

Low efficacy of albendazole against *Trichuris trichiura* infection in schoolchildren from Port Elizabeth, South Africa

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Background: Albendazole is one of two standard drugs for the control of soil-transmitted helminthiasis.

Methods: A total of 149 schoolchildren from Port Elizabeth, South Africa, were examined for soil-transmitted helminth infections using duplicate Kato-Katz thick smears before and 2 weeks after administration of albendazole (400 mg).

Results: *Trichuris trichiura* was the predominant soil-transmitted helminth species (prevalence 60.4%), followed by *Ascaris lumbricoides* (47.7%). While albendazole was highly efficacious against *A. lumbricoides* (cure rate [CR] 97.2%; egg reduction rate [ERR] 94.3%), it lacked efficacy against *T. trichiura* (CR 1.1%; ERR 46.0%).

Conclusions: Our study confirms low efficacy of single dose albendazole against *T. trichiura*. There is a need for safe and efficacious drugs against *T. trichiura*.

Keywords: Albendazole, *Ascaris lumbricoides*, Drug efficacy, Kato-Katz technique, South Africa, *Trichuris trichiura*

Introduction

South Africa is considered a moderate-burden country for soil-transmitted helminth (STH) infections, yet, there is a paucity of data.¹ Within the frame of a 3-year prospective epidemiological study entitled 'Disease, Activity and Schoolchildren's Health' (DASH) that is focussing on schoolchildren from poor neighbourhoods in Port Elizabeth, South Africa,^{2,3} a sub-study was implemented to assess the efficacy against STH infections of the anthelmintic drug albendazole.

Materials and methods

The study was carried out in Helenvale, situated in the northern part of Port Elizabeth, a coastal city located in the Eastern Cape province of South Africa (geographical coordinates: lat 34°07'54" to 33°57'29" S, long 25°36'00" to 25°55'49" E).^{2,3} Established in the 1950s, Helenvale is one of the oldest townships stemming from the apartheid era as a group area for coloured people. It is considered to be one of the poorest and most unsafe

neighbourhoods of the city, characterised by high unemployment, low levels of education, illicit drugs, alcohol abuse and gangsterism.

Grade 4 schoolchildren, aged 9–14 years, from a disadvantaged school (quintile 3) were included in the study. The school principal, teaching staff, schoolchildren and their parents or guardians were informed about the purpose and procedures of the study. Written informed consent (either in English, Xhosa or Afrikaans) was obtained from children's parents or guardians, while children assented orally. Children could withdraw at any time without further obligations.

Consenting children were provided stool containers with unique identifiers and invited to return the containers filled with a small portion of their morning stool the next day. Duplicate 41.7 mg Kato-Katz thick smears were prepared from each stool sample.⁴ Two slides were examined quantitatively under a microscope. Species-specific helminth egg counts were multiplied by a factor of 24 to obtain a proxy for infection intensity, as expressed by the number of eggs per gram of stool (EPG). Subsequently, a single 400 mg oral dose of albendazole (INRESA, Bartenheim, France) was administered to all children participating in the study owing to a STH prevalence of over

20%.⁵ Ingestion of the drug was directly observed. Two weeks after administration, all treated children were invited to submit another stool sample to be re-examined with the same diagnostic procedures.

Data were double-entered and validated using EpiData version 3.1 (EpiData Association, Odense, Denmark). Statistical analysis was done using STATA version 13.0 (STATA Corp., College Station, TX, USA). Drug efficacy was expressed as cure rate (CR; proportion of participants who were helminth egg positive before treatment and became egg-negative 2 weeks post-treatment) and egg reduction rate (ERR; reduction of the arithmetic mean helminth egg count after treatment compared to the baseline). A 95% CI was calculated for prevalence estimates. Statistical significance was defined as $p < 0.05$, while p -values were calculated using Pearson's χ^2 or paired t -test, as appropriate.

Results and Discussion

Complete data were available from 149 children: 76 girls (51.0%) and 73 boys. At baseline, 90 children were found to be infected with *Trichuris trichiura* (60.4%) and 71 with *Ascaris lumbricoides* (47.7%). No hookworm infections were found. Infection intensities were mainly light or moderate (Table 1). The highest prevalence of *T. trichiura* was observed among 11-year-old children (67.1%). Boys were significantly more often infected with *T. trichiura* than girls (71.2% vs 50.0%; $\chi^2=7.02$, $df=1$, $p=0.008$). Boys were also more often infected with

A. lumbricoides than girls (54.8% vs 40.8%), but this difference was not statistically significant ($p=0.087$).

A single dose of 400 mg albendazole lacked efficacy against *T. trichiura*. Only one of the 90 infected children at baseline appeared completely cured from this STH species at follow-up (observed CR 1.1%). In terms of infection intensity, the arithmetic mean faecal egg count of *T. trichiura* was reduced from 1082 to 584, owing to a moderate ERR of 46.0% ($t_{(148)}=2.48$, $p=0.007$). The number of moderate and heavy *T. trichiura* infections (≥ 1000 EPG) declined from 31 (20.8%) before treatment to 21 (14.1%) after the administration of albendazole.

A single dose of albendazole was highly efficacious against *A. lumbricoides*. At treatment follow-up, only two children were found positive for this STH species (CR 97.2%). The arithmetic mean *A. lumbricoides* egg count dropped from 10 959 EPG to 629 EPG, an ERR of 94.3% ($t_{(148)}=5.68$, $p < 0.001$). The prevalence of moderate and heavy *A. lumbricoides* infections (≥ 5000 EPG) decreased from 31.5% before to 1.3% after treatment.

The current study confirms that a single 400 mg oral dose of albendazole is highly efficacious against *A. lumbricoides*, but lacks efficacy against *T. trichiura* among school-aged children.⁶ In 2009, Stothard and colleagues reported low CRs for single dose albendazole against *T. trichiura* among preschool-aged children on Zanzibar Island.⁷ Recently, combination therapy (oxantel pamoate plus albendazole) showed higher CR and ERR compared to standard albendazole or mebendazole treatment.⁸

Only a few studies have examined the distribution of STHs in South Africa. For instance, Karagiannis-Voules and colleagues

Table 1. Prevalence and intensity of *Trichuris trichiura* and *Ascaris lumbricoides*, before and 2 weeks after treatment with a single dose of 400 mg albendazole, among 9- to 14-year-old schoolchildren in Port Elizabeth, South Africa, 2015

	Baseline		2 weeks after treatment ^a		
	n	<i>T. trichiura</i>	<i>A. lumbricoides</i>	<i>T. trichiura</i>	<i>A. lumbricoides</i>
Prevalence of infection, % (95% CI)					
Sex					
Male	73	71.2 (59.6–80.6)	54.8 (43.1–66.0)	69.9 (58.1–79.4)	1.4 (0.2–9.5)
Female	76	50.0 (38.7–61.3)	40.8 (30.1–52.4)	50.0 (38.7–61.3)	1.3 (0.2–9.1)
Total	149	60.4 (52.3–68.0)	47.7 (39.7–55.8)	59.7 (51.6–67.4)	1.3 (0.3–5.3)
CR ^b , %		NA	NA	1.1	97.2
Arithmetic mean EPG, n (95% CI)					
Total	149	1082 (639–1524)	10 959 (7325–14594)	584 (273–931)	629 (-251–1509)
ERR ^c , %		NA	NA	46.0	94.3
Intensity of infection					
Infected, n		90	71	89	2
Light ^d		59	24	68	0
Moderate ^e		28	38	20	1
Heavy ^f		3	9	1	1

^a Treatment according to WHO and national guidelines (single oral dose of 400 mg albendazole).

^b CR: cure rate (percentage of egg-positive children at baseline who became egg-negative after treatment).

^c ERR: egg reduction rate (reduction in the arithmetic mean faecal egg count at treatment follow-up compared to before treatment).

^d *A. lumbricoides* 1–4999 EPG; *T. trichiura* 1–999 EPG.

^e *A. lumbricoides* 5000–49 999 EPG; *T. trichiura* 1000–9999 EPG

^f *A. lumbricoides* $\geq 50 000$ EPG; *T. trichiura* $\geq 10 000$ EPG

reported slightly higher STH prevalences further north, in the province of KwaZulu-Natal.¹ Given the high prevalence and intensity of STH infections observed in our study, specific public health interventions are warranted but according to education authorities, preventive chemotherapy using either albendazole or mebendazole against STHs has thus far been neglected in the Helenvale neighbourhood.

Our study has several limitations. First, we only focussed on Grade 4 children attending a disadvantaged quintile 3 school in Port Elizabeth. Hence, our findings cannot be generalized for a broader population. Second, only single stool samples were collected before and after anthelmintic drug administration. It is conceivable that some infections, particularly those of light intensity, were missed.

Taken together, our findings from Port Elizabeth in South Africa suggest that a single 400 mg oral dose of albendazole is efficacious against *A. lumbricoides* but does not effectively manage *T. trichiura* infections in children. To control STH infections among school-aged children, public health measures are required, such as preventive chemotherapy, along with improvements in water, sanitation and hygiene (WASH). Moreover, there is a pressing need to use alternative and develop novel drugs and drug combinations that are safe and efficacious against *T. trichiura*.

Authors' contributions: IM, MG, UP, RdR, JU, CW and PS designed the study protocol. IM, LB, LZ and CW conducted the field work. CW was responsible for community sensitisation. IM, JU and PS analysed and interpreted the data, and drafted the manuscript. All authors critically reviewed and approved the manuscript prior to submission. IM and PS are the guarantors of the paper.

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Ethical approval: The study was cleared by the ethics committees of Northwest and Central Switzerland (EKNZ; reference no. 2014-179, approval date: 17 June 2014), the Nelson Mandela Metropolitan University (NMMU; study number H14-HEA-HMS-002, approval date: 4 July 2014), the Eastern Cape Department of Education (approval date: 3 August 2014) and the Eastern Cape Department of Health (approval date: 7 November 2014). The study is registered at ISRCTN registry under controlled-trials.com (unique identifier: ISRCTN68411960, registration date: 1 October 2014).

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