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Comparison of POC-CCA with Kato-Katz in Diagnosing *Schistosoma mansoni* Infection in a Pediatric L-Praziquantel Clinical Trial

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Introduction: Traditionally *Schistosoma mansoni* infection is diagnosed by the Kato-Katz method. Thick smears from each stool sample are prepared on slides and eggs are counted microscopically. Commercially available point-of-care circulating cathodic antigen (POC-CCA) cassette tests detect schistosomiasis antigens from urine samples in 20 minutes. POC-CCA results are qualitative or semi-quantitative: signal intensity is an indicator of the amount of worm antigens in the sample. Both methods were used in a phase II trial investigating the efficacy and safety of new pediatric formulations of praziquantel (PZQ) among children ≤6 years (NCT02806232). This secondary analysis evaluated the consistency of results between the Kato-Katz and POC-CCA methods.

Methods: POC-CCA was used to pre-screen for *S. mansoni* infection. Children with positive results were tested by the Kato-Katz method, and those with positive Kato-Katz results (>1 egg/1 occurrence) were enrolled. Participants (N=444) were treated with different formulations and doses of PZQ. POC-CCA and Kato-Katz were performed at 2–3 weeks after treatment to evaluate drug efficacy. Cure rate (CR) was defined as the proportion of participants with a negative result per POC-CCA, or no eggs in the stool samples per Kato-Katz. Kappa statistic was used to assess the agreement on cure status, and Spearman correlation between POC-CCA positivity and Kato-Katz egg counts was evaluated. Sensitivity and specificity of POC-CCA were calculated using Kato-Katz as a reference standard.

Results: CR per POC-CCA, measured 2–3 weeks after treatment, was 52% [95% confidence interval (CI): 48%, 57%] across all treatment arms except in infants aged 3–12 months. CR per Kato-Katz was 83% (95% CI: 79%, 87%). Kappa statistic was 0.16 (95% CI: 0.09, 0.23), indicating that the agreement was slightly better than by chance.

Relative to Kato-Katz, POC-CCA's sensitivity to detect infection was 70% and specificity was 57%. Spearman correlation coefficient between POC-CCA positivity and Kato-Katz egg counts was 0.26 (95% CI: 0.17, 0.34).

Conclusion: POC-CCA is sensitive and rapid for diagnosing *S. mansoni* infection, but its performance and consistency with Kato-Katz requires further investigation among young children.

Keywords: schistosomiasis, *Schistosoma mansoni*, point-of-care circulating cathodic antigen, Kato-Katz, praziquantel, pediatric, clinical trial

INTRODUCTION

Schistosomiasis is a neglected tropical disease affecting communities with limited access to safe water and adequate sanitation provision (1–3). The disease is caused by a parasitic worm of the genus *Schistosoma*, of which there are five species responsible for the major forms of disease (intestinal and urogenital schistosomiasis). The parasite infests water sources and transmission to humans occurs through the skin following routine contact with unsafe, infested water (3). It has been widely recognized that both pre-school-age and school-age children are at significant risk of schistosomiasis with at least 25 million infected, often with serious consequences to health (4, 5). The health impact includes anemia as well as poor growth, nutrition, and cognition in affected children (5). Recent studies suggest that, in highly endemic areas, children under 6 years of age, including infants, can carry a medium to heavy infection burden and that infection burden increases with age (6–8). The World Health Organization (WHO)-recommended treatment for schistosomiasis is praziquantel (PZQ) at a single oral dose of 40mg/kg body weight. This agent is effective in killing adult worms and indirectly triggers an immune response as the contents of the worms are released (1).

Traditionally *Schistosoma mansoni* infection is diagnosed by the Kato-Katz method according to WHO recommendations: two stool samples are collected from a person over 3 to 5 days and four Kato-Katz thick smears in total are read microscopically for egg counts (9, 10). However, the Kato-Katz test is not sufficiently sensitive to diagnose low egg counts, and therefore may over-estimate drug efficacy in clinical trials, especially in children with low infection intensity (11).

The Point-of-care circulating cathodic antigen (POC-CCA) cassette test, a commercially available tool, detects *Schistosoma* circulating antigens from adult worms that are ultimately secreted into urine. Test results can be observed on strips in about 20 minutes. The commercial provider claims that the kit can differentiate active from non-active infection (https://www.rapid-diagnostics.com/). POC-CCA positivity in urine samples may therefore be a more appropriate diagnostic tool in very young individuals who often have a low worm burden (12–14). Indeed, several studies have indicated that the POC-CCA test is a promising method for the diagnosis of intestinal schistosomiasis in pre-school-age and school-age children given its sensitivity, promptness of results and convenience (15–17).

POC-CCA and Kato-Katz have been compared in several surveillance studies, with POC-CCA consistently showing higher sensitivity. In a surveillance program in Tanzania among 404 children aged 9 to 12 years, 66.1% *vs* 28.7% of participants were positive for *S. mansoni* by POC-CCA and Kato-Katz, respectively (18). Similar results were observed in a prevalence study in Chad, although the prevalence was much lower: 6.9% by POC-CCA *vs* only 0.5% by the Kato-Katz method (19). Another study assessing the rate of *S. mansoni* infection in 979 HIV-positive adults in Tanzania reported positivity rates of 60.5% *vs* 47.3% by POC-CCA and Kato-Katz, respectively (20). Finally, a large study with more than 4000 children from areas endemic for schistosomiasis across five countries showed an overall prevalence of 55.2% by a single POC-CCA assay *vs* 38.8% by three Kato-Katz smears. The trend was similar in each individual country apart from Côte d'Ivoire, where the prevalence was 45.5% by a single POC-CCA assay *vs* 57.7% by three Kato-Katz smears (21).

Both Kato-Katz and POC-CCA methods were used in a phase II clinical trial investigating the efficacy and safety of new oral disintegrating tablet (ODT) formulations of PZQ among children aged ≤6 years in a single center in Côte d'Ivoire (NCT02806232) (ClinicalTrials.gov 22, 23). The trial assessed a racemate (rac-PZQ) formulation containing a mixture of R-(–)-Praziquantel (levo-PZQ or L-PZQ) and S-(+)-Praziquantel (dextro-PZQ or D-PZQ) in a 1:1 ratio, and the other one containing only L-PZQ, which is devoid of the biologically inactive D-PZQ enantiomer. It was concluded that both novel formulations were highly efficacious in pre-school-age children and L-PZQ ODT was efficacious in infants aged ≤2 years; no new safety concerns were identified (23).

Here, we present the results of the secondary analysis of this phase II clinical trial, evaluating the sensitivity and specificity of the POC-CCA assay and its concordance with the Kato-Katz method used to determine infection status at baseline before any treatment and over time after treatment.

METHODS

Full details of the conduct of the phase II trial (NCT02806232) are reported in the primary analysis (23). In brief, it was a two-part, open-label, dose-finding study of the efficacy and safety of PZQ formulations in children and infants infected with

S. mansoni in Côte d'Ivoire. In Part 1, children aged 2–6 years were randomized to receive commercially available rac-PZQ at 3x20 mg/kg (treatment arm 1, n=60) or 40 mg/kg (treatment arm 2, n=60); rac-PZQ ODT at 40 mg/kg (treatment arm 3, n=60) or 60 mg/kg (treatment arm 4, n=60); or L-PZQ ODT at 30 mg/kg (treatment arm 5, n=60), 45 mg/kg (treatment arm 6, n=60) or 60 mg/kg (treatment arm 7, n=60). The formulation and dose identified as optimal in terms of safety and efficacy in Part 1, i.e. 50 mg/kg L-PZQ ODT, was used in Part 2 for infants aged 13–24 months (treatment arm 8, n=20) and 3–12 months (treatment arm 9, n=4). The primary endpoint of the phase II trial was cure rate (CR) based on egg counts measured using the Kato-Katz method. POC-CCA urine cassette test was used as a pre-screening tool and as a secondary endpoint for CR at follow-up. No statistical comparison was planned between different treatments/formulations of PZQ. Rather, as accepted by the European Medicines Agency, the sample size for each treatment arm in Part 1 was determined to provide reasonable precision for the estimated CR.

The outcome of the POC-CCA test used in this trial was qualitative with four visual levels: negative, positive (+), positive (++), or positive (+++) (in positive results, more plusses were assigned to higher signal intensity and were used to indicate higher amounts of antigens in the sample). Details for this product can be found on the manufacturer's website: https://www.rapid-diagnostics.com/products.html. A semi-quantitative scoring system using a portable reader has since been developed and is gaining popularity. The device grades the test result in terms of a score (G-score) ranging from 1 to 10, with higher values indicating heavier infection (24). In our trial, we used the 4-level visual scores because the G-score system was not available when the clinical trial protocol was developed in 2017.

We defined the day when the treatment was administered as Day 1, and last measurement prior to study treatment was defined as baseline. Children from villages in endemic area were pre-screened (Day -28 to -1) for *S. mansoni* by POC-CCA, followed by Kato-Katz method, and for *S. haematobium* by the urine filtration method. Participants were included if they had positive results for both POC-CCA and Kato-Katz and a negative result for *S. haematobium* (i.e. participants with mixed infection were excluded).

Kato-Katz was performed at baseline and 2–3 weeks after treatment follow-up (Day 14–21; **Figure 1**). At each time point, two stool samples were collected from each participant on different days within a maximum of 5 days. Three Kato-Katz thick smears (41.7 mg) were prepared from each stool sample (for a total of six smears), and read under a microscope following the WHO Kato-Katz manual (25). Baseline infection intensity was defined as either light (1–99 eggs/gram) or moderate/heavy (≥100 eggs/gram). The participant was defined to be cured if egg count at the follow-up visit was 0.

Urine samples for POC-CCA testing were collected at follow-up visits to understand how worm burden changes over time after treatment, and to evaluate the sensitivity and specificity of POC-CCA as compared with Kato-Katz (**Figure 1**). Trace results were recorded as positive + infections for treatment arms 1 to 7; however, traces were considered negative when pre-screening for participants 3 months to 2 years old (arms 8 and 9) after observing that the majority of traces have negative results for Kato-Katz in this age group.

POC-CCA results were summarized by visits, age group and infection intensity at baseline. The analysis included the modified intent-to-treat population (mITT), defined as all participants who had baseline disease and did not use antimalarial medication during the study period (23). CR was defined as the proportion of participants with a negative result per POC-CCA or no eggs in stool sample per Kato-Katz at Day 14–21 of follow-up. Kappa statistic was calculated to assess the agreement on cure status between the two methods, overall and by infection intensity at baseline.

Spearman correlation between POC-CCA positivity and egg counts by Kato-Katz method at Day 14–21 of follow-up was also calculated. Sensitivity and specificity of POC-CCA were evaluated using Kato-Katz as the reference standard, though with reservations that the latter might not be perfectly sensitive especially among young children. These statistics were evaluated for the overall mITT population and each of the baseline infection intensity subgroups.

The trial was conducted in compliance with Good Clinical Practice and the Declaration of Helsinki. Written informed consent was obtained from one of the participant's parents, legal representatives, or guardians prior to any trial-related procedure. In addition, oral assent was recorded for children aged >3 years, if they were capable of doing so. The trial protocol and associated documents were approved by the Independent Ethics Committees/Institutional Review Boards in Switzerland and in Côte d'Ivoire.

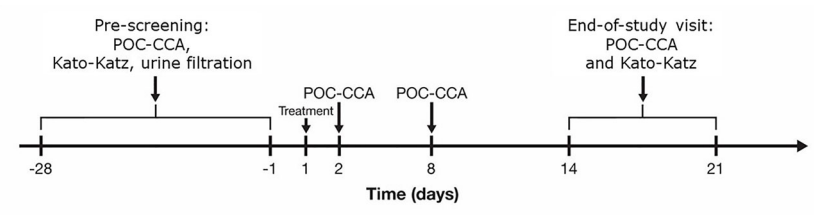

FIGURE 1 | Schedule of diagnostic assessments of infection burden. POC-CCA, point-of-care circulating cathodic antigen.

RESULTS

A total of 7906 subjects were pre-screened using the *S. mansoni* POC-CCA test; 710 children tested positive for *S. mansoni* by POC-CCA and Kato-Katz method, and negative for *S. haematobium* by the urine filtration method. Of these, N=444 met the inclusion/exclusion criteria and were enrolled and treated (23). The mITT population consisted of n=421 participants including n=10 participants who did not have POC-CCA results from the Day 14–21 follow-up visit and were imputed using last observation carried forward (LOCF) approach. Baseline characteristics have been published elsewhere (23). Briefly, all participants were Black, aged 0.5 to 6.9 years, 46% were female, and 62% had light infection.

In general, POC-CCA results showed a trend towards negativity over time. This trend was observed in all treatment arms, except treatment arm 9 which was composed of four infants <1 year of age. In most treatment arms, immediately on the day after treatment some participants become negative (~10%) or went from positive (+++) to positive (++) or positive (+) (**Figure 2**). By Day 8, about 40% of participants became negative by POC-CCA; by Day 14–21, over 50% became negative by POC-CCA. The trend over time was similar among the children with light infection at baseline (n=259) and those with moderate/heavy infection (n=162), but it is noticeable that at each visit there were more negative POC-CCA results for the light infection subgroup than for the moderate/heavy infection subgroup. For example, at the last follow-up visit the negative rates were 61.8% and 37.7% for light *vs* moderate/heavy infection, respectively.

The CR at the last follow-up visit (Day 14–21) per POC-CCA, ranging from 0% to 66.7%, was substantially lower than the CR based on Kato-Katz method in every treatment arm, ranging from 74.1% to 100% (**Table 1**, **Figure 2**). These results indicate that POC-CCA may be more sensitive in detecting the disease. No statistical comparison was performed, but the CRs per Kato-

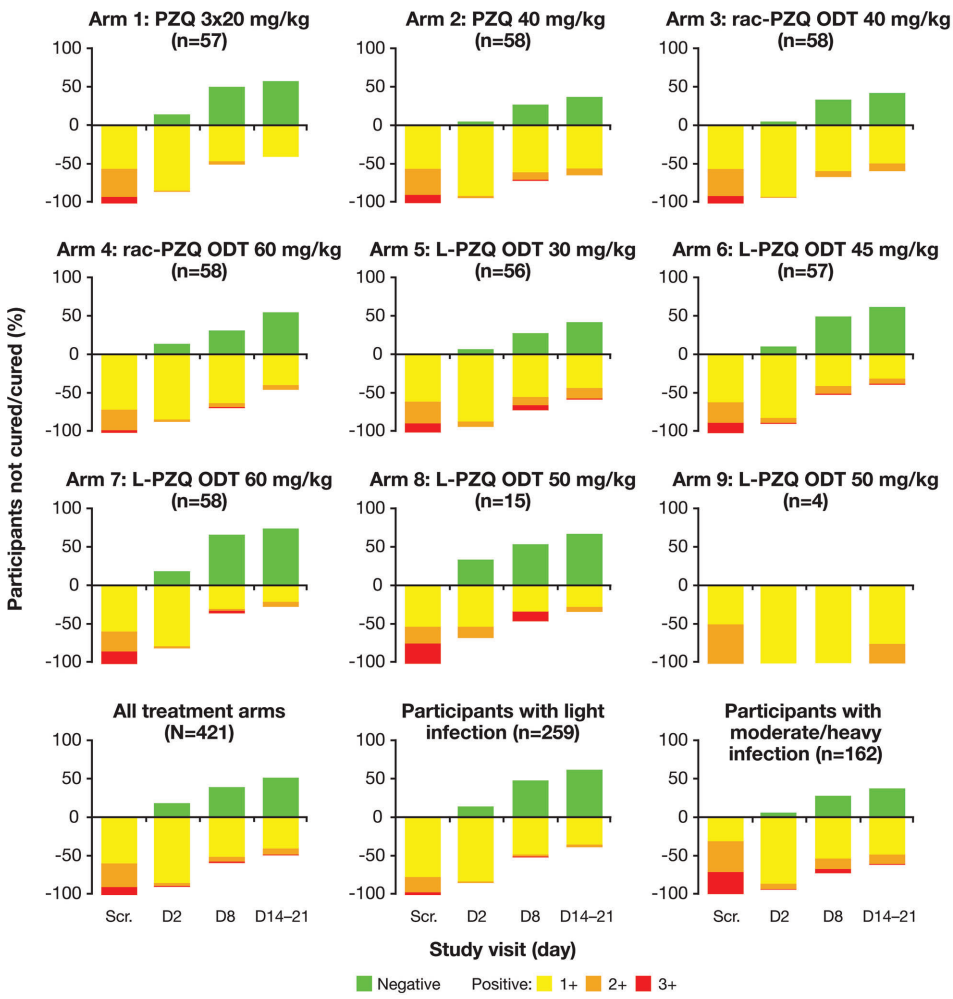

FIGURE 2 | POC-CCA results over time by treatment arm and by infection intensity. Participants' age: Treatment arms 1–7 (2–6 years); Treatment arm 8 (13–24 months); Treatment arm 9 (3–12 months). D, day; ODT, oral disintegrating tablet; POC-CCA, point-of-care circulating cathodic antigen; PZQ, praziquantel; rac, racemate; Scr., screening.

TABLE 1 | Day 14–21 follow-up cure rates [% (95% confidence interval)] per Kato-Katz and POC-CCA.

Assessment	Arm 1: PZQ 3x20 mg/kg (n = 57)	Arm 2: PZQ 40 mg/kg (n = 58)	Arm 3: rac-PZQ ODT 40 mg/kg (n = 58)	Arm 4: rac-PZQ ODT 60 mg/kg (n = 58)	Arm 5: L-PZQ ODT 30 mg/kg (n = 56)	Arm 6: L-PZQ ODT 45 mg/kg (n = 57)	Arm 7: L-PZQ ODT 60 mg/kg (n = 58)	Arm 8: L-PZQ ODT 50 mg/kg (n = 15)	Arm 9: L-PZQ ODT 50 mg/kg (n = 4)
Kato-Katz	89.5 (78.5, 96.0)	74.1 (61.0, 84.7)	81.0 (68.6, 84.7)	79.3 (66.6, 88.8)	78.6 (65.6, 88.4)	86.0 (74.2, 93.7)	89.7 (78.8, 96.1)	93.3 (68.1, 99.8)	100 (39.8, 100)
POC-CCA	57.9 (44.1, 70.9)	36.2 (24.0, 49.9)	41.4 (28.6, 55.1)	55.2 (41.5, 68.3)	42.9 (29.7, 56.8)	61.4 (47.6, 74.0)	72.4 (59.1, 83.3)	66.7 (38.4, 88.2)	0 (0, 60.2)

Participants' age: Treatment arms 1–7 (2–6 years); Treatment arm 8 (13–24 months); Treatment arm 9 (3–12 months).
ODT, oral dispersible tablet; POC-CCA, point-of-care circulating cathodic antigen; PZQ, praziquantel.

Katz were similar across different treatment arms. In contrast, the CR per POC-CCA varied across treatment arms: none of the four infants aged <1 year (treatment arm 9) became negative by POC-CCA on Day 14–21, but all of them were egg-free by the Kato-Katz method (**Table 1**, **Figure 3**). On the other hand, out of 15 participants aged 13–24 months, 10 became negative by POC-CCA, which is close to the treatment arms treated with ≥45 mg/kg L-PZQ ODT.

In the analysis of agreement between POC-CCA and Kato-Katz assessment at Day 14–21of follow-up, the Kappa coefficient was 0.16 (95% CI: 0.09, 0.23), suggesting that the agreement was only slightly better than what would be expected by chance (**Table 2**) (26). The agreement between POC-CCA and Kato-Katz was better in those with moderate/heavy infection than in those with light infection at baseline: Kappa coefficients were 0.23 (95% CI: 0.12, 0.33) and 0.04 (95% CI: -0.05, 0.14), respectively. Relative to Kato-Katz, sensitivity of POC-CCA to detect infection was 70% and specificity for cure was 57%. The most frequent discordant situation was POC-CCA-positive but "cured" per Kato-Katz (150 out of 421, 36%). In contrast, only 21 (5%) had negative POC-CCA but visible eggs in Kato-Katz. Among children with moderate/heavy infection at baseline, the sensitivity and specificity at Day 14–21 were 86% and 46%; among those with light infection at baseline, the sensitivity and specificity at Day 14–21 were 46% and 63%. The Spearman correlation coefficients between POC-CCA positivity and Kato-Katz egg counts were 0.52 (95% CI: 0.45, 0.59) for the overall mITT population, 0.50 (95% CI:0.37, 0.60) for moderate/heavy infection, and 0.17 (95% CI: 0.05, 0.29) for light infection at baseline. The overall Spearman correlation was 0.26 (95% CI: 0.17, 0.34) at Day 14–21 of follow-up.

DISCUSSION

Both Kato-Katz and POC-CCA methods have advantages and limitations. While POC-CCA may be particularly suitable for infection monitoring, Kato-Katz provides an egg count that allows for calculation of the egg reduction rate and is a widely used measure of treatment efficacy.

Current consensus is that POC-CCA is more sensitive than the Kato-Katz method in diagnosing *S. mansoni* infection, and a number of large studies recommend POC-CCA as an easy, rapid test with high sensitivity (12, 15, 16). The sensitivity of Kato-Katz varies with the number of stool samples and the number of thick smears per stool sample that are examined under the microscope. A recently published model of fecal egg-count data estimated the difference in sensitivity of the Kato-Katz method to be about 30% depending on whether 1 or 2 samples per patient were used for quantification (sensitivity was 50% and 80%, respectively). These results were applicable to patients with moderate infection (100–399 eggs/gram stool) (27). Another study showed that the proportion of positive samples analyzed by the Kato-Katz method increased from 11% to 19% for 4 *vs* 24 smears, respectively (28).

There are other diagnosis methods for *S. mansoni*, such as the Point-of-care circulating anodic antigen (POC-CAA) test and molecular approaches including PCR, real-time PCR, TaqMan®

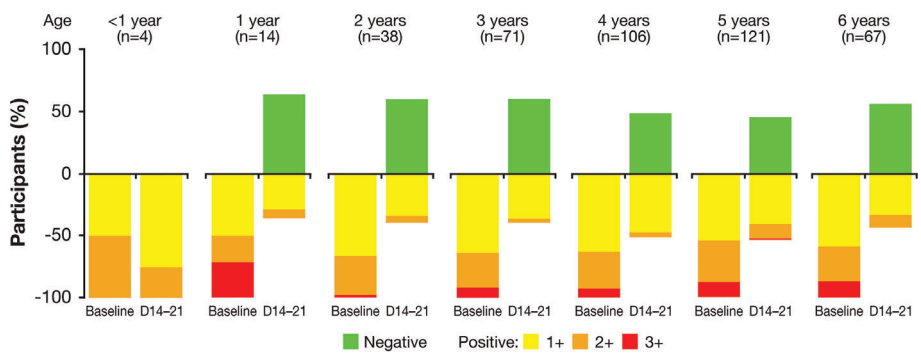

FIGURE 3 | POC-CCA results by age group, from baseline to 2–3 weeks after treatment. D, day; POC-CCA, point-of-care circulating cathodic antigen.

TABLE 2 | Sensitivity and specificity of POC-CCA, using Kato-Katz as standard, at 2–3 weeks after treatment.

	POC-CCA result	Kato-Katz result	
		Not cured	Cured
	Positive (+++)	2	0
	Positive (++)	15	16
	Positive (+)	33	134
	Negative	21	200
	Total	71	350
Cure rate	52.5%	83.1%	
Specificity	57.1%	Ref	
Sensitivity	70.4%	Ref	
Kappa coefficient	0.16 (95% CI: 0.09, 0.23)		
Spearman correlation coefficient	0.26 (95% CI: 0.17, 0.34)		

CI, confidence interval; POC-CCA, point-of-care circulating cathodic antigen.

fecal assays, SmMITLAMP (a LAMP-based method to detect *S. mansoni* DNA), etc. No conclusive results were obtained in various comparison studies (29–33), hence no consensus on a gold standard for the diagnosis of *S. mansoni* has been reached. One of the limitations of current molecular approaches is that they are based on the DNA of parasite eggs present in the stool. Detection is therefore linked to a minimum threshold and is subject to variations over time. Unlike egg DNA-based assays, POC-CAA and POC-CCA detect the presence of the parasite even in the absence of eggs (e.g. isolated males). In our trial, the diagnostic methods to measure disease control and cure in pre-school-age children were chosen based on previous experience in other age groups and programs, i.e. the Kato-Katz method and POC-CCA as a promising alternative method. The POC-CAA testing kit was not commercially available when the trial protocol was developed.

Due to the lack of a gold standard, the sensitivity and specificity of the POC-CCA assay were assessed in our trial relative to the Kato-Katz method (six smears from two samples), but with reservations. Barenbold et al. used a model with a latent variable to estimate the sensitivity and specificity of POC-CCA, avoiding the use of a gold standard; in their study, POC-CCA was characterized by high sensitivity (>95% for moderate/heavy infection and >75% for light infection) and >95% specificity across the infection spectrum (34). In another study in a low endemic area, when the reference standard was established using 16 Kato-Katz slides from three samples (12 from the first fecal sample, two from the second and two from the third), the comparison with POC-CCA revealed a sensitivity of 65.7%, a specificity of 80.4%, and Kappa coefficient of 0.27 (slightly higher than that observed in our trial) (35). Based on these results, the specificity of POC-CCA remains to be determined. There are also concerns about the lack of consistency with results obtained using the Kato-Katz method which remains the WHO-recommended method of diagnosis (9, 10).

Furthermore, possible reasons of simultaneous negative Kato-Katz and positive POC-CCA results have been summarized previously including infection with single-sex worms, infection with infertile female worms, host's anti-fecundity immunity (17), and cross-reactivity of POC-CCA in pregnant women (19). Absolute false POC-CCA is possible but was deemed relatively rare: a study of 100 children performed in a non-endemic area in Ethiopia showed that only one POC-CCA test (1%) had a trace positive result, while none of the children was identified to have any eggs per Kato-Katz (21). POC-CCA can also detect moderate/heavy *S. haematobium* infection (https://www.rapid-diagnostics.com/); however, it is highly unlikely that urogenital infection was the cause of false positive results in this trial, as participants with *S. haematobium* infection were excluded at screening. Although the possibility of a new urogenital infection between screening and post-treatment follow-up could not be excluded, the study period of 3–5 weeks was too short to allow for worm maturation to result in moderate/heavy infection.

The consistency between POC-CCA and Kato-Katz was modest in the clinical trial presented here. At the end of the trial, overall CRs were 74.1–100% with Kato-Katz and 0–72.4% with POC-CCA. The Kappa coefficient was modest (0.16; 95% CI: 0.09, 0.23), indicating that the agreement between Kato-Katz and POC-CCA was only slightly better than just by chance. The agreement between the two methods was more pronounced in individuals with moderate/heavy baseline infection than in individuals with light infection; indeed, we obtained a higher Kappa coefficient, sensitivity, and Spearman correlation for those with moderate/heavy infection. These results are in line with previous observations that POC-CCA is more sensitive than Kato-Katz method when used in surveillance studies (18–21).

In this trial, two stool samples were collected per participant and three smears were examined from each sample. With this standard procedure, one could expect higher sensitivity of the Kato-Katz method than in studies using fewer than six smears. However, the CR (which reflects the proportion of positive samples at follow-up) per Kato-Katz was higher than per POC-CCA. The high CR (possibly reflecting lower than expected sensitivity of Kato-Katz) could be linked to the fact that ~60% of the trial participants had light infection (1–99 eggs/gram feces) at baseline. In light infection, there is a chance of missing sparse eggs in stool samples examined by the Kato-Katz method due to human error, leading to a false negative result. In contrast, the chemical reaction-based POC-CCA is able to show some positivity as long as there are antigens excreted in the urine. Our data showed that the consistency between these two tests is greater when analyzing moderate/heavy infection and aligns with WHO's recommendation to use the Kato-Katz method to diagnose moderate/heavy infection (21, 25, 27). Due to the

general low sensitivity of stool sampling and possible observer bias, Kato-Katz often fails to detect light infection. However, for most of this trial (treatment arms 1 through 7; approx. 95% of participants) POC-CCA traces were recorded as positive (+), which partially explains much lower CR of POC-CCA compared with Kato-Katz. Another possible reason for the differences is that batches of POC-CCA can have variable quality leading to inconsistent positivity thresholds (information provided through personal communication with experts) (36).

Another possible reason for the difference in CRs per Kato-Katz and POC-CCA is that worm antigens may persist in the body longer than worms and eggs. Indeed, previous studies have shown that the number of antigen-positive, egg-negative individuals decreases after treatment with PZQ (34, 37). In this trial, the participants were assessed by POC-CCA until Day 14–21, and we noted a trend towards lower POC-CCA positivity over time. It is also important to note that classifying trace results as positive may have an influence on CRs. A longer follow-up should be used in future studies to assess the clearance time of *Schistosoma* antigens and compare it with the time required for egg clearance from stool.

This trial enrolled participants aged between 3 months and 6 years, i.e. younger than the populations included in the previous prevalence studies comparing the Kato-Katz method with POC-CCA. The younger age of the participants may have contributed to the difference in detection rate; we observed that many children aged <2 years had a positive POC-CCA result of ++ or +++, but showed no eggs by Kato-Katz. Notably, an ongoing prospective cohort study is assessing the use of POC-CCA for qualitative detection of *S. japonicum* in children ≥2 years of age (38). Future studies should assess the sensitivity of POC-CCA in the detection of *S. mansoni* in infants. A validated test with high sensitivity and specificity is urgently needed in the context of elimination of schistosomiasis, as it will provide researchers with benchmark CRs.

CONCLUSION

This phase II clinical trial showed a low level of correlation between the results derived using POC-CCA *vs* Kato-Katz, especially in light infection; this difference in test sensitivity may be more pronounced among children of pre-school age, whose infection is often light. POC-CCA is a convenient tool for evaluating the burden of *S. mansoni* over time. It is sensitive, quick, and affordable and may play an important role in schistosomiasis control programs, especially in developing countries. However, partly due to a lack of a gold standard, the absolute performance of POC-CCA has not been objectively quantified.

DATA AVAILABILITY STATEMENT

Any requests for data by qualified scientific and medical researchers for legitimate research purposes will be subject to Merck KGaA's Data Sharing Policy. All requests should be submitted in writing to Merck KGaA's data sharing portal https://www.merckgroup.com/en/research/our-approach-to-research-and-development/healthcare/clinical-trials/commitment-responsible-data-sharing.html. When Merck KGaA has a co-research, co-development, or co-marketing or co-promotion agreement, or when the product has been out-licensed, the responsibility for disclosure might be dependent on the agreement between parties. Under these circumstances, Merck KGaA will endeavor to gain agreement to share data in response to requests.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Independent Ethics Committees (IECs)/ Institutional Review Boards (IRBs): Ethikkommission Nordwest- und Zentralschweiz in Switzerland, the National Committee of Ethics and Research in Ivory Coast. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

EN'G, ÖY, EK-L, AT, EH, NA, MO, and WB designed the study. EN'G, DB, EH, NA, MO, ND, and FB supervised clinical patient management and ensured quality data collection. BH and XY analyzed the data. All authors contributed to the article and approved the submitted version.

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