by one to a core model comprising HIV status, age, and sex, none of these additional parameters were statistically significant (data not shown).

From all 243 participants (136 HIV-positive participants and 107 HIV-negative participants) with CAA levels available at study inclusion, only those who had follow-up CAA levels determined 3 months after treatment were included in the analysis of cure rates based on CAA levels (187 participants, including 108 HIV-positive participants and 79 HIV-negative participants). Applying a CAA cutoff value of 40 pg/mL, only 31% of HIV-positive participants (but 52% of HIV-negative participants) had test results negative for schistosomiasis 3 months after treatment (\( P < .01 \), by Fisher’s exact test). When stratified into 3 groups by HIV status and CD4+ cell count, as above, a statistically significant difference was revealed between HIV-positive participants with a CD4+ cell count <200 cells/\( \mu L \) and HIV-negative participants (\( P < .01 \)) and between HIV-positive participants with a CD4+ cell count \( \geq 200 \) cells/\( \mu L \) and HIV-negative participants (\( P < .05 \)), but no difference was revealed between HIV-positive participants with a CD4+ cell count <200 cells/\( \mu L \) and those with a CD4+ cell count \( \geq 200 \) cells/\( \mu L \) (\( P = .25 \)) (figure 1B). Logistic regression comparing HIV-positive versus HIV-negative participants, adjusted for age and sex, also showed a statistically significant difference (OR, 2.7; 95% CI, 1.4–5.0; \( P < .001 \)), with sex showing no effect (OR for female vs. male sex, 1.3; 95% CI, 0.6–2.9; \( P = .47 \)) but with the risk of remaining infected decreasing with age (OR per 10-year increase in age, 0.75; 95% CI, 0.55–1.01; \( P = .06 \)). When adding the same baseline values given above (i.e., CD4+ cell count, plasma HIV load, total WBC count, neutrophil count, monocyte count, basophil count, eosinophil count, lymphocyte count, platelet count, and hemoglobin level) to a core model comprising HIV status, age, and sex, none of these values (with the exception of plasma HIV load) were statistically significant (data not shown).

For plasma HIV load, an increasing risk of not clearing the infection with increasing HIV load at baseline was noted among the HIV-positive participants (OR per 0.1 log 10 copies/\( mL \) increase in HIV load, 1.07; 95% CI, 1.01–1.12; \( P < .05 \)).

As described elsewhere for the whole cohort [15], no difference between egg counts was observed at baseline between the HIV-positive group and the HIV-negative group for participants infected with S. haematobium (\( P = .94 \)) or for participants infected with S. mansoni (\( P = .55 \)) (table 1). Furthermore, the HIV-positive group and the HIV-negative group experienced a similar decrease in egg count from baseline to 3 months after treatment. For participants infected with S. haematobium, the mean difference in \( \Delta \) for egg counts (i.e., the mean \( \Delta \) value for the HIV-positive group minus the mean \( \Delta \)
Table 1. Baseline characteristics of study participants with schistosomiasis as determined by either egg count or circulating anodic antigen (CAA) level.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Schistosomiasis determined by egg count</th>
<th>Schistosomiasis determined by CAA level&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV-positive participants (n = 111)</td>
<td>HIV-negative participants (n = 95)</td>
</tr>
<tr>
<td>Sex, F/M</td>
<td>91/20</td>
<td>75/20</td>
</tr>
<tr>
<td>Age, mean years (95% CI)</td>
<td>33.3 (31.7–35.0)</td>
<td>29.5 (27.1–31.9)</td>
</tr>
<tr>
<td>Egg count in urine samples,&lt;sup&gt;c&lt;/sup&gt; geometric mean eggs/10 mL (95% CI)</td>
<td>6.03 (4.47–8.13)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>6.17 (4.37–8.51)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Egg count in fecal samples,&lt;sup&gt;h&lt;/sup&gt; geometric mean eggs/g (95% CI)</td>
<td>2.88 (1.82–4.68)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>2.40 (1.70–3.39)&lt;sup&gt;j&lt;/sup&gt;</td>
</tr>
<tr>
<td>CAA level, geometric mean pg/mL (95% CI)</td>
<td>4.07 (2.82–5.75)</td>
<td>2.95 (2.00–4.26)</td>
</tr>
<tr>
<td>CD4&lt;sup&gt;+&lt;/sup&gt; cell count, mean cells/μL (range)</td>
<td>379 (11–1355)</td>
<td>870 (195–1828)</td>
</tr>
<tr>
<td>HIV RNA load, mean log&lt;sub&gt;10&lt;/sub&gt; copies/mL (95% CI)</td>
<td>4.62 (4.45–4.79)</td>
<td>...</td>
</tr>
</tbody>
</table>

<sup>a</sup> Study participants with a CAA level $\geq$40 pg/mL were determined to have schistosomiasis.

<sup>b</sup> Comparisons between groups by Student’s $t$ test for all variables except for sex, for which the $\chi^2$ test was applied.

<sup>c</sup> Patients with *Schistosoma haematobium* infection and patients with *S. haematobium* and *Schistosoma mansoni* coinfection.

<sup>d</sup> $n = 100$.

<sup>e</sup> $n = 87$.

<sup>f</sup> $n = 101$.

<sup>g</sup> $n = 83$.

<sup>h</sup> Patients with *S. mansoni* infection and patients with *S. haematobium* and *S. mansoni* coinfection.

<sup>i</sup> $n = 26$.

<sup>j</sup> $n = 16$.

<sup>k</sup> $n = 25$. 
value for the HIV-negative group) was \(-0.11 \log_{10} \text{eggs/10 mL} \) (95% CI, \(-0.35 \) to \(0.13 \log_{10} \text{eggs/10 mL} \); \(P = .35 \)); a similar \(P \) value was found for participants infected with \(S. \) mansoni. An ANCOVA was performed with egg counts, CAA level at baseline, age, and sex as predictors. This confirmed a similar change in egg counts for the 2 HIV-infected groups (mean difference in egg counts [i.e., the mean value for the HIV-positive group minus the mean value for the HIV-negative group], \(0.0001 \log_{10} \text{eggs/10 mL} \); 95% CI, \(-0.13 \) to \(0.13 \log_{10} \text{eggs/10 mL} \); \(P = 1.00 \)), with effect of age (regression coefficient per 10-year increase in age, \(-0.08 \log_{10} \text{eggs/10 mL} \); 95% CI, \(-0.14 \) to \(-0.02 \log_{10} \text{eggs/10 mL} \); \(P < .05 \)) and egg count at baseline, but no effect of sex or CAA level at baseline.

No differences were found when performing an ANOVA after stratifying to the 3 groups by HIV status and CD4\(^+\) cell count (figure 2A). However, although there was, as described elsewhere [15], no difference in CAA levels at baseline between the HIV-positive and HIV negative groups (\(P = .71 \)), a Student’s \(t\) test of the decrease in CAA level between baseline and 3 months after treatment showed a lesser decrease in CAA level among HIV-positive patients (mean difference in \(\Delta\) value for CAA level, \(0.36 \log_{10} \text{pg/mL} \); 95% CI, \(0.12\)–\(0.60 \log_{10} \text{pg/mL} \); \(P < .01 \)). When performing an ANCOVA allowing for age and sex adjustments, similar results were found (mean difference in \(\Delta\) value for CAA level, \(0.43 \log_{10} \text{pg/mL} \); 95% CI, \(0.20\)–\(0.65 \log_{10} \text{pg/mL} \); \(P < .001 \)), with a significant effect of CAA level at baseline and age (regression coefficient per 10-year increase in age, \(-0.22 \log_{10} \text{pg/mL} \); 95% CI, \(-0.33 \) to \(-0.11 \log_{10} \text{pg/mL} \); \(P < .001 \)), but with
Figure 2. Decrease in mean egg count of urine and stool samples (A) and mean circulating anodic antigen level (B) at 3 months after treatment with a standard regimen of praziquantel, compared with baseline values. Study participants are stratified according to HIV status, and HIV-positive participants are additionally stratified according to CD4+ cell count, as follows: group 1, HIV-negative participants; group 2, HIV-positive participants with a CD4+ cell count <200 cells/μL; group 3, HIV-positive participants with a CD4+ cell count ≥200 cells/μL. For A, no statistically significant differences were found between strata. For B, no statistically significant difference was found between group 2 and group 3, but statistically significant differences were revealed between group 1 and group 2 ( ) and between group 1 and group 3 ( ). Error bars, 95% CIs.

no effect of sex (regression coefficient for female vs. male sex, 0.12 log10 pg/mL; 95% CI, −0.17 to 0.40 log10 pg/mL; P = .42). In multivariate linear regression analysis, performed in the same manner as for the analysis of egg counts, none of the additional parameters showed statistical significance.

When an ANOVA was performed after stratifying the participants into 3 groups (as defined above), it revealed that HIV-negative participants experienced a greater decrease in CAA level after treatment than did HIV-positive participants with a CD4+ cell count <200 cells/μL (mean difference in Δ value for CAA level, −0.47 log10 pg/mL; 95% CI, −0.83 to −0.11 log10 pg/mL; P = .01) or those with a CD4+ cell count ≥200 cells/μL (mean difference in Δ value for CAA level, −0.32 log10 pg/mL; 95% CI, −0.58 to −0.06 log10 pg/mL; P <.05). There was no statistically significant difference between HIV-positive participants with a CD4+ cell count <200 cells/μL and those with a CD4+ cell count ≥200 cells/μL with respect to decreases in CAA levels after treatment (P = .41) (figure 2B).

Similar results were obtained using the same ANOVA technique when HIV-coinfected participants were categorized according to the CDC classification system for HIV infection [22]. Although there were no differences when considering egg counts, differences were revealed with regard to CAA levels. Thus, both asymptomatic HIV-positive participants (CDC category A) and symptomatic HIV-positive participants (CDC categories B and C) experienced a less marked reduction in CAA level after treatment, compared with HIV-negative control participants with schistosomiasis (P = .018 and P = .008, respectively). There was no statistically significant difference in CAA level between asymptomatic HIV-positive participants with
DISCUSSION

Although egg counts revealed similar and satisfactory cure rates for HIV-positive and HIV-negative individuals with schistosomiasis following treatment with praziquantel, HIV-positive participants had significantly less clearance than did HIV-negative participants when CAA level was used as the diagnostic criterion. Likewise, there was an equal degree of decrease in egg count for HIV-positive participants and HIV-negative participants as a result of treatment, whereas the extent of the decrease in CAA level was lower among HIV-positive participants than among HIV-negative participants. We retrospectively measured levels of circulating cathodic antigen (CAA)—another schistosome gut-associated antigen—and these levels showed a similar pattern of lower clearance and decrease after treatment (data not shown).

Although several studies involving immunocompetent individuals have demonstrated lower cure rates after praziquantel treatment of schistosomiasis when cure is measured on the basis of CAA levels, compared with when cure is measured on the basis of egg counts, [23–25], the findings of the present study raise concern as to the function and efficacy of praziquantel for the immunocompromised HIV-infected individual.

Experimental animal studies, as well as clinical data, have shown that juvenile schistosomes 2–5 weeks of age are largely insensitive to praziquantel [26, 27]. These juveniles will, however, produce the schistosome gut-associated CAA and CCA, indicative of active infection. In the present study, the study population was characterized by harboring low intensities of schistosomiasis, suggestive of low transmission rates [15]. But more importantly, no differences were found in the cure rate as determined on the basis of egg counts. The different HIV groups had similar egg counts and CAA levels at baseline, and there was a strong correlation between them [15]. It is, therefore, unlikely that the observed difference in cure rates is caused by either prepatent infections of praziquantel-insensitive schistosomes or the lower sensitivity of egg counts in areas of low transmission.

With regard to assessment of efficacy of praziquantel on the basis of egg counts, our results are in accordance with those of previously published studies involving human subjects [11, 13]. This is in contrast to animal studies that have shown that praziquantel is not effective in immunodeficient mice [3]. Animal studies also showed restoration of praziquantel efficacy by passive transfer of infected mouse serum or a monoclonal antibody, suggesting a role for antibody-mediated schistosome clearance by praziquantel [4–6, 9]. Karanja et al. [11], therefore, commented that the presence of appropriate antibodies in the serum of both HIV-positive and HIV-negative individuals might partly explain the absence of an observed difference in praziquantel efficacy attributable to increased immunodeficiency. For our data, as for the data from the Kenyan study [11], a likely explanation for the discrepancy with regard to experimental animal studies may be that, in the murine model, the mice are initially immunocompromised and subsequently exposed to schistosomiasis. In our study, the sequence is likely to be the reverse; the study participants had probably been exposed to schistosomiasis as children, before they acquired their HIV-related immunodeficiency.

With regard to assessment of efficacy on the basis of CAA and CCA levels, our results are in contrast to the results of Karanja et al. [11], who identified equally decreased levels of CCA following praziquantel therapy. The amount of data included in our study is greater than the amount included in Karanja et al. [11], both with respect to combined schistosomiasis subgroups and with respect to each subgroup considered separately. Important clinical differences between our study and the Kenyan study [11] include the dominance of *S. haematobium* infections and *S. haematobium* and *S. mansoni* coinfections in our study, as opposed to *S. mansoni* infections alone in the Kenyan study. Contrasting findings could also be ascribed to much higher intensities of *S. mansoni* infection in the Kenyan study [11], compared with the low intensities of infection in our study. Our study had a very high proportion of female participants, in part reflecting the social demographics of the study area (where many men are migrant workers) and in part reflecting the greater willingness of females to enroll in the study. However, statistical analyses did not indicate that sex was an important factor in CAA clearance.

The persisting levels of CAA and CCA after treatment that we have identified correspond better with the demonstrated reduced efficacy of praziquantel in the experimental studies. One speculation could be that the antigens, although reported to disappear within days after treatment in healthy individuals [28], for some reason remain in the serum of the immunocompromised individual despite actual clearance of the source of production. However, another biologically more interesting assumption may be that, in the immunocompromised host, praziquantel is less capable of inducing eradication and instead affects the fecundity of adult schistosomes, thus reducing egg excretion but leaving the schistosomes metabolically active, as shown by the fact that antigen production is maintained. Secondary infections occurring during HIV infection could be a potential cause of the observed impaired clearance of worms as expressed by CAA level. However, asymptomatic HIV-positive participants had reduced CAA clearance, and no difference was detected in the HIV-positive group when participants were stratified according to the CDC clinical staging system. Thus, these data suggest that the reduced CAA clearance is caused by the HIV infection per se and not by the presence of secondary infections.
On the basis of other data originating from the Mupfure Schistosomiasis and HIV Cohort, we have suggested that treatment of schistosomiasis can impede an accelerated progression of HIV disease in the coinfected host [18]. With respect to the geographical concurrence of these 2 diseases, it is important to establish how the condition of the immunocompromised host who is infected with schistosomiasis is best diagnosed, treated, and monitored. Our study showed a discrepancy between monitoring of treatment efficacy on the basis of egg counts and monitoring of treatment efficacy on the basis of CAA levels, especially among HIV-positive participants. More research is needed to evaluate the dynamics involved and to resolve discrepancies between these data and previous data from Kenya [11]. Our data suggest that praziquantel may be only partly efficient in eradicating adult schistosome worms in the immunocompromised host, but it may be more effective in reducing adult worm fecundity; this may be misinterpreted as treatment success by traditional diagnostic measures. Although reducing the egg burden is the target with respect to reducing schistosomiasis morbidity, the possible continued presence of metabolically active worms might sustain immune system activation, leading to increased HIV replication. Eventually, it may be necessary to develop and implement different schistosomiasis treatment guidelines for HIV-positive subjects that involve either repeated treatment and/or higher doses of praziquantel.

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