RESEARCH NOTE

EFFICACY OF SINGLE DOSE ALBENDAZOLE TREATMENT OF SOIL-TRANSMITTED HELMINTHS AMONG INDIGENOUS CHILDREN IN MALAYSIA

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Abstract. Albendazole, a synthetic nitroimidazole with a broad spectrum antinematode and anticathode activities, has been routinely used to treat soil-transmitted helminths (STH) infection. In Malaysia, STH infection prevalence is significantly higher among indigenous (Orang Asli) community, which resides in an environment highly susceptible to STH infection. Efficacy of a single dose albendazole (400 mg) treatment against *Ascaris lumbricoides* (AL, large roundworm) and *Trichuris trichiura* (TT, whipworm) was evaluated among Orang Asli children (n = 68, 2-17 years of age) who never or at least one month prior had undergone deworming treatment. The prevalence of both AL and TT was 85%. The overall cure rate among all age groups was 93% for AL and 41% for TT while egg reduction rates among uncured participants were 99.9% and 55.7 % for AL and TT, respectively. Infection with AL was mainly of mild intensity, which was nearly absent following treatment, while TT infection mainly was of mild to moderate intensity, which was reduced by about 50% after treatment. In conclusion, a single dose albendazole treatment was effective in treatment of *Ascaris lumbricoides* and to lesser extent of *Trichuris trichiura* infection among Orang Asli children, suggesting a higher dosage of albendazole would be required for effective treatment of whipworm infection.

Keywords: albendazole, cure rate, efficacy, indigenous children, Malaysia, soil-transmitted helminth

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INTRODUCTION

Soil-transmitted helminth (STH) infection is still prevalent despite progress in urbanization and modernization, with more than 1.5 billion people infected annually worldwide, mainly children because they often play outdoors without adequate foot protection (Savioli *et al*, 2004; Hartini and Mohamed Kamel, 2010). Common soil-transmitted helminths are *Ancylostoma duodenale* (old world hookworm), *Ascaris lumbricoides* (large roundworm), *Necator americanus* (new world hookworm), *Strongyloides stercoralis* (roundworm), and *Trichuris trichuria* (whipworm) (Hartini and Mohamed Kamel, 2010).

STH infection is medically important as etiology of anemia and nutritional deficiency, with high intensity of infection lead to low cognitive function, malaise and poor growth rate (Wong *et al*, 2016). In Malaysia *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm infections are most commonly detected (Ahmed *et al*, 2011). Four kinds of anthelmintic drugs, namely, albendazole, ivermectin, mebendazole, and praziquantel are recommended, the most widely used being a single dose of albendazole (400 mg) or mebendazole (500 mg), except in pregnant women in first trimester due to risk of teratogenicity and embryotoxicity and children under 1 year of age (WHO, 2006).

Previous studies in Malaysia have paid attention to efficacies of STH drug treatment but few have focused on reduction of the burden of infection. Here, intensities of *Ascaris lumbricoides* and *Trichuris trichiura* infection pre- and post-treatment with single-dose albendazole and percent cure rate were determined among indigenous (Orang Asli) children in two communities in Selangor, Malaysia. The findings should give insight on the efficacy of single dose albendazole to various intensity of STHs found in the studied area and this should guide whether continuing using albendazole for STHs controlling for the Orang Asli communities is possible.

MATERIALS AND METHODS

Study area and participants

The study was conducted in two indigenous settlements, Kampung Sungai Lalang 3°03'14.4"N 101°52'17.4"E (latitude: 3.001338; longitude: 101.876742) and Kampung Kachau Luar 3°00'56.0"N101°54'14.2"E (latitude: 2.9611225; longitude: 101.82103), Hulu Langat, Selangor, Malaysia from June to September 2019. Both villages are located approximately 12 km from the main town, surrounded by hills and forests, and each has a population of 200 [approximately 90 being children (2-17 years of age)]. Participants were limited to the children population. Inclusion criteria were children 2-17 years of age permanently residing in the villages. Exclusion criteria were children with a previous history of taking deworming medicine, currently under any long-term medication, with severe disease or thalassemia, or pregnant (teenagers).

The study protocol was approved by Human Ethical Committee of UniKL [UNIKL REC /2020/003] and Department of Aboriginal Affairs of Malaysia (JAKOA) [ref: JAKOA/PP.30.032.Jld 46(95)], with prior consent from village leaders. Prior Informed consent was obtained from parents of each participant through verbal communication and voice recording.

Stool collection and examination

Participants or their parents were given sterile wide mouth, screw-cap specimen containers with a scoop to aid fecal collection. Fecal sample from each participant was collected pre- and post-drug treatment. Each specimen container was tagged with subject identification number, house number, date and time of stool collection. A 30 ml aliquot of 70% alcohol was added to each container, which was transported on ice to UniKL Mestech and stored at 4°C until used (within 24 hours). Helminth eggs in samples were analyzed using a floatation technique (Nisha *et al*, 2016) and recorded as egg/g fecal sample (epg) using a McMaster slide. Egg count of each sample was conducted in duplicate. Infection intensity was categorized as mild (1-4,999 *A. lumbricoides* or 1-999 *T. trichiura* epg), moderate (5,000-49, 999 *A. lumbricoides* or 1,000-99,991 *T. trichiura* epg) and heavy (≥50,000 *A. lumbricoides* or ≥10,000 *T. trichiura* epg) (WHO and UNICEF, 2004.

Albendazole treatment

During July 2019 stools were collected from participating children and subsequently administered, in the presence of a member of the research team, a single dose of albendazole (400 mg) (ZENTEL; GlaxoSmithKline, London, UK) as a single tablet (to children 13-19 years of age) or as 10 ml suspension (to children 2-12 years of age). Post-treatment collection of stool samples was carried out one month after treatment. Efficacy of treatment is based on cure rate (CR) and egg reduction rate (ERR) as follow:

$$CR = \frac{\text{number of egg-negative samples post-treatment}}{\text{number of egg-positive samples pre-treatment}} \times 100$$

$$ERR = \frac{\text{GM FEC at pre-treatment - GM FEC at post-treatment}}{\text{GM FEC at pre-treatment}} \times 100$$

where GM FEC refers to geometric mean of fecal egg count

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 24 (IBM, Armonk, NY). Gender and age group are defined as categorical variables (qualitative data) and presented as frequency and percentage. Using a chi-square test, a *p*-value <0.050 is considered significant.

RESULTS

Socio-demographic profile and STH prevalence of participants

Orang Asli children (*n* = 68; 35 females and 33 males), 2-17 years of age were enrolled in the study, with 7-12 years old being the predominant age group (Table 1). Only *A. lumbricoides* and *T. trichiura* eggs were found in pre-treatment stool samples, a combined prevalence of 85%, highest prevalence of the former helminth among children 7-11 years of age and that of the latter among children of 12-17 years of age. There is a significant association of children age group with *T. trichiura* infection (*p*-value = 0.029).

Efficacy of albendazole treatment

One month following a single treatment with 400 mg of albendazole, stool egg counts were again examined, showing an overall CR of 93% and 41% and ERR among uncured participants of 99.9% and 55.7% for *A. lumbricoides* and *T. trichiura*, respectively, with *T. trichiura*-infected children in 7-11 years of age group responding significantly better than those in the other age groups (Table 2). At pre-treatment, 78% of *A. lumbricoides* infection was considered as mild intensity based on WHO's criteria (WHO and UNICEF, 2004) which was reduced to 7% post-infection, while for *T. trichiura*,

Table 1

Socio-demographic characteristics of Orang Asli participants and prevalence of soil-transmitted helminths infection, Selangor, Malaysia

Characteristic	Number (%) (*n* = 68)	Number of samples (% prevalence)	
		Ascaris lumbricoides	*Trichuris trichiura*
Gender			
Male	33 (48)	26 (79)	27 (82)
Female	35 (52)	32 (91)	31(91)
Age group, years			
2-6	22 (32)	18 (82)	17 (77)
7-11	33 (48)	31 (94)	29 (88)
12-17	13 (20)	9 (69)	12 (92)
Overall	68 (100)	58 (85)	58 (85)

Table 2

Cure rate and egg reduction rate for *Ascaris lumbricoides* and *Trichuris trichiura* infections following single albendazole dose (400 mg) of Orang Asli children in Selangor, Malaysia (June to September 2019)

Helminth species	Age group (years)	Number of participants		Cure rate (%)	GM FEC** (EPG)		Egg reduction rate (%)
		Cured	Uncured		Before	After	
Ascaris lumbricoides	2-6	16	2	88.9	4488.1	5.6	99.9
	7-11	29	2	93.5	4119.4	3.3	99.9
	12-17	9	0	100.0	N/A	N/A	N/A
Overall		54	4	93.1	24907.4	8.9	99.9
Trichuris trichiura	2-6	4	13	23.5	638.2	344.1	46.1
	7-11	17	12	58.6*	443.1	231.0	47.9
	12-17	3	9	25.0	733.3	229.2	68.7
Overall		24	34	41.4	1814.7	804.3	55.7

*p-value = 0.029 compared to the other two age groups: **Calculation was performed only in the uncured group

EPG: number of eggs per gram of feces; GM FEC: geometric mean of fecal egg count; mg: milligram; N/A: not applicable

pre-treatment stool demonstrated both mild (83%) and moderate (14%) infection intensity, which was reduced post-treatment to 50 and 7% respectively (data not shown).

DISCUSSION

The study shows similar prevalence of *A. lumbricoides* and *T. trichiura* among Orang Asli children in Selangor, Malaysia, and a single albendazole dose results in a better treatment outcome for *A. lumbricoides* compared to *T. trichiura* infection, in agreement with an earlier survey among indigenous children (Penggabean *et al*, 1998). A single dose of albendazole resulted in 100% cure against ascariasis among school children in Sumatra, Indonesia (Putra *et al*, 2016). Similar findings among were reported among school children 4-18 years of age Cameron, Ethiopia, Tanzania, and Vietnam (Levecke *et al*, 2014; Samuel *et al*, 2014). Steinmann *et al* (2011) reported children ≥5 years of age in Nongang, PR China involving, triple-dose albendazole produces higher efficacy against *T. trichiura* compared to single dose of albendazole, but no difference was observed against *Ascaris*.

In the present study, a McMaster chamber technique was used to determine egg counts of *A. lumbricoides* and *T. trichiura* (WHO and UNICEF, 2004). This method allowed eggs to float on the surface rather than sink to bottom following centrifugation, thereby facilitating egg identification under a light microscope (10x magnification). This method is simpler than other methods such as Kato Katz technique (Albonico *et al*, 2012)

Intensity of *A. lumbricoides* infection in our study children mainly was mild, similar to a previous study at Pos Legap, Perak, Malaysia, which reported 6% heavy infection among school children of standards 1 to 3 about 200 kids (Wong *et al*, 2016). However, Ahmed *et al* (2011) reported moderate to heavy infection of *A. lumbricoides* among aboriginal children in primary school (Sekolah Kebangsaan Satak) about 200 to 300 people in Pahang, Malaysia. Most of the eggs observed were fertile due to the moist and warm soil in the villages (Hartini and Mohamed Kamel, 2010). Following treatment, four children in our study group (6%) still had mild infection. Samuel *et al* (2017), in Ambo Town, Western Ethiopia also observed mild infection remaining after a single dose albendazole treatment, as did Speich *et al* (2014) in Pemba Island, Tanzania with samples collected two weeks post-treatment.

For *T. trichiura* infection, majority of the children had mild to moderate infection intensity, which was reduced by half with albendazole treatment, similar to findings from studies carried out in 2014 and 2016 at Pemba Island, Tanzania and Port Elizabeth, South Africa respectively (Speich *et al*, 2014; Müller *et al*, 2016). Speich *et al* (2014) noted in Tanzania heavy infection of *T. trichiura* is not cured one month post-treatment with albendazole. A single dose albendazole has good efficacy for *Trichuris* infection of mild intensity (Steinmann *et al*, 2011). Although the presence of albendazole resistance was not investigated, re-infection is the most likely explanation

when children are exposed to *Trichuris*-highly contaminated soil (Ahmed *et al*, 2011).

Association between children age group (7-11 years) and cure rate was observed only for *T. trichiura* infection as *A. lumbricoides* infection in all age groups was nearly absent post-treatment. However, Narain et al (2004) in Assam, India found no significant association between age group and cure rate for all STH infection. This might be due to differences in life style, ethnicity and parasite strain.

The limitations of the study were language barrier, which resulted in reduced participation of parents, and time constraint.

In conclusion, a single dose albendazole (400 mg) is effective in treating Orang Asli children with *Ascaris lumbricoides* but not *Trichuris trichiura* infection, suggesting that increased dosing regimen might be necessary for elimination of the latter soil-transmitted helminth infection among indigenous children in Malaysia.

ACKNOWLEGEMENT

We would like to acknowledge all the parents and children from Kampung Sungai Lalang and Kampung Kachau Luar whom willingly participated in this study. We would also like to thank Department of Aboriginal Affairs of Malaysia (JAKOA) and Universiti Kuala Lumpur - Institute of Medical Science Technology (UniKL MESTECH) to give us permission to conduct this study at the Orang Asli village.

REFERENCES

Ahmed A, Al-Mekhlafi HM, Choy S, *et al*. The burden of moderate-to-heavy soil-transmitted helminth infections among rural malaysian aborigines: an urgent need for an integrated control programme. *Parasit Vectors* 2011; 4: 242.

Albonico M, Ame SM, Vercruysse J, Levecke B. Comparison of the Kato-Katz thick smear and McMaster egg counting techniques for monitoring drug efficacy against soil-transmitted helminths in schoolchildren on Pemba Island, Tanzania. *Trans R Soc Trop Med Hyg* 2012; 106: 199-201.

Hartini Y, Mohamed Kamel AG. Ascariasis among Orang Asli children at Pos Lenjang, Pahang, Malaysia. *Med Health* 2010; 5: 60-5.

Levecke B, Montresor A, Albonico M, *et al*. Assessment of anthelmintic efficacy of mebendazole in school children in six countries where soil-transmitted helminths are endemic. *PLoS Negl Trop Dis* 2014; 8: e3204.

Müller I, Beyleveld L, Gerber M, *et al*. Low efficacy of albendazole against *Trichuris trichiura* infection in schoolchildren from Port Elizabeth, South Africa. *Trans R Soc Trop Med Hyg* 2016; 110: 676-8.

Narain K, Medhi GK, Rajguru SK, Mahanta J. Cure and reinfection patterns of geohelminthic infections after treatment in communities inhabiting the tropical rainforest of Assam, India. *Southeast Asian J Trop Med Public Health* 2004; 35: 512-7

Nisha M, Kumarasamy V, Ambu S, Davamani F, Mak JW. Factors associated with intestinal parasite infections in a resettled indigenous community in Malaysia. *Int J Trop Dis Health* 2016; 12: 1-7.

Penggabean M, Norhayati, Oothuman P, Fatmah MS. Efficacy of albendazole in the treatment of *Trichuris trichuria* and *Giardia* intestinalis infection in rural Malay communities. *Med J Malaysia* 1998; 53: 408-12.

Putra DS, Dalimunthe W, Lubis M, Pasaribu S, Lubis C. The efficacy of single-dose albendazole for the treatment of ascariasis. *Paediatr Indones* 2016; 49: 97-103.

Samuel F, Degarege A, Erko B. Efficacy and side effects of albendazole currently in use against *Ascaris*, *Trichuris* and hookworm among school children in Wondo Genet, southern Ethiopia. *Parasitol Int* 2014; 63: 450-5.

Samuel F, Demsew A, Alem Y, Hailesilassie Y. Soil transmitted helminthiasis and associated risk factors among elementary school children in ambo town, western Ethiopia. *BMC Public Health* 2017; 17: 791.

Savioli L, Albonico M, Engels D, Montresor A. Progress in the prevention and control of schistosomiasis and soil-transmitted helminthiasis. *Parasitol Int* 2004; 53: 103-13.

Speich B, Ame SM, Ali SM, *et al*. Oxantel pamoate-albendazole for *Trichuris trichiura* infection. *N Engl J Med* 2014; 370: 610-20.

Steinmann P, Utzinger J, Du ZW, *et al*. Efficacy of single-dose and triple-dose albendazole and mebendazole against soil-transmitted helminths and *Taenia* spp.: a randomized controlled trial. *PLoS One* 2011; 6: e25003.

Wong WK, Foo PC, Roze MNM, Pim CD, Subramaniam P, Lim BH. Helminthic infection and nutritional studies among Orang Asli children in Sekolah Kebangsaan Pos Legap, Perak. *Can J Infect Dis Med Microbiol* 2016: 1326085.

World Health Organization (WHO). Preventive chemotherapy in human helminthiasis, 2006 [cited 2020 Mar 18]. Available from: URL: https://apps.who.int/iris/bitstream/handle/10665/43545/9241547103_eng.pdf;jsessionid=774B7B7D3FD0289ED-B5AC5DEE9217FF2?sequence=1

World Health Organization and United Nations Children's Fund (WHO and UNICEF). Prevention and control of schistosomiasis and soil-transmitted helminthiasis, 2004 [cited 2020 Mar 18]. Available from: URL: https://www.who.int/intestinal_worms/resources/en/ppc_unicef_finalreport.pdf?ua=1