



Effect of Mass Drug Administration with a Single Dose of Albendazole on *Ascaris lumbricoides* and *Trichuris trichiura* Infection among Schoolchildren in Yangon Region, Myanmar

Jong-Yil Chai^{1,2,*†}, Woon-Mok Sohn^{3,†}, Sung-Jong Hong⁴, Bong-Kwang Jung¹, Sooji Hong¹, Seon Cho¹, Jong-Bok Park¹, In-Sung Kim¹, Sunkyoung Kim¹, Keon-Hoon Lee¹, Hoo-Gn Jeoung¹, Thi Thi Htoon⁵, Htay Htay Tin⁵

¹Institute of Parasitic Diseases, Korea Association of Health Promotion, Seoul 07649, Korea; ²Department of Tropical Medicine and Parasitology, Seoul National University College of Medicine, Seoul 03080, Korea; ³Department of Parasitology and Tropical Medicine, and Institute of Health Sciences, Gyeongsang National University School of Medicine, Jinju 52727, Korea; ⁴Department of Environmental Medical Biology, Chung-Ang University College of Medicine, Seoul 06974, Korea; ⁵National Health Laboratory, Yangon 11191, Myanmar

Abstract: Soil-transmitted helminths, including *Ascaris lumbricoides* and *Trichuris trichiura*, are important intestinal parasites mostly affecting younger people in developing countries. In 2014-2015, we performed mass fecal examinations targeting a total of 2,227 schoolchildren in 3 districts (South Dagon, North Dagon, and Hlaing-thar-yar) of Yangon Region, Myanmar, using the Kato-Katz thick smear technique. The egg positive children were subjected to a mass drug administration (MDA) using a single oral dose of 400 mg albendazole. The pre-treatment egg positive rate (EPG/person) of *A. lumbricoides* averaged 17.2% (15,532); it was 25.2% (21,796), 14.2% (11,816), and 12.8% (12,983) in 3 districts, respectively, and that of *T. trichiura* averaged 19.4% (1,074), and was 24.1% (1,040), 12.3% (852), and 21.2% (1,330) in 3 districts, respectively. Follow-up fecal examinations performed 4 months post-MDA revealed considerable decreases of *A. lumbricoides* prevalence (EPG/person) to av. 8.3% (12,429), and 13.7% (17,640), 8.0% (7,797), and 4.5% (11,849) in 3 districts, respectively. However, *T. trichiura* did not show any recognizable decrease in the prevalence (EPG/person) remaining at av. 18.2% (862), and 18.5% (888), 11.5% (812), and 23.3% (887) in 3 districts, respectively. The results demonstrated difficulty in short-term control of *T. trichiura* by MDA using albendazole and suggested necessity of either a long-term MDA (> 10 years) or changing the albendazole regimen into 2-3-day course (total 800 or 1,200 mg), or using an alternative drug/drug combination.

Key words: *Ascaris lumbricoides*, *Trichuris trichiura*, prevalence, effect of control, albendazole, schoolchildren, Myanmar

Soil-transmitted helminths (STHs), including *Ascaris lumbricoides*, hookworms, and *Trichuris trichiura*, are the most common intestinal parasites affecting more than 1.5 billion people worldwide [1]. These infections affect especially children in developing countries and are associated with poor growth, reduced physical activity, and impaired learning ability [2]. In Myanmar, the prevalence of *A. lumbricoides* and *T. trichiura* among schoolchildren has been high, whereas that of hookworms has been comparatively low [2-4].

Repeated mass fecal examinations followed by mass drug

administration (MDA), environmental sanitation including remodeling of latrines and prohibition of night soil fertilizers, and health education for improving personal hygiene are the 3 basic control strategies for STH infections [5]. Among these, MDA using a proper anthelmintic drug is the most feasible and efficient method. Anthelmintics most popularly used for STH control are albendazole and mebendazole [1]; the recommended regimen of albendazole is 400 mg given in a single dose [4,6], and that of mebendazole is 100 mg in a single dose [6]. However, the sensitivity of each helminth species to MDA and anthelmintic drugs varies depending on the species (*A. lumbricoides*, hookworms, or *T. trichiura*) and might also be associated with drug resistance of helminths [1].

The Korea Association of Health Promotion (KAHP), Seoul, Korea undertook an international health promotion project entitled, "Korea-Myanmar Health Promotion Project for Ele-

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*Corresponding author (cyj@snu.ac.kr)

†These authors contributed equally to this work.

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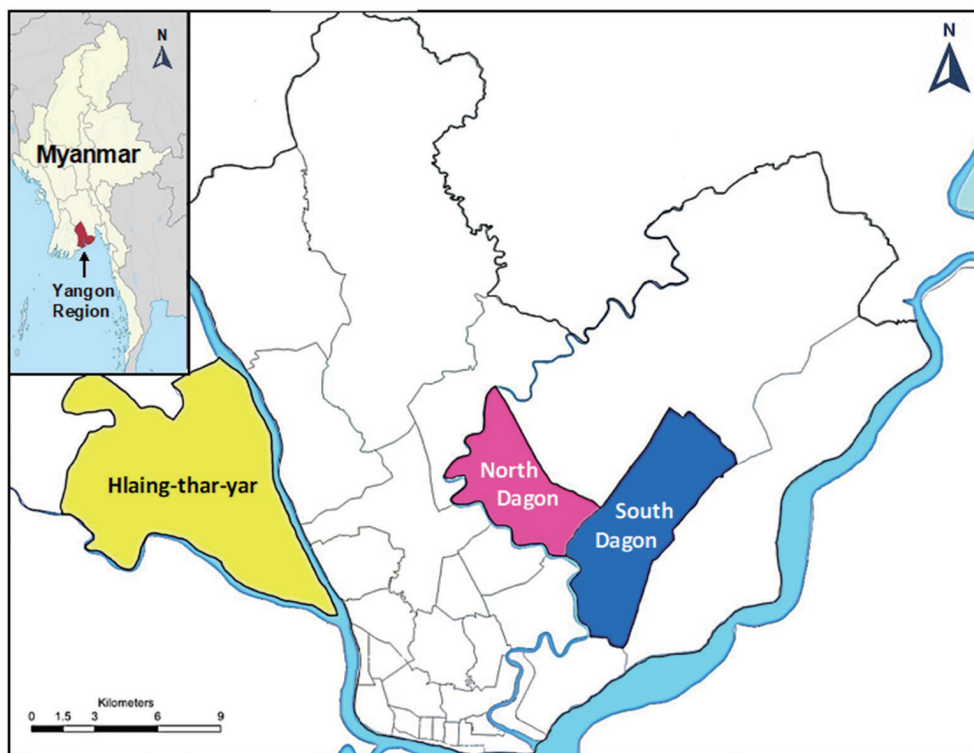


Fig. 1. Map showing the surveyed areas in Yangon Region, Myanmar. Schoolchildren of 20 primary schools in 3 districts (South Dagon, North Dagon, and Hlaing-thar-yar) were subjected for this study.

mentary Schoolchildren of the Vulnerable Areas around Yangon, Myanmar". The main purpose of the project was intestinal parasite control among schoolchildren under the agreement between 2 countries (as of 16 June 2013; IRB was not available at the time of this survey). In 2014-2015, we performed mass fecal examinations targeting schoolchildren in 20 Basic Education Primary Schools (BEPS) located in 3 districts (South Dagon, North Dagon, and Hlaing-thar-yar) of Yangon Region. MDA was performed on egg positive children using a single oral dose of albendazole. Follow-up fecal examinations were done 4 months later. The short-term (4-month) control efficacy in response to MDA appeared to be quite different between *A. lumbricoides* (high efficacy) and *T. trichiura* (poor efficacy). The purpose of this paper is to present the results of MDA with analyses of the factors related to the effect of control.

The 20 BEPS consisted of 6 schools in South Dagon, 6 schools in North Dagon, and 8 schools in Hlaing-thar-yar district (Fig. 1). Fecal examinations were performed on a total of 2,227 schoolchildren (aged 6-8 years, including almost the same numbers of boys and girls) using the Kato-Katz thick

smear technique (1 smear per child). The results revealed that the egg positive rate of any kinds of helminths averaged 30.9%; the rate being 40.4% (33.3-52.0% by school) in South Dagon, 21.9% (8.1-54.2%) in North Dagon, and 30.2% (23.0-38.7%) in Hlaing-thar-yar (Table 1). The egg positive rate (EPG/person) of *A. lumbricoides* averaged 17.2% (15,532), and by district 25.2% (21,796), 14.2% (11,816), and 12.8% (12,983), respectively, and that of *T. trichiura* averaged 19.4% (1,074), and by district 24.1% (1,040), 12.3% (852), and 21.2% (1,330). The egg positive rate of hookworms was 0.2% on average, and by district 0.1%, 0.1%, and 0.4%, and that of *Opisthorchis viverrini*/minute intestinal flukes (MIF) averaged 0.1%, and by district 0.1%, 0.0%, and 0.1%, in 3 districts, respectively (Table 1). The results were not significantly different ($P > 0.05$) between boys and girls (data not shown).

MDA was performed on a selective treatment manner, and a total of 688 helminth egg positive cases were given each a single oral dose of 400 mg albendazole (Shinpoong Pharm Co., Seoul, Korea). Two trematode egg positive children were given additionally praziquantel 40 mg/kg in a single dose. The MDA coverage rate exceeded 95-98% in each school but there were a

Table 1. Prevalence of *Ascaris lumbricoides*, *Trichuris trichiura*, and other helminths among schoolchildren in 3 districts of Yangon area, Myanmar (2014-2015)

District/school code	No. exam.	Egg positive rate (%)					
		Any helminths ^a	<i>Ascaris lumbricoides</i>	<i>Trichuris trichiura</i>	Hook-worms	<i>Opisthorchis viverrini</i> /MIF ^b	Others ^c
South Dagon							
BEPS ^d -A	84	34.5	16.7	25.0	1.2	1.2	4.8
BEPS-B	50	52.0	30.0	44.0	0	0	0
BEPS-C	132	46.2	32.6	26.5	0	0	2.3
BEPS-D	198	33.3	17.7	19.2	0	0	1.0
BEPS-E	125	38.4	27.2	20.0	0	0	0.8
BEPS-F	124	46.8	31.5	24.8	0	0	1.6
Subtotal	713	40.4	25.2 ^e	24.1	0.1	0.1	1.7
North Dagon							
BEPS-G	79	12.7	6.3	6.3	0	0	1.3
BEPS-H	131	54.2	45.0	26.7	0	0	2.3
BEPS-I	135	8.1	3.0	6.7	0	0	0.7
BEPS-J	169	8.3	3.0	5.3	0	0	0.6
BEPS-K	107	13.1	1.9	13.1	0	0	0
BEPS-L	64	46.9	34.4	18.8	1.6	0	3.1
Subtotal	685	21.9	14.2 ^f	12.3	0.1	0	1.2
Hlaing-Thar-yar							
BEPS-M	163	23.0	11.7	15.3	0	0	2.5
BEPS-N	79	25.3	10.1	21.5	0	0	0
BEPS-O	96	24.0	8.3	18.8	0	0	0
BEPS-P	141	33.3	11.3	21.3	0.7	0	4.3
BEPS-Q	75	38.7	13.3	33.3	1.3	0	0
BEPS-R	86	33.7	11.6	23.3	1.2	0	1.2
BEPS-S	111	32.4	17.1	22.5	0	0.9	0.9
BEPS-T	78	34.6	20.5	20.5	0	0	1.3
Subtotal	829	30.2	12.8 ^g	21.2	0.4	0.1	1.6
Total	2,227	30.9	17.2 ^h	19.4	0.2	0.1	1.5

^aHelminth egg positive rates were not significantly different between boys and girls ($P > 0.05$).

^bMinute intestinal fluke.

^cOthers included eggs of *Enterobius vermicularis* and *Trichostrongylus* sp.

^dBasic Education Primary School.

^eUnfertilized egg positive rate was 16.7% and fertilized egg positive rate was 16.0%.

^fUnfertilized egg positive rate was 8.5% and fertilized egg positive rate was 8.5%.

^gUnfertilized egg positive rate was 9.3% and fertilized egg positive rate was 6.8%.

^hUnfertilized egg positive rate was 11.4% and fertilized egg positive rate was 10.2%.

few children dropped-out from the MDA (data not shown). The significance of differences in the prevalence before and after the MDA were statistically evaluated using the student's *t*-test.

At 4 months after the MDA, follow-up fecal examinations (1 Kato-Katz smear for each child) were performed on the same schools, and the efficacy of the MDA for reduction of *A. lumbricoides* and *T. trichiura* prevalence and worm burden was assessed. Possible bias due to a few new attendees in each school was neglected. The efficacy of the MDA was evaluated to be fairly satisfactory for *A. lumbricoides* as the pre-treatment average egg positive rate of 17.2% was decreased to lower than half level, 8.3% ($P < 0.05$) (Fig. 2), and the pre-treatment EPG/person of 15,532 decreased to 12,429 after the MDA ($P > 0.05$) (Fig. 3). This decreasing trend of *A. lumbricoides* was similar

among 3 districts (Figs. 2, 3) and also recognizable among different schools, although some schools, like BEPS-A, B, I, and Q, showed no significant decreases in the prevalence ($P > 0.05$) (data not shown).

However, the efficacy of the MDA against *T. trichiura* was far from satisfactory (Fig. 2). The average pre-treatment egg positive rate, 19.4%, in 3 districts was not significantly decreased after the MDA which remained at 18.2% at follow-up examinations ($P > 0.05$) (Fig. 2), although the average EPG of infected schoolchildren was decreased a little, from 1,074 to 862 ($P > 0.05$) (Fig. 3). Insignificant and minor decreasing trends ($P > 0.05$) were seen in 2 districts, South Dagon and North Dagon (Figs. 2, 3), and a slight increase ($P > 0.05$) in the prevalence vs a remarkable decrease in EPG/person appeared in

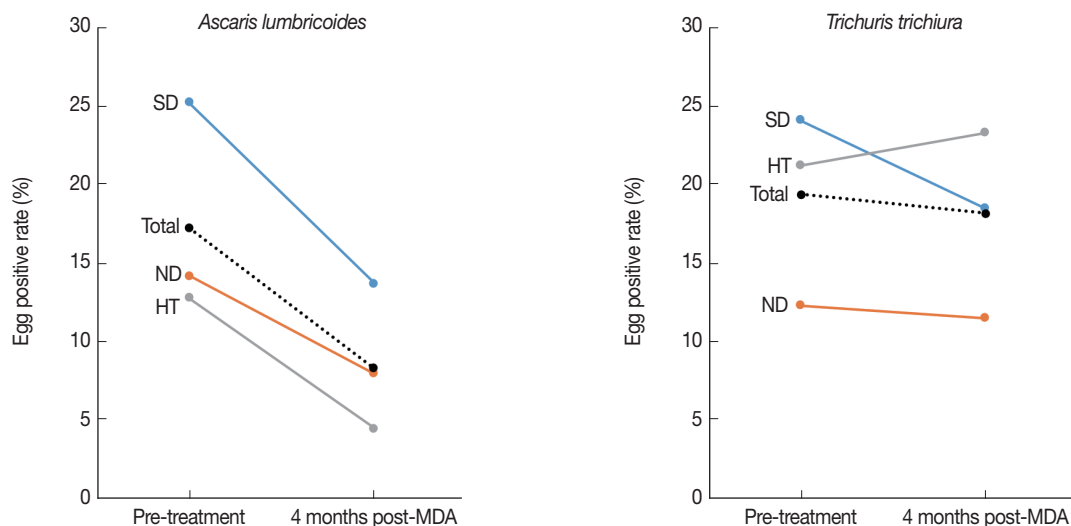


Fig. 2. Pre- and post-MDA prevalences of *Ascaris lumbricoides* and *Trichuris trichiura* among schoolchildren in 3 districts of Yangon Region, Myanmar. SD, South Dagon; ND, North Dagon; HT, Hlaing-thar-yar.

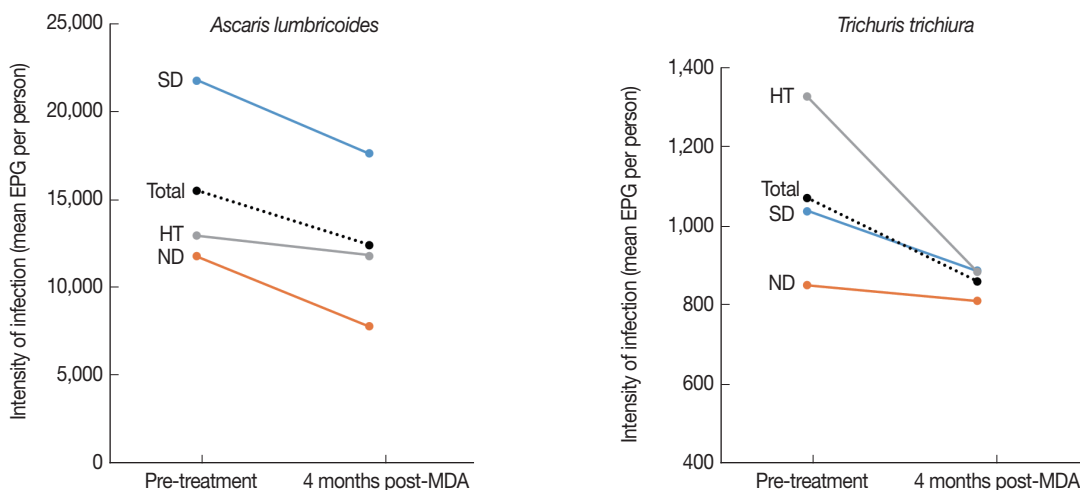


Fig. 3. Pre- and post-MDA intensity of infection (average EPG/person) of *Ascaris lumbricoides* and *Trichuris trichiura* among schoolchildren in 3 districts of Yangon Region, Myanmar. SD, South Dagon; ND, North Dagon; HT, Hlaing-thar-yar.

Hlaing-thar-yar district (Figs. 2, 3). The majority of individual schools revealed more or less decreasing trends, while some of them, including BEPS-H, O, Q, R, and T schools, showed slightly increasing trends in the prevalence of *T. trichiura* (data not shown).

The high sensitivity of *A. lumbricoides* to benzimidazoles (albendazole and mebendazole) has been well documented [6,7]. The cure rate of albendazole (400 mg) for *A. lumbricoides* infection was reported to be 82-100% [6] or 93.2-97.3% [7]. However, the sensitivity of *T. trichiura* to albendazole or mebendazole has been reported to be generally low and unsatisfactory [1,6,7]. The cure rate of 400 mg single oral dose of

albendazole for treating *T. trichiura* infection was reported to be 27-81% [6] or less, 21.0-42.5% [7].

Our study demonstrated that the efficacy of MDA using a single dose of albendazole was fairly good for reduction of the prevalence and intensity of infection of *A. lumbricoides* (from 17.2% to 8.3% in average egg positive rate and from 15,532 to 12,429 in EPG/person) at 4 months post-MDA. A large portion of 8.3% in prevalence at follow-up was regarded to be due to reinfection during 4 months after the MDA. However, its efficacy was far from satisfactory for short-term control of *T. trichiura*. The average prevalence before the MDA was 19.4% but it remained to be still high after 4 months, 18.2%. The egg

reduction was fairly remarkable in Hlaing-thar-yar district but less remarkable in 2 other districts. The failure in reduction of *T. trichiura* prevalence could be due to 2 basic factors; one is limitation of the drug efficacy, and the other is rapid reinfection after the MDA. However, the importance of reinfection may not be so great considering the biology and life cycle of *T. trichiura*. The pre-patent period of *T. trichiura* was estimated to be 101-114 days in a human volunteer after an experimental intake of eggs [10]. It is thus unlikely that *T. trichiura* worms reinfected after the MDA produced a sufficient amount of eggs. Therefore, a more important factor may be the drug efficacy limitation of albendazole against *T. trichiura*.

Various workers have reported limited efficacy of albendazole and mebendazole for individual treatment of *T. trichiura* infection [1,6-9]. However, these drugs can be used in MDA because of considerable egg reduction rates, 77.0-99.0% [6] or 39.0-60.6% [7]. In particular, a long-term repeated use of albendazole or mebendazole at provincial or national level, up to 10 or more years (once or twice a year), markedly reduced the prevalence of *T. trichiura* in China [11,12] and also in Cambodia (unpublished observations). In our study, egg reduction of *T. trichiura* was fairly remarkable after the MDA in Hlaing-thar-yar district. These together indicate that a prolonged use of benzimidazoles must be beneficial for long-term control of *T. trichiura*.

However, it should be reminded that Moser et al. [1,7] demonstrated a considerable temporal decrease of benzimidazole efficacy against trichuriasis, possibly in part due to an emergence of drug resistance. For example, 73% egg reduction rate of *T. trichiura* by albendazole in 1995 dropped down to 43% in 2015, and 91% egg reduction rate of *T. trichiura* by mebendazole in 1995 dropped down to 55% in 2015 [1]. Cure rates of albendazole also fell from 38.6% in 1995 to 16.4% in 2015 [7]. These decreases in efficacy could be explained by study-related confounders or by anthelmintic drug resistance [1]. Further studies are required to identify single nucleotide polymorphisms in the parasite gene which is associated with the drug resistance [1].

Our study clearly demonstrated difficulty in short-term control of *T. trichiura* by MDA using 400 mg single dose of albendazole and suggested the necessity of either a prolonged use of albendazole or use of an alternative regimen of albendazole or an alternative anthelmintic drug in the surveyed region of Myanmar. In this respect, sustained use of albendazole (400 mg single dose) for more than 10 years, or trial of new regi-

mens of albendazole, for example, 400 mg daily for 2-3 days, might be considered. However, the latter method seems not so feasible and not convenient for MDA, and repeated drug intake in each child may provoke untoward effects. Increasing the single dose of albendazole, for example, to 600 mg revealed no better efficacy than the recommended dose (400 mg) in treating *T. trichiura* infection [8].

Alternative drugs for *T. trichiura* include tribendimidine, ivermectin, oxantel pamoate, and moxidectin [1]. One or more of these drugs in combination with albendazole can be new candidates for use against *T. trichiura* [1,9]. In particular, oxantel pamoate alone or in combination with albendazole showed higher cure and egg reduction rates than albendazole alone [9]. However, oxantel pamoate is currently unavailable in Myanmar and will be expensive if imported from foreign countries. In the study of Speich et al. [9], oxantel pamoate and the matching placebo were self-manufactured at the University of Basel, Switzerland. Albendazole plus ivermectin, albendazole plus tribendimidine, and albendazole plus moxidectin can be other drug combinations for possible use in *T. trichiura* infection [1].

In our study, the egg positive rate of *O. viverrini*/MIF among the schoolchildren was very low, <0.1% on average. It is comparable with our previous report from the same districts targeting village people who revealed 0.7% egg prevalence of *O. viverrini*/MIF among 2,057 subjects examined [13]. The only adult worm (n = 1) harvested after chemotherapy and purging of an egg-positive villager was identified as *O. viverrini* [13]. Some *Enterobius vermicularis* eggs (among others; Table 1) were also detected from a few schoolchildren; however, this does not reflect the true figure of *E. vermicularis* infection because anal swab examinations should be done to properly evaluate the status of this nematode infection. It is worth to mention that our group separately performed anal swab examinations on a total of 761 schoolchildren in the same 3 districts of Yangon Region, and the average egg positive rate of *E. vermicularis* appeared to be very high, 47.2% [14].

Taken together, our study (MDA) using a single oral dose (400 mg) of albendazole showed a successful result for short-term (4 months) control of *A. lumbricoides* in primary schools of 3 districts in Yangon Region. However, its efficacy was not satisfactory in short-term control of *T. trichiura* in the same districts. Either prolonged use of albendazole for more than 10 years or changing the albendazole regimen into 2-3-day course (total 800 mg or 1,200 mg), or use of an alternative drug, for

example, oxantel pamoate, may bring about better control efficacy against *T. trichiura* infection in this region.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest related to this study.

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