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ORIGINAL ARTICLE

Integrated community-based intervention for urinary schistosomiasis and soil-transmitted helminthiasis in children from Caxito, Angola

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Background: Schistosomiasis and soil-transmitted helminths (STH) infections are major public health problems. We aimed to study the 6-mo impact of mass drug administration with praziquantel and albendazole on urinary schistosomiasis and STH.

Methods: We examined children (aged 2–15 y) from one hamlet, who provided urine and faeces samples at baseline (n=197), 1 mo (n=102) and 6 mo (n=92); 67 completed the protocol.

Results: At baseline, 47/67 (70.1%) children presented *Schistosoma haematobium* (75.8% in the baseline total sample) and 12/67 (17.9%) with STH (30.5% in the initial sample, p=0.010). Among the children, 47.3% had heavy *Schistosoma haematobium* infection. The most frequent STH was *Trichuris trichiura* in 9.0%. We also found *Hymenolepis nana* (13.2%) and *Plasmodium falciparum* (9.1%) infections and anaemia (82.1%). One mo after chemotherapy there was a significant (p=0.013) reduction of *Schistosoma haematobium* prevalence (23.5%) and a high egg reduction rate (86.9%). Considering the sample of 67 children, the mean egg concentration was 498 at baseline, 65 at 1 mo and 252 at 6 mo ($p<0.05$). We also observed a reduction in STH infections, 50% in *Ascaris lumbricoides*, 33.3% in *T. trichiura* and 50% in hookworms. At 6 mo, the prevalence of *Schistosoma haematobium* (76.1%) was similar to the baseline and the STH reduction was not significant.

Conclusions: Longitudinal studies have reported many losses in these settings, but we were able to show that mass drug administration for control of schistosomiasis and STH present low effectiveness, that reinfections occur rapidly and that stand alone anthelmintic therapy is not a sustainable choice.

Keywords: chemotherapy, mass drug administration, *Schistosomiasis haematobia*, soil-transmitted helminths

Introduction

Helminth infections have a massive impact on the morbidity and mortality of human populations globally.[1] *Schistosoma haematobium*, *Ascaris lumbricoides*, *Trichiura trichuris* and hookworm infections affect 290.6, 804.4, 477.4 and 471.8 million people worldwide, respectively.[2] These infections are endemic in Angola, where the prevalence of *Schistosoma haematobium*, hookworms, *A. lumbricoides*, *T. trichiura* and *Hymenolepis nana* were reported to be high (10–17, 4–6.7, 15–17, 7–14 and 6–7%, respectively) in preschool and school-age children in the Dande municipality (Bengo province, Angola) in 2010.[3] Additionally, some of those species also share their geographical distribution with malaria, and therefore co-infections were reported. Among comorbidities associated with these infections, we find bladder and kidney pathologies, chronic inflammation, respiratory and gastrointestinal problems, chronic blood loss, immunity and anaemia.[1,4–9]

In Angola, it is expected that there will be adoption of integrated therapeutic mass drug distribution of praziquantel and albendazole in deworming campaigns, as described in the National Sanitary Development Plan for 2012–2025 (approved by Angolan Ministry of Health in 2012). However, research into the impact of an integrated approach is urgently needed, as it

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could help to clarify key aspects such as behavioural change related to health education, clean water provision, environmental sanitation and programme control adherence, which would help to improve these interventions.

Here, we investigated the 6-mo impact of a community-based integrated therapeutic intervention with praziquantel, albendazole and Coartem (if tested positive for malaria), in the reinfection of schistosomiasis, geohelminths and malaria and in the occurrence of anaemia.

Materials and methods

Study site

We conducted this investigation in Cabungo, one hamlet of the study area of Centro de Investigação em Saúde de Angola (CISA), located in the Dande municipality (Bengo, northern Angola). The structure, dynamics and geographical distribution of the population of this area are monitored by the Health and Demographic Surveillance System, previously described by Costa and coworkers.[10] The initial list provided by Demographic Health Survey consisted of 824 inhabitants, including 364 children aged 2–15 y. The research team integrated two DHS technicians and updated the list of children during the baseline, identifying 209 (57.4%) children present, who were all invited and participated in the study.

Study design, participants and data collection

This was an interventive prospective study, conducted between December 2012 and December 2013. Cabungo was selected by convenience, based on the high rates of schistosomiasis.[4] On the first day of the baseline, the study team went from house to house to identify and invite children aged 2–15 y and to distribute containers for sample faeces. On the second day, the population was concentrated in a designated place for a previously arranged community meeting, where we collected all urine, faeces and blood samples, applied the questionnaire with signed consent and administered the drugs. During the two follow-ups, we met participants at the same designated place. Six mo after the second follow-up, the team returned to the participants' homes to inquire about reasons for non-adherence. Trained field workers conducted the questionnaire to obtain demographic and socioeconomic data and child morbidity history. We provided a container (1 d prior to survey) to collect one faecal sample per participant while urine samples were collected in containers provided to participants upon arrival on the survey day. Both samples were stored in ice at 4°C until transportation to the CISA laboratory where they were refrigerated. Kato-Katz smears were performed by CISA expert technicians for the diagnosis of *Schistosoma mansoni*, soil-transmitted helminths (STH) (such as hookworms, *A. lumbricoides* and *T. trichiuria*), *H. nana* and *Taenia* spp. Urogenital schistosomiasis (*Schistosoma haematobium*) was diagnosed by examination of the pellet resulting from 10 ml centrifuged urine and eggs count, according to WHO protocol.[11] We were not able to use the membrane for filtration method in this project; however, the local availability of equipment and laboratory technicians ensured good execution of the centrifugation method, whose effectiveness in concentrating the eggs does not cause any morphological changes to either the helminth eggs or larvae.[12] Capillary blood samples were collected for diagnosis of malaria by rapid diagnostic test (SD BIOLINE Malaria Ag P.f/P.v, Standard Diagnostics Inc.) and for measurement of haemoglobin levels with the HemoCue system (HemoCue 201+, Angelholm, Sweden). All children took a single dose of praziquantel (40 mg/kg) and albendazole (400 mg) under direct observation at the first visit and 6 mo later. The children who tested positive for *Plasmodium falciparum* were treated with Coartem (artemether/lumefantrine 20/120), in accordance with the national therapeutic guidelines for uncomplicated malaria at all evaluation time points. The national malaria control programme recommends treatment for asymptomatic individuals (human reservoirs) with positive Rapid Diagnostic Test (RDT) for *plasmodium* at all opportunities, in order to reduce continuous transmission by the mosquito bite.[13,14] In addition, one long-lasting insecticide-treated bednet was provided for each child who participated in this study. Follow-up visits occurred 1 and 6 mo after initial drug delivery and parasitological examination. Malaria treatment was performed on all visits.

Reasons for dropout were investigated performing an additional structured questionnaire, performed 6 mo after the second follow-up with the same respondents. In these questionnaires we also asked respondents for suggestions of possible solutions to improve adherence.

Table 1. Cut-offs for intensity of infection and thresholds used to define anaemia

Infections	Light	Moderate	Heavy
Schistosoma haematobium (no. of eggs/10 ml of urine)	1–49		≥50
A. lumbricoides (no. of eggs/gram of faeces)	1–4999	5000–49 999	≥50 000
T. trichiura (no. of eggs/gram of faeces)	1–999	1000–9999	≥10 000
Hookworms (no. of eggs/gram of faeces)	1–1999	2000–3999	≥4000
H. nana (no. of eggs/gram of faeces)	1–1999	2000–9999	≥10 000
Anaemia in children (g/dl)	**Mild**	**Moderate**	**Severe**
<5 y	9.0–11.0	7.0–8.9	<7
5–11 y	11.0–11.4	8.0–10.9	<8
12–14 y	11.0–11.4	8.0–10.9	<8

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Statistical analysis

Data were entered into the CISA database and then exported to SPSS Statistics for Windows version 20.0 and R version 3.0.1 (IBM, Armonk, NY, USA). Analyses were performed to determine prevalence and intensity reduction, intensity and reinfection rates resulting from *Schistosoma haematobium*, geohelminths and *H. nana* infections, 1 and 6 mo after treatment.

Prevalences were calculated as the frequencies of the outcome over the total samples with valid results. The intensity of *Schistosoma haematobium* infections and of intestinal parasites was recorded according to WHO[15] (Table 1). Also, the age-specific severity of anaemia was defined as recommended by WHO.[16,17]

The prevalence reduction rate (PRR) was calculated as:

$$\frac{\%\text{ prevalence before the treatment} - \%\text{ prevalence after the treatment}}{\%\text{ prevalence before treatment}} * 100$$

The intensity reduction rate (IRR) was calculated as:

$$\frac{\text{Geometric mean of eggs before the treatment} - \text{geometric mean eggs after the treatment}}{\text{geometric mean before the treatment}} * 100$$

The post-treatment reinfection rates were calculated as:

$$\frac{\text{Number of children who became positive after the treatment}}{\text{Number of children who turned negative after the treatment}} * 100$$

χ^2 McNemar's, paired sample t and Wilcoxon related samples tests were used to compare difference in the prevalence and intensity of infections. The threshold for significant level was 0.05.

Ethical aspects

This study was approved by the Ethical Committee of the Ministry of Health of Angola. Informed consent was obtained by signature from the parents or guardians of children. Schistosomiasis, geohelminth and malaria infections were treated. Children with anaemia were referred to the nearest health-care centre. The project team at the study site provided education sessions for all people present and returned the results of parasitological examinations to the parents and guardians of the children who participated in the study.

Results

In this study, we enrolled 209 children (110 boys and 99 girls aged 2–15 y, with a median age of 6 y). Those who showed no compliance to drug therapy at the baseline, failed to provide urine, faeces and blood samples, or had invalid data or examination results and refused to repeat the procedure, were excluded from the analysis. Most of these dropouts were children who cried, vomited or choked upon medication. Some did not give urine or stool samples and their parents or guardians did not bring them back to repeat the procedure. Others were absent from the residences during the study period. Exclusions, dropouts and the number of followed children are presented in Table 2.

In total, 142 lost to follow-up were questioned concerning the reasons for their absence at the evaluation time points. The main reported reason for lost to follow-up was spending school holidays in the capital for the Christmas vacation (33.1%, 47/142) and quarterly break (21.8%, 31/142). The other reasons were the side effects of medication reported by participants (16.2%, 23/142 and 11.3%, 16/142) and the unavailability of the caregiver to take the child to the evaluation (4.2%, 6/142 and 5.6%, 8/142) during the first and second evaluations, respectively.

About 100 respondents suggested possible solutions to improve adherence, including family counselling regarding sanitation and hygiene (45%, 45/100) and door-to-door notification of the follow-up dates (29%, 29/100).

Children within the lost to follow-up group were significantly more frequently infected with STH than children within the followed group (Table 3); 80% of the children diagnosed with STH were lost to follow-up (p=0.010). We found no significant differences between participants and losses to follow-up among all other variables.

We investigated participants' knowledge, attitudes and practices (KAP) with regard to schistosomiasis, geohelminths and malaria and also behaviour regarding water, sanitation and hygiene (WASH) at the baseline (Table 4). All children were reported to have contact with dams, ponds, rivers or irrigation canals, and 57.6% (114/197) of them had two or more contacts per day and were infected with *Schistosoma haematobium*. Water from those sources was reported to be used mainly for bathing and playing. About 39.7% of the children were reported to drink treated water, and they were significantly infected with *Schistosoma haematobium* (21.2%, *p*=0.001) and *T. trichuria* (2.0%, *p*=0.001). It was noted that 34.0% of the households had latrines; however, most latrine users had more *Schistosoma haematobium* (50%) than STH infections, but the difference was not significant. Correct knowledge concerning *Schistosoma haematobium* was significant in 17.7% (p= 0.001) of participants infected by the disease, of whom 20.7% (p=0.001) had already urinated blood. Those that maintained contact with animals were also more infected with *Schistosoma haematobium* (22.7%, p=0.007).

Parasitological characteristics of the participants

At the baseline, 75.8% (150/198) of all children delivering urine samples presented *Schistosoma haematobium*. From those, 10.8% were light, and 62.7% were heavy infections. Among those providing faeces samples, 30.5% (60/197) were infected with at least one STH, 13.7% (27/197) with *A. lumbricoides*, 14.7% (29/197) with *T. trichiura* and 5.1% (10/197) with hookworms. Other helminths identified at the baseline were *H. nana* (10.2%, 20/197) and *Strongyloides stercoralis* (3.6%, 7/197). Prevalence of malaria among children successfully delivering blood samples was 6.9% (14/203).

Among the 67 children successfully completing the study of helminths infections, the prevalence of *Schistosoma haematobium* varied from 70.1% (47/67) to 53.7% (36/67) and 76.1% (51/67) between the baseline, first and second follow-up, respectively. This corresponded to a 23.5% PRR between the

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Table 2. Exclusions and denominators used for prevalence estimation within evaluation time points

Time points	*Schistosoma haematobium*		Soil-transmitted helminths (STH)		*Hymenolepis nana*		*Plasmodium falciparum*		Anaemia	
Enrolled	no. enrolled=209		no. enrolled=209		no. enrolled=209		no. enrolled=209		no. enrolled = 209	
Baseline (0)	180	29 excluded	178	31 excluded	176	33 excluded	193	16 excluded	202	7 excluded
Evaluation - treatment										2 no data
		11 no urine		12 no faeces		12 no faeces		1 no data		
		13 missed PZQ		14 missed ALB		16 missed PZQ		10 previous treatment		5 invalid data
		5 invalid data		5 invalid data		5 invalid data		5 invalid data		
1 mo post-treatment (1)	102	78 excluded	110	68 excluded	110	66 excluded	125	68 excluded	133	69 excluded
										63 lost to follow-up
Evaluation (0)→(1)		17 no urine		8 no faeces		8 no faeces		62 lost to follow-up		6 invalid data
		58 lost to follow-up		55 lost to follow-up		53 lost to follow-up		6 invalid data		
		3 invalid data		5 invalid data		5 invalid data				
6 mo post-treatment (6a)	67	35 excluded	67	43 excluded	68	42 excluded	77	48 excluded	82	51 excluded
		29 lost to follow-up		5 no faeces		5 no faeces		44 lost to follow-up		47 lost to follow-up
Evaluation (1)→(6a)		6 invalid data		34 lost to follow-up		34 lost to follow-up		4 invalid data		4 invalid data
Treatment				4 invalid data		3 invalid data				
6 mo post-treatment (6b)	92	88 excluded	87	91 excluded	86	90 excluded	100	93 excluded	105	97 excluded
		17 no urine		6 no faeces		6 no faeces		87 lost to follow-up		91 lost to follow-up
Evaluation (0)→(6b)		63 lost to follow-up		82 lost to follow-up		80 lost to follow-up		6 invalid data		6 invalid data
Treatment		8 invalid data		3 invalid data		4 invalid data				

ALB, albendazole; PZQ, praziquantel; (0), baseline; (1) 1 mo; (6a), 6 mo after first treatment; (6b), 6 mo after baseline.

baseline and first follow-up (p=0.013), and to an increase of prevalence either between the first and second follow-up (PRR: 41.7%, p=0.003) but not between the baseline and second follow-up (PRR: 8.6%, p=0.424).

At the same time, 77 children were submitted to malaria RDT and the positive cases were treated by plasmodial infection. The prevalence of malaria was 9.1% (7/77), 10.4% (8/77) and 2.6% (2/77) at the three time points of the study, respectively (Table 5).

The intensity of *Schistosoma haematobium* infections, 1 mo after the first administration of praziquantel, was reduced by 86.9% (p<0.001), and heavy infections dropped from 62.7 to 34.3%. However, between the first and second follow-ups, the intensity of infection increased considerably (p<0.001). At all evaluation time points, no heavy infections were observed for either STH or *H. nana*. Moderate infections were only observed for *A. lumbricoides* at the baseline, cleared after the first administration of albendazole, and for *T. trichiura* 6 mo after treatment.

We observed that some negative results in the baseline became positive at the first follow-up, namely, 6.0% (4/67) of *Schistosoma haematobium*, 3.0% (2/67) of *A. lumbricoides*, 4.5% (3/67) of *T. trichiura*, 1.5% (1/67) of hookworms, 1.5% (1/67) of *H. nana* and 3.9% (3/77) of *P. falciparum*. Reinfections at the second follow-up occurred only for *Schistosoma haematobium* (85.7%, 12/14) and *A. lumbricoides* (33.3%, 1/3).

Prevalence of anaemia among all children presenting at the baseline (Table 3) was 76.8% (159/207, CI: 70.5 to 82.4), of which 66.7% (106/159, CI: 60.9 to 76.0) was moderate and only 3.8% (6/159, CI: 1.4 to 8.3) was severe. Among the 67 children who completed the all-infections study, 55.1% (37/67) had anaemia (of which 14, 38 and 3% was mild, moderate and severe, respectively). From the baseline to the second follow-up period, a prevalence reduction of 25.9% (p=0.230), or 55.2 to 40.9%, was observed. In the analysis of the association between anaemia and the infections studied (Table 4), we found that moderate anaemia predominated. All cases of severe anaemia (n=6, 3.0%) and most cases of moderate anaemia

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Table 3. Main characteristics of participants and dropouts in the study

Variables	Baseline	Participants (0→6)	Lost to follow-up (0→6)	p-value (participants vs lost to follow-up)
Sex	N=209	N=67	N=142	
Male	110 (52.6%, CI: 45.6 to 60.0)	41 (37.3%, CI: 28.2 to 47.0)	69 (62.7%, CI: 53.0 to 71.8)	0.120
Female	99 (47.4%, CI: 40.4 to 54.4)	26 (26.3%, CI: 17.9 to 36.1)	73 (73.7%, CI: 63.9 to 82.1)	
Age	N=209	N=67	N=142	
Median	6.0	6.0	6.0	0.382
Preschool age	93 (44.5%, CI: 37.6 to 51.5)	30 (32.3%, CI: 22.9 to 42.7)	63 (67.7%, CI: 57.3–77.1)	1.000
School age	116 (55.5%, CI: 48.5–62.4)	37 (31.9%, CI: 23.6–41.2)	79 (68.1%, CI: 58.8–76.4)	
Attend school	N=208	N=66	N=142	
No	116 (55.8%, CI: 48.7 to 62.6)	40 (34.5%, CI: 25.9 to 43.9)	76 (65.5%, CI: 56.1 to 74.1)	0.419
Yes	92 (44.2%, CI: 37.4 to 51.3)	26 (28.3%, CI: 19.4 to 38.6)	66 (71.7%, CI: 61.4 to 80.6)	
Schistosoma haematobium	N=198	N=67	N=131	
No	48 (24.2%, CI: 18.4 to 30.8)	20 (41.7%, CI: 27.6 to 56.8)	28 (58.3%, CI: 43.2 to 72.4)	0.254
Yes	150 (75.8%, CI: 69.2 to 81.6)	47 (31.3%, CI: 24.0 to 39.4)	103 (68.7%, CI: 60.6 to 76.0)	
STH	N=197	N=67	N=130	
No	137 (69.5%, CI: 62.6 to 75.9)	55 (40.1%, CI: 31.9 to 48.9)	82 (59.9%, CI: 51.1 to 68.1)	0.010
Yes	60 (30.5%, CI: 24.1 to 37.4)	12 (20.0%, CI: 10.8 to 32.3)	48 (80.0%, CI: 67.7 to 89.2)	
H. nana	N=197	N=68	N=129	
No	177 (89.8%, CI: 84.8 to 93.7)	59 (33.3%, CI: 26.4 to 40.8)	118 (66.7%, CI: 59.2 to 73.6)	0.428
Yes	20 (10.2%, CI: 6.3 to 15.2)	9 (45.0%, CI: 23.1 to 68.5)	11 (55.0%, CI: 31.5 to 76.9)	
P. falciparum	N=208	N=77	N=131	
No	194 (93.3%, CI: 89.0 to 96.3)	70 (36.1%, CI: 29.3 to 43.3)	124 (63.9%, CI: 56.7 to 70.7)	0.450
Yes	14 (6.7%, CI: 3.7 to 11.0)	7 (50.0%, CI: 23.0 to 77.0)	7 (50.0%, CI: 23.0 to 77.0)	
Anaemia	N=207	N=82	N=125	
No	48 (23.2%, CI: 17.6 to 29.5)	17 (35.4%, CI: 22.2 to 50.5)	31 (64.6%, CI: 49.5 to 77.8)	0.610
Yes	159 (76.8%, CI: 70.5 to 82.4)	65 (40.9%, CI: 33.2 to 48.9)	94 (59.1%, CI: 51.2 to 66.8)	

STH, soil-transmitted helminths

(n=66, 33.3%) were infected with *Schistosoma haematobium*. Infections by *A. lumbricoide*, *H. nana* and *P. falciparum* were not found in any case of severe anaemia. We also verified that all the severe cases occurred in the preschool-age children and that they presented a slightly higher prevalence of anaemia than the school-age children (73 vs 69%).

Approximately 52% of the participants reported transient adverse events postmedication. The most mentioned were belly pain, headache, dizziness and fatigue. No cases were taken to the health facility.

Discussion

Previous cross-sectional studies conducted by CISA have already reported a high prevalence of *Schistosoma haematobium*, STH, *H. nana* and *P. falciparum* in children within this geographical area of Angola.[3] For the children who completed the protocol, prevalence decreased in the first month but rose again in the sixth month, being similar to the baseline.

A high loss of follow-up was observed in this study (67%), a situation common in many regions of Africa.[18] However, the families of dropout children recognised the benefit of the study and suggested that the research team move from house to house advising families in order to improve adherence to the study.

Controlling infections with integrated doses of praziquantel and albendazol resulted in a considerable egg reduction rate but a low reduction in *Schistosoma haematobium* prevalence 1 mo after treatment. Lee and coworkers[19] performed a similar comprehensive intervention with chemotherapy, health education and water supply, and achieved a low reduction of *Schistosoma haematobium* prevalence of 13.5% after 6 mo of follow-up. At the same time, more reduction was found in the village where there was a water supply.

Considering that during the duration of our study there was no supply of drinkable water, those events may suggest a continuous contact with cercarial contaminated water. We observed that almost a third of these children were highly knowledgeable about the diseases and knew that the parasites were caught in the collection of water and in the faeces or contaminated food, but they continued to go two or more times a day to the irrigation canal, lake or pond to take baths and draw water for domestic use. Although this suggests other strategies of persuasion to provide adequate KAP,[20] we did not see any alternatives for them to obtain water of sufficient quantity for

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Table 4. Baseline demographic and knowledge, attitudes and practices regarding infections

Characteristics	*Schistosoma haematobium*		*A. lumbricoide*		*T. trichuria*		Hookworms		*H. nana*		*P. falciparum*	
	n (%)	p	n (%)	p	n (%)	p	n (%)	p	n (%)	p	n (%)	p
Overall	197		190		197		197		197		209	
Demographic characteristics												
Gender												
Boys	77 (38.9)	0.274	8 (4.2)	0.027	17 (8.6)	0.092	1 (0.5)	0.297	12 (6.1)	0.058	104 (49.8)	0.448
Girls	73 (36.9)	-	17 (8.9)	-	8 (4.1)	-	1 (0.5)	-	4 (0.2)	-	91 (43.5)	-
Grouped age												
Preschool-age children	57 (28.8)	0.013	12 (6.3)	0.522	8 (4.1)	0.209	1 (0.5)	0.447	9 (4.6)	0.289	89 (42.6)	0.214
School-age children	93 (47.0)	-	13 (6.8)	-	17 (8.6)	-	3 (1.5)	-	7 (3.6)	-	106 (50.7)	-
Water, sanitations and hygiene practices (WASH)												
Water contact												
Once a day or less	36 (18.2)	0.317	7 (3.7)	0.837	6 (3.0)	0.818	1 (0.5)	0.967	2 (1.0)	0.202	4 (1.9)	0.741
Twice a day or more	114 (57.6)	-	18 (9.5)	-	19 (9.6)	-	3 (1.5)	-	14 (7.1)	-	10 (4.8)	-
Drinking treated water (with lye, alum or boiling)	42 (21.2)	0.001	13 (6.8)	0.060	4 (2.0)	0.029	0	-	6 (3.0)	0.864	71 (36.0)	0.520
Use of latrine	99 (50.0)	0.335	22 (11.6)	0.996	16 (8.1)	0.996	4 (2.0)	0.129	9 (4.6)	0.503	7 (3.3)	0.221
Hand washing after defecation	48 (24.2)	0.713	6 (3.2)	0.482	10 (5.1)	0.240	2 (1.0)	0.376	7 (3.6)	0.209)	7 (3.3)	0.103
Use of soap in hand washing	19 (5.1)	0.528	3 (1.6)	0.154	1 (0.5)	0.712	0	-	0	-	0	-
Knowledge, attitude and practices (KAP)												
Knowledge of schistosomiasis	35 (17.7)	0.001	8 (4.2)	0.947	7 (3.6)	0.029	1 (0.5)	0.186	5 (2.5)	0.975	4 (1.4)	0.226
Already urinated blood	41 (20.7)	0.001	11 (5.8)	0.538	11 (5.6)	0.630	1 (0.5)	0.547	7 (3.6)	0.723	6 (2.9)	0.774
Have been treated for schistosomiasis	68 (34.3)	0.069	18 (9.5)	0.013	9 (4.6)	0.111	3 (1.5)	0.327	9 (4.6)	0.647	6 (2.9)	0.542
Knowledge of the intestinal parasites	19 (9.6)	0.162	4 (2.1)	0.397	1 (0.5)	0.223	1 (0.5)	0.375	2 (1.0)	0.860	4 (1.9)	0.038
Already had blood in the stool	103 (52.0)	0.162	18 (9.5)	0.862	17 (8.6)	0.672	3 (1.5)	0.878	12 (6.1)	0.751	10 (4.8)	0.943
Have been treated for STH	122 (61.6)	0.519	19 (10.0)	0,393	16 (8.1)	0.008	3 (1.5)	0.679	12 (6.1)	0.393	161 (77.0)	0.763
Usually have contact with animals (dog, cat, monkey)	45 (22.7)	0.007	5 (2.6)	0.478	8 (4.1)	0.539	1 (0.5)	0.931	3 (1.5)	0.443	2 (1.0)	0.209
Knowledge of malaria	9 (4.5)	0.629	2 (1.1)	0.612	0	-	1 (0.5)	0.088	0	-	9 (4.3)	0.118
They slept last night under bednets	124 (62.6)	0.823	20 (10.5)	0.709	23 (11.7)	0.210	4 (2.0)	0.365	14 (7.1)	0.635	12 (5.7)	0.799
Anaemia												
Mild	33 (16.7)	0.160	7 (3.7)	-	6 (3.0)	0.194	0	-	6 (3.0)	0.104	2 (1.0)	-
Moderate	66 (33.3)	-	13 (6.8)	-	15 (7.6)	-	2 (1.0)	-	3 (1.5)	-	10 (4.8)	-
Severe	6 (3.0)	-	0	-	1 (0.5)	-	1 (0.5)	-	0	-	0	-

STH, soil-transmitted helminths

households, or to use only family or community latrines in order to leave the main places where they become infected. We found significant associations of *Schistosoma haematobium* with school-age children (p=0.013), drinking water (p=0.001), knowledge, blood in urine and contact with animals (p=0.001) and *A. lumbricoides* associated with girls (p=0.027).

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Table 5. Effect of the intervention on the occurrence of the parasites in children completing the study

Indicators	*Schistosoma haematobium* (N=67)	STH (N=67)			*H. nana* (N=67)	*P. falciparum* (N=77)
		A. lumbricoides	*T. trichiura*	Hookworms		
Baseline pretreatment (0)						
No. of children infected	47	4	6	2	9	7
Prevalence: % (95% CI)	70.1 (57.7 to 80.7)	6.0 (1.7 to 14.6)	9.0 (3.4 to 18.5)	3.0 (0.4 to 10.4)	13.4 (6.2 to 23.6)	9.1 (3.7 to 17.8)
Infection level: % (95% CI)						
Light	7.5 (2.5 to 16.6)	1.5 (0.0 to 8.0)	9.0 (3.4 to 18.5)	3.0 (0.4 to 10.4)	13.2 (6.2 to 23.6)	-
Moderate	-	4.5 (0.9 to 12.5)	0	0	0	-
Heavy	62.7 (41.3 to 87.5)	0	0	0	0	-
GM eggs count (95% CI)	498 (312 to 795)	4413 (11 to 13145)	168 (60 to 366)	55 (48 to 61)	93 (72 to 117)	-
1 mo post-treatment (1)						
No. of children infected	36	2	4	1	1	8
Prevalence: % (95% CI)	53.7 (41.1 to 66.0)	3.0 (0.4 to 10.4)	6.0 (1.7 to 14.6)	1.5 (0.0 to 8.0)	1.5 (0.0 to 7.9)	10.4 (4.6 to 19.4)
Infection level: % (95% CI)						
Light	19.4 (10.8 to 30.9)	3.0 (0.4 to 10.4)	6.0 (1.7 to 14.6)	1.5 (0.0 to 8.0)	1.5 (0 to 7.9)	-
Moderate	-	0	0	0	0	-
Heavy	34.3 (23.2 to 46.5)	0	0	0	0	-
GM eggs count (95% CI)	65 (50 to 84)	51 (0 to 134)	269 (120 to 437)	24[3]	24[3]	-
PRR (0→1): % (p-value)[1]	23.5 (0.013)	50.0 (0.688)	33.3 (0.727)	50.0 (1.000)	88.6 (0.021)	−14.3 (1.000)
ERR (0→1): % (p-value)[2]	86.9 (<0.001)	98.8 (0.356)	60 (0.626)	-	-	-
New cases in %	6.0 (4/67)	3.0 (2/67)	4.5 (3/67)	1.5 (1/67)	1.5 (1/67)	3.9 (3/77)
6 mo post-treatment (6)						
No. of children infected	51	3	2	0	8	2
Prevalence: % (95% CI)	76.1 (64.1 to 85.7)	4.5 (0.9 to 12.5)	3.0 (0.4 to 10.4)	0.0 (0.0 to 5.4)	11.9 (5.2 to 21.9)	2.6 (0.3 to 9.1)
Infection level: % (95% CI)						
Light	11.9 (5.3 to 22.2)	4.5 (0.9 to 12.5)	1.5 (0.0 to 8.0)	0	11.8 (5.2 to 21.9)	-
Moderate		0	1.5 (0.0 to 8.0)	0	0	-
Heavy	64.2 (42.5 to 89.2)	0	0	0	0	-
GM eggs count (95% CI)	252 (162 to 391)	477 (24 to 1320)	344 (192 to 509)	0[3]	115 (86 to 150)	-
PRR (1→6): % (p-value)[1]	−41.7 (0.003)	−50.0 (1.000)	50.0 (0.625)	100	−686.7 (0.039)	75.0 (0.109)
PRR (0→6): % (p-value)[1]	−8.6 (0.424)	25.0 (1.000)	66.7 (0.289)	100	10.6 (1.000)	71.4 (0.180)
ERR (1→6): % (p-value)[2]	−287.2 (<0.001)	−835.3 (0.357)	28.0 (0.626)	-	-	-
ERR (0→6): % (p-value)[2]	49.4 (0.986)	89.2 (0.411)	−104.8	-	−23.7 (0,210)	-
Reinfection in %	85.7 (12/14)	33.30 (1/3)	0.0 (0/5)	0.0 (0/2)	0.0 (0/9)	40.0 (2/5)

ERR, eggs reduction rate; GM, geometric mean of eggs count per 10 ml urine or 1 g of faeces in positive cases; PRR, prevalence reduction rate: (0→1) baseline to 1 mo, (1→6) 1 to 6 mo and (0→6) baseline to 6 mo after treatment.
[1]McNemar test; [2]paired sample t test; [3]number of eggs.

In addition, 1 mo after the integrated drug administration, we observed a reduction in the prevalence of *A. lumbricoides*, *T. trichiura*, hookworms and *H. nana* (only statistically significant for *H. nana*). Despite not being statistically significant, the intensity of infections in those children remaining infected with *A. lumbricoides* and *T. trichiura* also decreased and moderate infections of *A. lumbricoides* were cleared, results that are concordant with other studies showing that albendazole successfully lowers the intensity of those infections.[21,22] However, 3.0, 4.5, 1.5 and 1.5% of new *A. lumbricoides*, *T. trichiura*, hookworms and *H. nana* infections were observed, respectively, suggesting possible contact between children and contaminated environments, food and/or water between evaluation time points. This hypothesis is reinforced by the reinfection rates observed for *A. lumbricoides* and its consequent prevalence increase 6 mo after treatment. Similarly, and despite no reinfection with *H. nana* being observed at the end of the study, a significant prevalence increase was also verified for hymenolepiasis.

In the present study, it appears that both praziquantel and albendazole presented some apparent failure or low effectiveness in the treatment of the studied infections. A change in the prescription pattern of praziquantel should also be considered, as it was suggested that a single treatment regimen of praziquantel may be unable to clear immature stages of *Schistosoma haematobium*.[21–23] Further investigation discriminating between reinfections and recurrent infections would help clarify these matters. Additionally, it must also be considered that a long prepatent period (approximately 6–8 wk) was reported for *Schistosoma haematobium*, in which eggs may continue to be released from tissues, even after the clearance of the worms.[24] This could lead to the overestimation of positive cases and thus influence the results presented here.

Further studies are recommended in the case of a modest reduction in helminth infection observed after taking albendazole drugs.[25–27]

Regarding *P. falciparum*, the prevalence increased from baseline to first follow-up, with 3.9% of new cases, but decreased after the second follow-up, where 40% of reinfections were observed. This prevalence variation is certainly associated with seasonality of malaria risk since the first follow-up was at the peak of the risk season for malaria. The treatment of malaria was performed in this study for ethical reasons and the evolution of its prevalence was subject to several biases, such as seasonality. Moreover, the distribution of bednet in the baseline could be a potential confounder when evaluating the effect of the intervention.

Prevalence of anaemia at the baseline, among the 67 children who completed the study, was very high (82.0%). This prevalence reduced, but not significantly. All cases of anaemia were infected with *Schistosoma haematobium* and this infection was the only one found in cases of severe anaemia. In fact, *A. lumbricoide*, *H. nana* and *P. falciparum* were not found in any severe case. We attributed the strong influence of *Schistosoma haematobium* to the occurrence or severity of anaemia, as described in other studies, but other causes of anaemia were not investigated in this study.[3]

Participants in this study reported transient cases of medication side effects that usually occur with this type of intervention.[28]

A limitation of this study is the absence of some parasitological examinations (that should be carried out on at least three urine and faeces samples collected on different days), which would allow a better estimation of the intensity of the infection, also enabling the variability described in the excretion of eggs during the day to be overcome. On the other hand, recurrent infections and reinfections weren't discriminated here.

In Angola, historical annual deworming with albendazole was performed in schools and reported cases of haematuria were treated in health units. Consequently, a low therapeutic coverage was reported regarding the goals recommended by WHO for the Africa region.[29] The strategic plan for neglected tropical diseases 2012–2015 included in the new National Sanitary Development Plan already foresees the adoption of integrated preventive chemotherapy with distribution of praziquantel, albendazole and ivermectin in campaigns of deworming, to reach a therapeutic coverage of 80–100% in school-age children and 70–95% in communities between 2017–2021, in line with WHO recommendations.[30] Thus, we believe that this study highlights some key aspects that should be considered in order to maximise the effectiveness of future approaches in the Angolan context, such as the strategy and monitoring of mass drug administration, environmental and health education for behavioural change, provision of drinking water for hygiene and sanitation in communities.

Longitudinal studies have reported many losses in these settings, but we were able to show that mass drug administration for control of schistosomiasis and STH presents low effectiveness, that reinfections occur rapidly and that stand alone anthelmintic therapy is not a sustainable choice. In the context of our country, drug effectiveness should be studied for its suitability.

Authors' contributions: ML, SN, MB, HB and PS conceived and designed the study. CM, ML, MB performed the experiments. ML, SM, CM, MB and CF analyse the data and wrote the paper. All author read and approved the final manuscript.

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References

1 Hotez PJ, Brindley PJ, Bethony JM, et al. Helminth infections: the great neglected tropical diseases. J Clin Invest. 2008;118(4):1311–21.

2 Herricks JR, Hotez PJ, Wanga V, et al. The global burden of disease study 2013: What does it mean for the NTDs? PLoS Negl Trop Dis. 2017;11(8):e0005424.

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3 Sousa-Figueiredo JC, Gamboa D, Pedro JM, et al. Epidemiology of malaria, schistosomiasis, geohelminths, anemia and malnutrition in the context of a demographic surveillance system in northern Angola. PLoS One. 2012;7(4):e33189.

4 Magalhães RJS, Langa A, Sousa-Figueiredo JC, et al. Finding malaria hot-spots in northern Angola: the role of individual, household and environmental factors within a meso-endemic area. Malar J. 2012; 11(1):385.

5 Schüle SA, Clowes P, Kroidl I, et al. Ascaris lumbricoides infection and its relation to environmental factors in the Mbeya region of Tanzania, a cross-sectional, population-based study. PLoS One. 2014;9(3):e92032.

6 Soares Magalhães RJ, Langa A, Pedro JM, et al. Role of malnutrition and parasite infections in the spatial variation in children's anaemia risk in northern Angola. Geospatial Health. 2013;7(2):341–54.

7 Dickson R, Awasthi S, Williamson P, et al. Effects of treatment for intestinal helminth infection on growth and cognitive performance in children: systematic review of randomised trials. BMJ. 2000;320 (7251):1697–701.

8 Gyorkos TW, Gilbert NL, Larocque R, et al. Re-visiting Trichuris trichiura intensity thresholds based on anemia during pregnancy. PLoS Negl Trop Dis. 2012;6(9):e1783.

9 Lewis FA, Tucker MS. Schistosomiasis. New York, NY: Springer; 2014, 47–75.

10 João Costa M, Rosário E, Langa A, et al. Setting up a demographic surveillance system in northern Angola. Afr Popul Stud. 2012;26(2): 133–146.

11 World Health Organization. Manual of basic techniques for a health laboratory, 2nd ed. Geneva, Switzerland: World Health Organization; 2003.

12 Mirante C, Clemente I, Zambu G, et al. Comparing concentration methods: parasitrap® versus Kato-Katz for studying the prevalence of Helminths in Bengo province, Angola. Afr Health Sci. 2016;16(3): 698–703.

13 Moonen B, Cohen JM, Snow RW, et al. Operational strategies to achieve and maintain malaria elimination. Lancet. 2010;376(9752): 1592–1603.

14 Chen I, Clarke SE, Gosling R, et al. 'Asymptomatic' malaria: a chronic and debilitating infection that should be treated. PLoS Med. 2016;13 (1):e1001942.

15 World Health Organization. Basic laboratory methods in medical parasitology. Geneva, Switzerland: World Health Organization; 1991.

16 Ahmed AM, Abbas H, Mansour FA, et al. Schistosoma haematobium infections among schoolchildren in central Sudan one year after treatment with praziquantel. Parasit Vectors. 2012;5(1):108.

17 Montresor A, Crompton DWT, Hall A, et al. Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level: a guide for managers of control. WHO/CTD/SIP/98.1 programmes. 1998. http://apps.who.int/iris/handle/10665/63821 (Accessed January 12 2019).

18 Saathoff E, Olsen A, Kvalsvig JD, et al. Patterns of geohelminth infection, impact of albendazole treatment and re-infection after treatment in schoolchildren from rural KwaZulu-Natal/South-Africa. BMC Infect Dis. 2004;4(1):27.

19 Lee Y-H, Jeong HG, Kong WH, et al. Reduction of urogenital schistosomiasis with an integrated control project in Sudan. PLoS Negl Trop Dis. 2015;9(1):e3423.

20 Sady H, Al-Mekhlafi HM, Atroosh WM, et al. Knowledge, attitude, and practices towards schistosomiasis among rural population in Yemen. Parasit Vectors. 2015;8(1):436.

21 Tchuem Tchuenté L-A, Momo SC, Stothard JR, et al. Efficacy of praziquantel and reinfection patterns in single and mixed infection foci for intestinal and urogenital schistosomiasis in Cameroon. Acta Trop. 2013;128(2):275–83.

22 Tchuenté L-AT, Shaw DJ, Polla L, et al. Efficacy of praziquantel against Schistosoma haematobium infection in children. Am J Trop Med Hyg. 2004;71(6):778–82.

23 Botros S, Pica-Mattoccia L, William S, et al. Effect of praziquantel on the immature stages of Schistosoma haematobium. Int J Parasitol. 2005;35(13):1453–7.

24 Loker ES. A comparative study of the life-histories of mammalian schistosomes. Parasitology. 1983;87(Pt 2):343–69.

25 Newton S, Terryah S, Boakye D, et al. Hookworm infection among school age children in Kintampo north municipality, Ghana: nutritional risk factors and response to albendazole treatment. Am J Trop Med Hyg. 2013;89(3):540–8.

26 Prichard RK, Basáñez M-G, Boatin BA, et al. A research agenda for helminth diseases of humans: intervention for control and elimination. PLoS Negl Trop Dis. 2012;6(4):e1549.

27 Vercruysse J, Albonico M, Behnke JM, et al. Is anthelmintic resistance a concern for the control of human soil-transmitted helminths? Int J Parasitol Drugs Drug Resist. 2011;1(1):14–27.

28 Samuel F, Demsew A, Alem Y, et al. Soil transmitted helminthiasis and associated risk factors among elementary school children in Ambo town, western Ethiopia. BMC Public Health. 2017;17(1):791.

29 World Health Organization. WHO country report 2010 Angola. 2010. https://www.who.int/countries/ago/en/ (Accessed January 12 2019).

30 Utzinger J, Brattig NW, Kristensen TK. Schistosomiasis research in Africa: how the CONTRAST alliance made it happen. Acta Trop. 2013; 128(2):182–95.

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