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Comparison of Kato-Katz thick-smear and McMaster egg counting method for the assessment of drug efficacy against soil-transmitted helminthiasis in school children in Jimma Town, Ethiopia

Teshome Bekana[a], Zeleke Mekonnen[b], Ahmed Zeynudin[b], Mio Ayana[b], Mestawet Getachew[c], Jozef Vercruysse[d] and Bruno Levecke[d,*]

[a]Department of Biomedical Science, Faculty of Public Health and Medical Science, Mettu University, Mettu, Ethiopia; [b]Department of Medical Laboratory Sciences and Pathology, College of Public Health and Medical Sciences, Jimma University, Jimma, Ethiopia; [c]Department of Pharmacy, College of Public Health and Medical Sciences, Jimma University, Jimma, Ethiopia; [d]Department of Virology, Parasitology and Immunology, Ghent University, Belgium

*Corresponding author: Tel: +32 9 264 74 04; E-mail: Bruno.Levecke@UGent.be

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Background: There is a paucity of studies that compare efficacy of drugs obtained by different diagnostic methods.

Methods: We compared the efficacy of a single oral dose albendazole (400 mg), measured as egg reduction rate, against soil-transmitted helminth infections in 210 school children (Jimma Town, Ethiopia) using both Kato-Katz thick smear and McMaster egg counting method.

Results: Our results indicate that differences in sensitivity and faecal egg counts did not imply a significant difference in egg reduction rate estimates.

Conclusion: The choice of a diagnostic method to assess drug efficacy should not be based on sensitivity and faecal egg counts only.

Keywords: Anthelminthic drug efficacy, Egg reduction rate, Ethiopia, Kato-Katz thick smear, McMaster egg counting method, Soil-transmitted helminths

Introduction

To fight soil-transmitted helminthiasis (STH) caused by *Ascaris lumbricoides*, *Trichuris trichiura* and the hookworms (*Ancylostoma duodenale* and *Necator americanus*), WHO recommends mass drug administration (MDA) programmes in which a single oral dose of albendazole (ALB) or mebendazole are administered without prior diagnosis. Currently, a worldwide upscale in MDA programmes is underway in Africa, Asia and Latin America, with the ultimate goal to eliminate STH as a public health problem. Although this unprecedented commitment is in place, it also creates the need for periodically evaluating the efficacy of drugs to detect any change in drug efficacy due to emerging anthelminthic resistance.[1] To date, there are various diagnostic methods available to assess drug efficacy, including the WHO recommended Kato-Katz thick smear,[2] and the recently introduced McMaster egg counting method.[3] However, these methods have been mainly evaluated in terms of their diagnostic performance (sensitivity and faecal egg counts [FECs]),[3] but rarely for their ability to accurately estimate drug efficacy.[4] Therefore, we compared Kato-Katz and McMaster for the assessment of drug efficacy against STH in school children in Jimma Town (Ethiopia) applying the recently published WHO guidelines on the assessment of drug efficacy.[5]

Materials and methods

Study design

The study was embedded in a larger epidemiological survey carried out in Jimma Town, Ethiopia.[6] The objectives of this epidemiological study were to evaluate a sampling strategy based on pooling of stool samples and to assess the infection intensity of STH across seasons in 14 primary schools.[6] To assess the efficacy, we applied the currently published WHO guidelines on the assessment of drug efficacy.[5] An overview of the different steps at the field can be watched at https://www.youtube.com/watch?v=hyEoBcqnqxU. In short, children were asked to provide a stool sample during the pre-intervention survey. A single dose of ALB (Zentel®; GlaxoSmithKline Pharmaceuticals Ltd, Mumbai, Maharashtra, India; batch number L298) was administered to

all subjects excreting STH eggs. Stool samples were processed using both Kato-Katz (https://www.youtube.com/watch?v=WpcZejHa_jM) and McMaster (https://www.youtube.com/watch?v=rkSGe-L4Sec; https://www.youtube.com/watch?v=bwIFyZ7NrFw).[1,2] Fourteen days post-treatment, stool samples were again collected and processed by the two diagnostic methods. The aim was to enrol at least 50 children excreting eggs, either on McMaster or Kato-Katz, for each of the STH species, separately.[5]

Statistical analysis

The sensitivity and mean FEC were calculated for each of the two FEC methods. For this, we used the combined results of both methods as the diagnostic 'gold' standard, assuming a specificity of 100% for both methods. Finally, egg reduction rate (ERR) was calculated for each method using the following formula[5]:

$$\text{ERR}\,(\%) = 100 \times \left(1 - \frac{\text{arithemtic mean of FEC at follow-up}}{\text{arithmetic mean of FEC at baseline}}\right)$$

Differences in sensitivity, mean FEC and ERR between FEC methods were assessed by a permutation test (10 000 iterations) taking into account the correlation in outcome between the two FEC methods. The level of significance was set at $p<0.05$. In addition, we compared the two methods in classifying the efficacy of the drugs into 'satisfactory', 'doubtful' and 'reduced'. This classification was based on the criteria recently proposed by WHO.[5]

Ethical approval

The school teachers and children were informed about the objectives and procedures of the study prior to actual data collection. The written consent form was prepared in two commonly used local languages (Afaan Oromo and Amharic) and delivered to the parents/guardians of all participating children. Only those children (i) who were willing to participate, (ii) whose parents or guardians signed the written informed consent form and (iii) who provided at least 5 g of stool were included in the study.

Results and Discussion

The sensitivity, mean FEC and ERR for each of the two FEC methods are summarised in Table 1. Differences in sensitivity between methods were observed for *A. lumbricoides* and hookworm infections, where Kato-Katz detected significantly more *A. lumbricoides* infections (97.9% vs 83.5%; p=0.002) and McMaster more hookworm infections (81.3% vs 53.3%; p=0.004). For *T. trichiura*, no significant difference in sensitivity was observed (McMaster 88.6% vs Kato-Katz 89.4%; p=0.89). Compared to Kato-Katz, McMaster yielded considerably lower FECs for both *A. lumbricoides* (10 631 eggs per gram of stool [EPG] vs 20 496 EPG; p<0.001), but higher FEC for hookworms (148 EPG vs 253 EPG; p=0.003). For *T. trichiura,* the FECs were comparable (McMaster 564 EPG vs Kato-Katz 643 EPG; p=0.49). Overall, ERR results were high for *A. lumbricoides* (>99.0%) and hookworms (>85.0%), but low for *T. trichiura* (>55.0%). The Kato-Katz resulted in higher ERRs than McMaster for both *T. trichiura* (65.8% vs 55.8%) and *A. lumbricoides* (>99.9% vs 99.9%). For hookworm, McMaster resulted in a higher ERR (87.9% vs 85.9%). Between both methods there was a only a significant difference in ERR for *A. lumbricoides* with Kato-Katz resulting in slightly higher ERR (p<0.001). There was no disagreement in classifying the efficacy of ALB for all STH species. Both methods classified the efficacy of ALB as 'satisfactory' for *A. lumbricoides* and *T. trichura*, but as 'doubtful' for hookworms. The observed differences in sensitivity and FEC can be explained by the differences in operational procedures and inherent shortcomings of the methods.[3] Despite these differences in sensitivity and FECs, both methods provided comparable ERR results and agreed in classifying the efficacy, as recently proposed by WHO. Although the applied WHO guidelines are designed to assess drug efficacy and, hence, may not allow a powerful comparison of ERR results across diagnostic methods for *T. trichiura* and hookworms, our study suggest that differences in sensitivity and FECs do not imply a difference in ERR estimates. Hence, it highlights that the choice of a diagnostic method to assess drug efficacy should not be based on sensitivity and FECs only.

Table 1. The overall sensitivity, mean FEC and ERR after administration of albendazole based on Kato-Katz and McMaster for STH infections in school children in Jimma Town, Ethiopia. $n_{baseline}$ and $n_{follow\text{-}up}$ represent the number of students excreting eggs at baseline and follow-up, respectively

	A. lumbricoides ($n_{baseline}$=94; $n_{follow\text{-}up}$=3)	*T. trichiura* ($n_{baseline}$=147; $n_{follow\text{-}up}$=99)	Hookworm ($n_{baseline}$=58; $n_{follow\text{-}up}$=17)
Sensitivity (%) (95% CI)			
McMaster	83.5[a] (76.3; 90.7)	88.6 (84.6; 92.3)	81.3[a] (72.0; 89.3)
Kato-Katz	97.9 (94.8; 100)	89.4 (85.4; 93.1)	53.3 (42.7; 64.0)
Mean FEC (EPG) (95% CI)			
McMaster	10631[b] (6526; 15957)	564 (403; 781)	253[a] (171; 355)
Kato-Katz	20496 (12718; 29905)	643 (385; 1014)	148 (90; 217)
ERR (%) (95% CI)			
McMaster	99.9[b] (99.7; 100)	55.8 (33.2; 70.6)	87.9 (80.1; 93.5)
Kato-Katz	>99.9 (>99.9; 100)	65.8 (36.7; 77.9)	85.9 (68.9; 96.0)

EPG: eggs per gram; ERR: egg reduction rate; FEC: faecal egg count; STH: soil-transmitted helminthiasis.
[a] p<0.005.
[b] p<0.001.

Authors' contributions: ZM and BL designed the study protocol; TB, MG and ZM carried out the field and laboratory work; BL analysed the data; TB and BL wrote the paper; ZM, AZ and JV critically revised the manuscript. All authors read and approved the manuscript. TB is the guarantor of the paper.

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Competing interests: None.

Ethical approval: The epidemiological survey in which this study was embedded was approved by the Ethical Committee of Jimma University [RPGC/09/2011] and Ghent [2011/374].

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