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High levels of *Schistosoma mansoni* infections among schoolchildren in central Sudan one year after treatment with praziquantel

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Abstract

A longitudinal study was conducted to evaluate the impact of praziquantel (PZQ) for the treatment of *Schistosoma mansoni* infection among schoolchildren in Al Gunaid in Central Sudan. A cohort of schoolchildren (6–15 years of age) was investigated before and 1 year after treatment with a single dose of PZQ 40 mg/kg. Parasitological examinations for *S. mansoni* were performed before and after treatment, and prevalence and intensity of infection were analysed. Of 2741 schoolchildren recruited from six elementary schools at baseline, 2521 were successfully traced and re-examined at follow-up, with two complete sets of longitudinal parasitological data on *S. mansoni*. Boys showed significantly higher prevalence of *S. mansoni* infection than girls. A single dose of PZQ reduced the overall prevalence of *S. mansoni* infection by 36.7% (from 59.1 to 37.4%) and the intensity of infection by 41.1% (from 116.7 to 68.7 eggs per gram of stool) 1 year after treatment. The reduction in prevalence was significantly higher among the group of children with heavy infections (by 76.1%, from 6.7 to 1.6%) and among girls (by 54.1%, 42.3 to 19.4%) at 1 year after treatment. Thus, in spite of a significant reduction in the prevalence and intensity of *S. mansoni* infection 1 year after PZQ treatment, the prevalence of the disease was still high and further research is needed on this topic.

Introduction

Schistosoma haematobium and *S. mansoni* are the main forms of human schistosomiasis that exist in Africa, including Sudan. There are around 165 million people in sub-Saharan Africa with this disease. Approximately 112 million suffer from urinary schistosomiasis and approximately 54 million suffer from intestinal schistosomiasis (Chitsulo *et al.*, 2000; Van der Werf *et al.*, 2003; Steinmann *et al.*, 2006). The highest prevalence and intensity of schistosomiasis are usually found among schoolchildren (Jordan & Webbe, 1993).

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Both *S. haematobium* and *S. mansoni* are endemic in Sudan, which is an African country with a population of approximately 40 million people and one of the world's most underdeveloped regions (Ahmed *et al.*, 1996). In Sudan, the risk for schistosomiasis is widespread, especially in the major irrigation systems in the Gezira area between the Blue and White Nile Rivers. Indeed, we have recently observed a high prevalence of schistosomiasis in the different regions of Sudan among different populations, including schoolchildren (Ahmed *et al.*, 2010; Mahgoub *et al.*, 2010).

The mainstay of the current strategy recommended by the World Health Organization (WHO) against schistosomiasis is morbidity control through preventive chemotherapy with praziquantel (PZQ) (WHO, 2002, 2006).

Several national control programmes for schistosomiasis are now being implemented across sub-Saharan Africa including Sudan, where mass therapy with PZQ is the cornerstone of these programmes. Recently, studies have reported the successful implementation of these national control programmes for schistosomiasis using an annual treatment strategy through school-based PZQ administration to schoolchildren and community-based administration to adults at high risk, and their great impact on reducing morbidity and infections (Kabatereine *et al.*, 2007; Zhang *et al.*, 2007). The assessment of using annual PZQ treatment for schoolchildren is fundamental for both caregivers and health planners. The present longitudinal study aimed to investigate the prevalence and intensity of *S. mansoni* infection 1 year after treatment with PZQ among schoolchildren in Al Gunaid in central Sudan.

Methods

Parasitological surveys

This was one of the collaborative projects between the University of Khartoum and the Ministry of Health in Sudan, and it was part of a pilot programme for schistosomiasis control that aimed at regularly treating primary schoolchildren for schistosome infection. This longitudinal study was conducted in Al Gunaid, which is an agricultural area in central Sudan, during the period September 2007 to October 2008. The study was conducted in six elementary schools (for boys and girls). All the children in these six schools were included in this study. Students who had been administered PZQ in the past 6 months were excluded from this cohort. These schools included students of both gender in the elementary levels from level 1 up to level 8. Permission from the Education and Health Vice Chancellor and village head (sheikh) of this area was obtained. Then, the school authorities and parents/guardians of children were approached for participation in the study. The students were then briefed by the principals and headmasters, who thereafter sought parental consent for the students who took part in the study.

Two parasitological surveys were carried out, one before treatment and the other 1 year after treatment to determine the prevalence and intensity of schistosomiasis among these schoolchildren. The collected samples were examined for the presence of *S. haematobium* eggs in a 10-ml sample of terminally voided urine using the sedimentation technique, and for the presence of *S. mansoni* eggs in the faeces using the modified Kato technique.

Stool examination

Qualified laboratory scientists performed microscopic examination of stool specimens to detect *S. mansoni* hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* eggs using the Kato–Katz technique (Teesdale & Amin, 1976). Stool samples were collected and duplicate slides were prepared from each stool sample. Thick stool smears were prepared using plastic templates (40.0 g) and examined within 30–60 min under a light microscope. The smears were left to clear for at least 24 h and were re-examined for the detection of *S. mansoni* eggs. The numbers of eggs detected from each Kato–Katz thick smear were counted to express the infection intensity as the number of eggs per gram of stool (epg). The mean epg reading of two slides was considered as the final reading. Data gathered were used to calculate the cumulative prevalence and intensity of infection, which was classified on the basis of epg as light <100 epg, moderate 100–399 epg and high ≥ 400 epg (WHO, 1999). *Schistosoma haematobium* eggs were investigated in the urine by membrane filtration.

Treatment of children

Treatment of children in all primary schools in the entire district was carried out by health teams (trained nurses and medical officers) as part of the treatment campaign. The study team assisted this health team with treatment and also recorded and observed the treatment of the study schoolchildren. All schoolchildren were treated for schistosome infection with a single dose of 40 mg/kg praziquantel, without considering the infection status, using 600 mg praziquantel tablets, which can be subdivided into four segments of 150 mg. The health team provided a dosing sheet that showed the correct dosage for different body weights. Children infected with other helminths received albendazole orally.

Ethics

The study received ethical clearance from the Research Board of Communicable Disease, Ministry of Health, Sudan.

Data analysis

Data were entered into the computer using SPSS for windows version 16.0 (SPSS Inc., Chicago, Illinois, USA) and double checked before analysis. The chi-square test was used to compare the differences in the prevalence (proportions) of infection. ANOVA was used to compare differences in the intensity of infection (egg count in epg). A value of $P < 0.05$ was regarded significant. Reduction in the prevalence and intensity (egg count in epg) was calculated using the formulae below (Montresor *et al.*, 1998).

Prevalence reduction

$$= ((\%\ \text{prevalence before treatment} - \%\ \text{prevalence 1 year after treatment})/(\%\ \text{prevalence before treatment})) \times 100\%$$

Reduction in the intensity

$$= ((\%\ \text{mean epg before treatment} - \%\ \text{mean epg 1 year after treatment})/(\%\ \text{mean epg before treatment})) \times 100\%$$

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Table 1. The prevalence and intensity of *Schistosoma mansoni* infections in children from six schools in Al Gunaid in Central Sudan.

School	Baseline			One year post-treatment		
	Children examined	Prevalence (95% CI)	Intensity (95% CI)	Children examined	Prevalence (95% CI)	Intensity (95% CI)
El Kidaiwa	659	65.2 (61.5–68.8)	111.6 (111.4–111.7)	614	36.7 (32.9–40.5)	86.2 (85.9–86.4)
Id El Sheikh	265	32.1 (26.6–37.8)	39.9 (39.6–40.1)	236	16.9 (12.5–22.1)	30.9 (30.3–31.4)
El Hodour	562	18.7 (15.6–22.0)	47.4 (47.0–47.7)	517	5.4 (3.7–7.6)	32.2 (31.4–32.9)
El Talha	459	73.8 (69.6–77.7)	119.8 (119.6–119.9)	423	44.7 (39.9–49.4)	59.7 (59.3–60.0)
Magharba	328	78.3 (73.6–82.5)	189.0 (188.8–189.1)	303	59.4 (53.8–64.8)	98.0 (97.8–98.1)
El Ingaz	468	86.1 (82.7–89.0)	191.7 (191.6–191.8)	428	62.4 (57.7–66.8)	106.0 (105.8–106.1)
Total	2741	59.1 (57.2–60.9)	116.7 (116.6–116.8)	2521	37.4 (35.5–39.3)	68.7 (68.5–68.8)

Intensity was calculated as geometric mean egg-count/g; CI, confidence interval.

Results

Of 2741 schoolchildren recruited at baseline, 2521 were successfully traced and re-examined at baseline and followed up with two complete sets of longitudinal parasitological data on *S. mansoni*. Data of children who dropped out or missed the follow-up survey were not significantly different to those included in both surveys (data not shown).

The mean age of these children was 9.8 years (range, 6–15 years). Only 13 cases of *S. haematobium* were detected in the first survey. This is the reason why S. *haematobium* infection was not investigated in the second survey; hence, only the results of *S. mansoni* infection are presented in this report. Only a few cases (1.7%, 1.4%, 0.8% and 0.4%) of *Hymenolepis nana*, hookworm, *T. trichiura* and *A. lumbricoides*, respectively, were detected. Table 1 summarizes the parasitological results of *S. mansoni* infection in children examined at baseline and 1 year after treatment. Generally, boys had significantly higher prevalence rates and intensity of *S. mansoni* infection than girls (table 2). While the prevalence of *S. mansoni* infection ranged from 18.7 to 86.1% with an overall prevalence of 59.1%, geometric egg counts ranged from 39.9 to 191.7 epg with a mean of 116.7 epg among all children.

A single dose of PZQ significantly reduced the prevalence of *S. mansoni* infection by 36.7% (from 59.1 to 37.4%) and the intensity of infection by 41.1% (from 116.7 to 68.7 epg) 1 year after treatment. A reduction in both prevalence and intensity of infection was found in all age groups and in both boys and girls (table 2). While there was a significantly higher reduction of prevalence of *S. mansoni* infection among girls in comparison with boys, there was no significant difference in the reduction of prevalence among different age groups. There was no significant difference in the reduction of the intensity of infection between the gender or age groups (table 3).

Importantly, the reduction in prevalence (76.1%) was significantly higher in children with heavy infection ($P < 0.001$). Before treatment, the proportion of schoolchildren with heavy infections accounted for 6.7%. This decreased to 1.6% at 1 year after treatment (table 4).

Discussion

To our knowledge, this is the first published report to have investigated the effect of PZQ on *S. mansoni* infection 1 year after treatment in a large cohort of Sudanese schoolchildren. The main findings of the current study were a high prevalence of *S. mansoni* infection, especially among boys, and that a single treatment with PZQ reduced the overall of prevalence of *S. mansoni* infection by 36.7% (from 59.1 to 37.4%) and intensity of infection by 41.1% (from 116.7 to 68.7 epg) 1 year after treatment. The reduction in *S. mansoni* infection was significantly higher among the group of children with heavy infection, i.e. by 76.1% (from 6.7 to 1.6%) 1 year after treatment. The high total prevalence and the large proportion of heavy infection that we found indicate that, according to WHO criteria, regular treatment of schoolchildren in

Table 2. The prevalence and intensity of *Schistosoma mansoni* infections in children from six schools in Al Gunaid in Central Sudan at baseline and 1 year post treatment, relative to gender and age.

Variable	Baseline			One year post-treatment		
	Children examined	Prevalence (95% CI)	Intensity (95% CI)	Children examined	Prevalence (95% CI)	Intensity (95% CI)
Boys	1488	75.7 (73.4–77.8)	148.3 (148.2–148.3)	1327	55.5 (52.7–58.1)	86.3 (86.2–86.3)
Girls	1253	42.3 (39.5–45.0)	84.6 (84.4–84.7)	1194	19.4 (17.2–21.7)	51.1 (50.8–51.3)
Total	2741	59.1 (57.2–60.9)	116.7 (116.6–116.8)	2521	37.4 (35.5–39.3)	68.7 (68.5–68.8)
Age $<$ 10 years	1409	60.7 (58.1–63.2)	120.2 (120.1–120.2)	1276	37.7 (37.1–42.3)	70.2 (70.0–73.3)
Age $\geq$ 10 years	1332	57.4 (54.7–60.0)	112.7 (112.5–112.8)	1245	35.2 (32.5–37.9)	67.2 (67.0–67.3)
Total	2741	59.1 (57.2–60.9)	116.7 (116.6–116.8)	2521	37.4 (35.5–39.3)	68.7 (68.5–68.8)

Intensity was calculated as geometric mean egg-count/g; CI, confidence interval.

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Table 3. Reduction (% (95% confidence interval)) in the prevalence and intensity of *Schistosoma mansoni* infections in children from six schools in Al Gunaid in Central Sudan, relative to gender and age.

Variables	Reduction in prevalence	Reduction in the intensity
Boys	26.7 (19.1–36.3)	41.8 (34.0–49.9)
Girls	54.1 (40.6–65.4)	39.6 (30.7–49.0)
P	0.001	0.7
Age < 10 years	37.9 (26.3–50.5)	41.6 (33.0.–50.5)
Age ≥ 10 years	38.7 (28.9–50.3)	40.4 (32.4–48.6)
P	0.5	0.9

this area is indeed necessary (WHO, 2002). The high prevalence of *S. mansoni* infection in boys has been observed in eastern Sudan as well as in this study (Mahgoub *et al.*, 2010). This could be explained by different water-contact patterns.

In the current study, although the prevalence of *S. mansoni* infection was significantly decreased, it was still high (37.4%). It seems more likely that the relatively high post-treatment prevalence was not an indication of a high proportion of active infections after treatment, but that they were caused by new infections. Yet, the possibility of treatment failure and/or new infections exists. However, some reports emerged recently that indicate the ability to differentiate between PZQ resistance in *Schistosoma* and re-infections (Lamberton *et al.*, 2010). We have recently observed a full (100%) cure rate with PZQ (after 4 weeks) in 46 schoolchildren with *S. mansoni* infection in eastern Sudan (Mohamed *et al.*, 2009). However, in eastern Sudan, the prevalence of *S. mansoni* infection was only 15.9% and only one child had heavy infection (Mohamed *et al.*, 2009). Interestingly, in Burkina Faso, a prevalence of *S. mansoni* infection of 13.6% and intensity of infection of 22.4 epg in a cohort of schoolchildren were significantly reduced to 1.5% and 2.9 epg, respectively, 2 years after PZQ treatment (Touré *et al.*, 2008). Full cure rates with PZQ have rarely been recorded in endemic areas, but cure rates of 85–90% are generally achieved. Therefore, the rationale behind this and similar programmes in other countries is not to eliminate infection in a given area, but to keep infection intensity low in this vulnerable age group in order to prevent serious morbidity (WHO, 1993). Immature schistosome worms are insensitive to PZQ. It is therefore argued that low cure rates and observed treatment failures are due to the presence of immature worms in the patients at the time they are treated (Gryseels *et al.*, 2001), an argument supported by the higher cumulative cure rates achieved when two treatments were given a few weeks apart (Utzinger *et al.*, 2000).

Table 4. Reduction (% (95% confidence interval)) in the prevalence and intensity of *Schistosoma mansoni* infections in children from six schools in Al Gunaid in Central Sudan, relative to the level of infections.

Infection level, epg	Cumulative results: % (95% confidence interval)		Reduction in the prevalence rate
	Baseline	One year post-treatment	
Negative	40.8 (38.9–42.6)	62.6 (60.6–64.4)	–
Light	33.0 (31.2–34.8)	25.8 (24.1–27.5)	21.8 (13.3–35.4)
Moderate	19.4 (18.0–20.9)	10.0 (8.8–11.2)	48.5 (32.6–65.4)
Heavy	6.7 (5.8–7.7)	1.6 (1.1–2.1)	76.1 (76.1–93.7)
Total	59.1 (57.3–61.0)	37.4 (35.5–39.3)	36.7 (26.5–47.3)

However, there is much debate about whether PZQ has become less effective because of the potential emergence of drug resistance. When PZQ was used for treating intestinal schistosomiasis in northern Senegal, cure rates of only 18–39% were obtained (Stelma *et al.*, 1995). Following extensive use of PZQ in Egypt for the treatment of *S. mansoni*-infected patients, with PZQ at 40 mg/kg and after an additional two treatments, the latter at 60 mg/kg, 1.6% of the patients were still passing viable eggs (Ismail *et al.*, 1996).

In our study, the reduction in *S. mansoni* infection was significantly higher among the group of children with heavy infection. Cure rates based on egg counts are usually overestimated because of the inherent insensitivity of the methods for counting eggs routinely used in endemic areas. Thus, for example, Kato–Katz thick-smear examinations performed on only 1 day indicated higher cure rates compared with those carried out over several days (Utzinger *et al.*, 2000). The examination of three or more specimens per child would most certainly have led to even higher estimates of total prevalence, but we do not believe that this would have substantially changed our results. All this indicates that the reporting of infection intensity is not only important because it is a better indicator of population morbidity than prevalence (Jordan & Webbe, 1993) but that intensity is also a more reliable marker of treatment success, defined as the removal of egg-laying worms. This is especially important when relying on single egg counts to assess the effectiveness of the intervention, which is usually the case in treatment programmes and larger field studies (Davis, 2004).

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