

EFFICACY OF SINGLE DOSE ALBENDAZOLE ON THE PREVALENCE AND INTENSITY OF INFECTION OF SOIL-TRANSMITTED HELMINTHS IN ORANG ASLI CHILDREN IN MALAYSIA

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Abstract. The efficacy of a single-dose 400mg albendazole to treat *Ascaris*, *Trichuris* and hookworm infection was studied in Orang Asli community. Kato-Katz examination was performed on fecal samples which were collected before treatment, 1 and 4 months after treatment. A total of 123 children were involved in all three surveys. The cure rate of *Ascaris* infection was 97.4% and the egg reduction after treatment was 99.9%. The cure rate for hookworm infection was 93.1% with 96.6% egg reduction. Although the cure rate was low in *Trichuris* infection (5.5%), egg reduction was more evident (49.1%). The reinfection rate at 4 months after treatment was 54.5%, 3.6% and 10.3% for *Ascaris*, *Trichuris* and hookworm infection, respectively. Within 4 months after treatment almost one-fifth children with *Ascaris* and hookworm infection reached pre-treatment intensity infection. In *Trichuris* infection, however more than half of the children reached their pre-treatment intensity infection at 4 months after treatment. Findings suggest that 4-monthly targeted periodic treatment with 400 mg single-dose albendazole in highly endemic areas can have a significant impact on intensity infection of *Ascaris* and hookworm, but not on *Trichuris* infection.

INTRODUCTION

It is estimated that nearly a billion of the world's population are currently infected with *Ascaris*, and similar figures may apply to *Trichuris* and hookworm infection (soil-transmitted helminths, STH) (WHO, 1987). These infections continue to be global health problems, particularly among children, in poor community in developing countries (Salvioli *et al.*, 1992). Improvement in sanitation, water supply, housing conditions together with improvement of economic status in endemic areas have proven to be effective strategies in controlling STH infection (Henry, 1981, 1988; Ismail *et al.*, 1987, 1989; Che Ghanj *et al.*, 1989). However, constraints at the national and individual levels, control infection using the above mentioned control methods have become unrealistic and it also takes long time. In recent years the availability of single-dose broad spectrum anthelmintics has helped in reducing worm burden in endemic community. Studies have shown that periodic chemo-

therapy strategy has successfully lowered the intensity of infection of *Ascaris* (Thien-Hlaing *et al.*, 1987; Hall *et al.*, 1992).

The aim of this study was to evaluate the efficacy of single-dose 400mg albendazole in reducing the prevalence (measured by cure rate) and the intensity infection (reduction in egg counts) in a highly endemic area for STH in Malaysia. The reinfection rate and the status of intensity infection four months after treatment were also measured to determine the most appropriate targeted-treatment schedules for control measures.

MATERIALS AND METHODS

This study was part of a larger investigation conducted among residents of 6 Orang Asli (Abo-origines) villages in the District of Dengkil, Selangor, Malaysia situated 50 km from Kuala Lumpur. Each village comprised a very small population and most of the residents worked as palm oil estate laborers, rubber tapers, farmers or doing odd jobs such as fishing and selling forest

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products. Most of them lived in single-roomed houses made of bamboo and wood. Almost all the house in the villages had no electricity, no pipe water nor toilet facilities. The residents used well or river water for daily use and defecated in open ground among the bushes.

In all 205 children (95 males and 110 females) aged 1-13 years old were included in this study. Stool samples were collected from the children and those found infected were treated, under supervision, with a single 400 mg albendazole. All samples were examined by the Kato-Katz technic and intensity of infection of *Ascaris*, *Trichuris* and hookworm was measured indirectly as egg counts per gram (epg). Harada-Mori culture was done on all samples to identify hookworm species and also to detect *Strongyloides stercoralis*. Stool samples were collected and examined again at 1 and 4 months after treatment. In all 123 children were examined in all three phases of the study to evaluate the efficacy of treatment and reinfection rate occurred after 4 months of treatment. Egg counts and the changes in the intensity of infection before and after treatment were compared by a Student's *t*-test after logarithmic transformation of data and by Wilcoxon test, respectively.

RESULTS

The prevalence rates of *Trichuris*, *Ascaris* and hookworm infection before treatment in the cohort of 123 children examined in this study were 89.4%, 62.6% and 23.6%, respectively. The age-specific prevalence before treatment, 1 and 4 months after treatment, for each species is shown in Fig 1a, 1b and 1c. The prevalence of *Ascaris* and hookworm infection in every age group was reduced significantly following 1 and 4 months after treatment. However in *Trichuris* infection significant reduction in prevalence was only seen 1 month after treatment.

More than one-third (38.2%) of the children had moderate and severe infection of *Ascaris*; and two-thirds (68.0%) of the children had moderate and severe infection of *Trichuris*. However only 2.4% of the children had moderate infection of hookworm. The age-specific mean egg counts before treatment, 1 and 4 months after treatment for each species are shown in Fig 2a, 2b, 2c. There was a significant

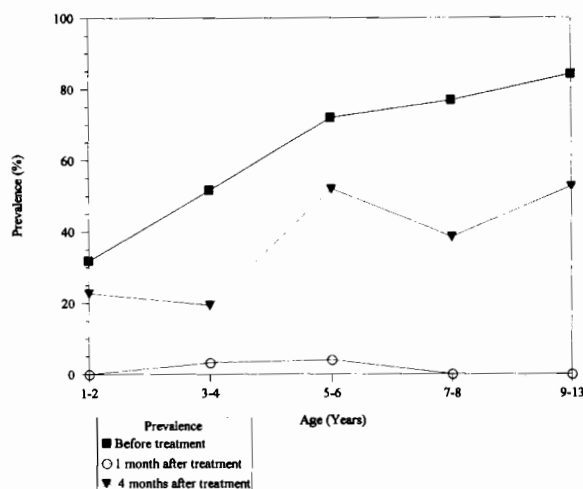


Fig 1a—Age specific prevalence of *Ascaris* before treatment 1 and 4 months after treatment.

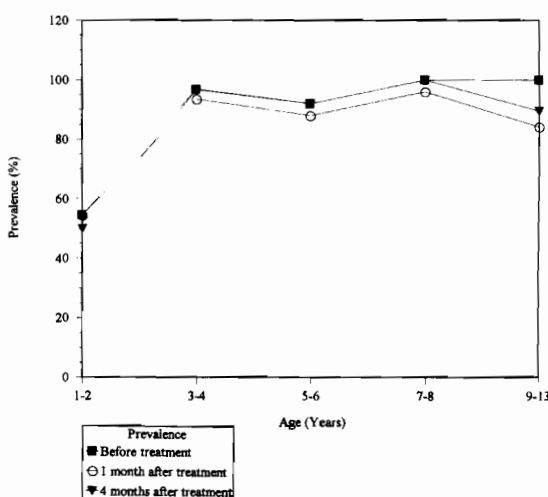


Fig 1b—Age specific prevalence of *Trichuris* before treatment 1 and 4 months after treatment.

reduction in the mean egg counts in every age group between before treatment and 1 month after treatment in *Ascaris*, *Trichuris* and hookworm infection. The overall cure rate for *Ascaris* was 97.4% and the egg reduction rate was 99.9%. The cure rate of hookworm infection was 93.1% and the reduction of egg counts was 96.6%. The effect of treatment was much less marked in *Trichuris* infection with only 5.5% cure rate. The impact of albendazole, however was more evident on the mean egg counts of *Trichuris*, with an overall reduction of 49.1%. Reinfection rate of *Ascaris*, *Trichuris* and hookworm

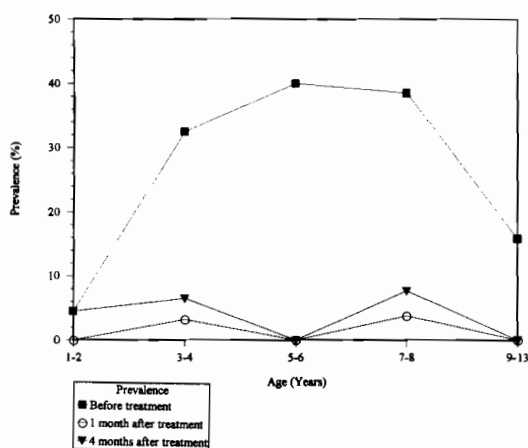


Fig 1c—Age specific prevalence of hookworm infection before treatment, 1 and 4 months after treatment.

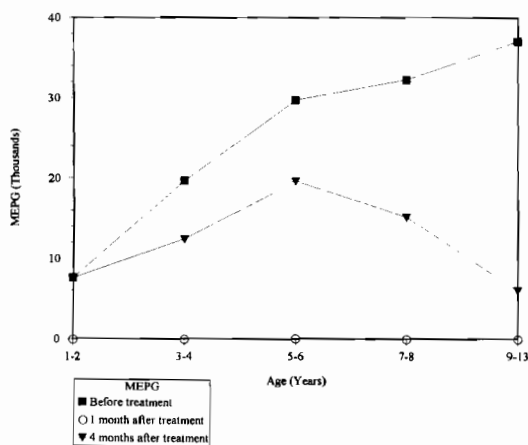


Fig 2a—Age specific mean egg per gram (MEPG) of *Ascaris* before treatment 1 and 4 months after treatment.

was 54.5%, 3.6% and 10.3%, respectively (Table 1).

Table 2 shows the changes in the intensity of STH infection at 1 and 4 months after treatment. Thirty-six (78.0%) children who were negative for *Ascaris* remained negative at 4 months of observation. Among children who had mild intensity of *Ascaris* infection 29 (96.7%) were cured of infection at 1 month after treatment. Four months after treatment 19 (65.5%) and 7 (23.3%) remained negative and in mild infection respectively. As for the children in the moderate group infection, 16 (96.7%) children were cured of infection at 1 month after

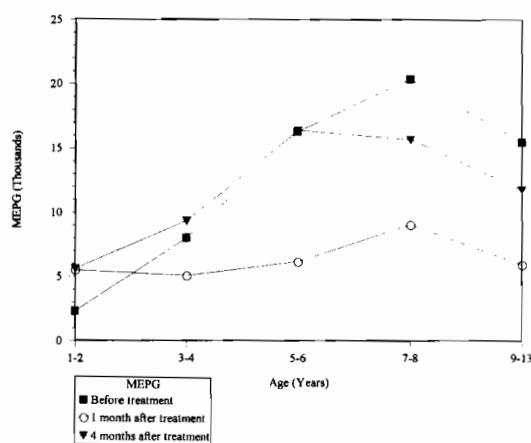


Fig 2b—Age specific mean egg per gram (MEPG) of *Trichuris* before treatment 1 and 4 months after treatment.

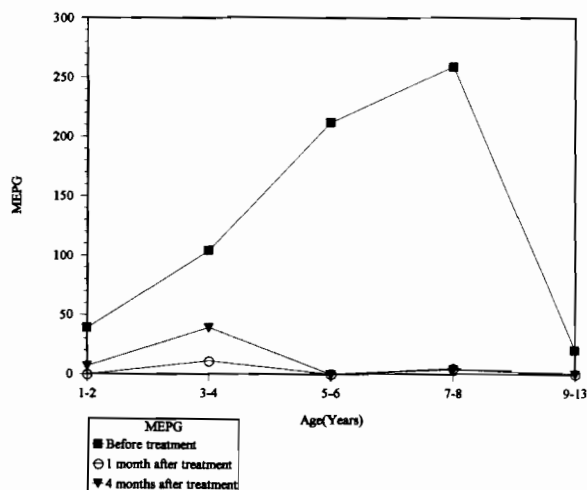


Fig 2c—Age specific mean egg per gram (MEPG) of hookworm before treatment 1 and 4 months after treatment.

treatment and 1 (5.9%) remained with moderate infection. At 4 months after treatment 8 (47.1%) and 3 (17.6%) children remained negative and moderate infection respectively. In the severe intensity group, all 30 (100.0%) children were cured of infection 1 month after treatment. However at 4 months after treatment 6 (20.0%) and 10 (33.3%) children remained negative and with severe infection, respectively. The differences in the changes of infection intensity at 1 and 4 months after treatment were significant. Only 6 (46.2%) children who were negative for *Trichuris* remained negative

Table 1

Cases of *Ascaris*, *Trichuris* and hookworm infection before treatment (1), 1 month (2) and 4 months (3) after treatment.

Infection	No. of cases			Cure rate (%)	Reinfection rate (%)	Mean eggs/gram			Egg reduction (%) paired <i>t</i> -tests
	1	2	3			1	2	3	
<i>Ascaris</i>	77	2	44	97.4	54.5	39,814	32	18,796	99.9%, <i>t</i> =9.26, <i>df</i> =76, <i>p</i> =0.0000
<i>Trichuris</i>	110	104	108	5.5	3.6	13,904	7,084	13,181	49.1%, <i>t</i> =3.97 <i>df</i> =109, <i>p</i> =0.0000
Hookworm	29	2	5	93.1	10.3	464	16	46	96.6%, <i>t</i> =3.39, <i>df</i> =28, <i>p</i> =0.002

at 4 months of observation. Among children who had mild *Trichuris* infection, 4 (15.4%) children were cured of infection 1 month after treatment and 17 (65.4%) children remained at mild infection. Four months after treatment 1 (3.8%) and 13 (50.0%) children remained negative and with mild infection, respectively. As for the children in the moderate infection group 2 (4.5%) were cured of infection. At 4 months after treatment 2 (4.5%) and 23 (52.3%) children remained negative and with moderate infection respectively. In the severe intensity group all 40 (100.0%) children were not cured of infection after 1 month of treatment. However 6 (15.0%) and 12 (30.0%) children had mild and moderate infections respectively. At 4 months after treatment 30 (75.0%) children remained with severe infection. The differences in the changes of infection intensity were only significant at 1 month after treatment.

Ninety-three (98.9%) children who were negative for hookworm remained negative at 4 months of observation. Among children who had mild hookworm infection, 24 (92.3%) children were cured of infection at 1 month after treatment and 2 (7.7%) remained with mild infection. Four months after treatment 21 (80.0%) and 5 (19.2%) children remained negative and with mild infection, respectively. As for the children in the moderate group infection, all 3 (100.0%) children were cured of infection. At 4 months after treatment all children remained negative. The differences in the changes of infection intensity at 1 and 4 months after treatment were significant.

DISCUSSION

This study indicated that STH infection is highly endemic in this community as shown by the high prevalence, with more than one-third and two-thirds of the children having moderate and severe infections of *Ascaris* and *Trichuris*, respectively. The efficacy of single-dose 400 mg albendazole was higher in *Ascaris* infection compared to hookworm and *Trichuris* infections: the cure rate was 97.4% in *Ascaris* infection compared to 93.1% in hookworm infection but only 5.5% in *Trichuris* infection. The effect of albendazole on egg reduction was very impressive in *Ascaris* and hookworm infection, with 99.9% and 96.6% egg reduction, respectively. Although the cure rate for *Trichuris* infection was low, the egg reduction of 49.1% was significant. High cure rates and egg reduction rates of *Ascaris* and hookworm infection with single-dose albendazole was reported in many studies (Pene *et al*, 1982; Ramalingam *et al*, 1983; Sinniah and Chew, 1988; Foo *et al*, 1989; Sinniah *et al*, 1990; Ismail *et al*, 1990; Jongsuksuntigul *et al*, 1993; Albonico *et al*, 1994).

In contrast, studies on the effect of single-dose 400 mg albendazole in the treatment of *Trichuris* infection is varied with most studies reporting low curative effect (Kan, 1984; Sinniah and Chew, 1988; Foo *et al*, 1989; Sinniah *et al*, 1990; Ismail *et al*, 1990; Albonico *et al*, 1994; Hall and Nahar, 1994). One study showed high drug efficacy (Jongsuksuntigul *et al*, 1993), but this was still less effective

Table 2

Changes in infection intensity according to species before treatment and after treatment (1 month and 4 months).

Before treatment (n)	Months after treatment							
	1				4			
	N(%)	Mi(%)	Mo(%)	S(%)	N(%)	Mi(%)	Mo(%)	S(%)
<i>Ascaris</i>								
N(46)	46 (100.0)	-	-	-	36 (78.0)	4 (8.7)	6 (13.0)	-
Mi(30)	29 (96.7)	1 (3.3)	-	-	19 (65.5)	7 (23.3)	3 (10.0)	1 (3.3)
Mo(17)	16 (94.1)	1 (5.9)	-	-	8 (47.1)	3 (17.6)	3 (17.6)	3 (17.6)
S(30)	30 (100.0)	-	-	-	6 (20.0)	5 (16.7)	9 (30.0)	10 (33.3)
	Wilcoxon Z=-7.5645, p=0.0000				Wilcoxon Z=-3.5512, p=0.0004			
<i>Trichuris</i>								
N(13)	10 (76.9)	3 (23.1)	-	-	6 (46.2)	6 (46.2)	1 (7.7)	-
Mi(26)	4 (15.4)	17 (65.4)	4 (15.4)	1 (3.8)	1 (3.8)	13 (50.0)	11 (42.3)	-
Mo(44)	2 (4.5)	17 (38.6)	20 (45.4)	5 (11.4)	2 (4.5)	7 (15.9)	23 (52.3)	12 (27.3)
S(40)	-	6 (15.0)	12 (30.0)	22 (55.0)	-	2 (5.0)	8 (20.0)	30 (75.0)
	Wilcoxon Z=-3.5862, p=0.0003				Wilcoxon Z=-0.9467, p=0.3438			
<i>Hookworm</i>								
N(94)	94 (100.0)	-	-	-	93 (98.9)	1 (1.1)	-	-
Mi(26)	24 (92.3)	2 (7.7)	-	-	21 (80.0)	5 (19.2)	-	-
Mo(3)	3 (100.0)	-	-	-	3 (100.0)	-	-	-
	Wilcoxon Z=-4.5407,p=0.0000				Wilcoxon Z=-4.0629,p=0.0000			
Intensity of infection (WHO, 1987)								
	<i>Ascaris</i>				<i>Trichuris</i> and hookworm			
N=Negative	epg=0				epg=0			
Mi=Mild	epg=1-9,999				epg=1-1,999			
Mo=Moderate	epg=10,000-49,000				epg=2,000-9,999			
S=Severe	epg=50,000 and above				epg=10,000 and above			

when compared to *Ascaris* and hookworm infection. The reasons for the differences in the results in many of the studies are unknown. However drawing from experience in our study, a high percentage of children with moderate and severe infections of *Trichuris* infection may be one explanation why efficacy of albendazole is poor. A study by Foo *et al* (1989) showed that the efficacy of albendazole against *Trichuris* depends on the intensity of infection, *ie*, the cure rate was lower in severe infection compared to mild infection and this was also seen in this study. In contrast, a study by Hall and Nahar (1994) in Bangladesh indicated that single-dose 400 mg albendazole gave very poor cure rate although more than 70% of the subjects studied had light infections of *Trichuris*. Studies have shown that by giving 400 mg albendazole daily for three days, the cure rate improved to 80.0% and 91.5% (Hall and Nahar, 1994; Pangga-bean *et al*, unpublished data). The low cure rate for *Trichuris* infection in our study and significant egg reduction rate could be explained by the higher efficacy of single-dose 400 mg albendazole in affecting the fecundity of the female worm rather than the clearance of *Trichuris* worms.

Field studies describing reinfection of *Ascaris*, *Trichuris* and hookworm infection following single-dose 400 mg albendazole have been reported before (Albonico *et al*, 1995; Oothuman *et al*, 1995). Study by Oothuman *et al* (1995) showed a reinfection rate of *Ascaris* and *Trichuris* at 3 months following 400 mg/daily albendazole for 2 days of 18.8% and 45.8%, respectively. In this study the results indicated that more than 50.0% and 10.0% of the cured children respectively were reinfected again with *Ascaris* and hookworm respectively at 4 months after treatment.

Almost one-fifth of the children reinfected with *Ascaris* reached their pre-treatment intensity at 4 months post-treatment. For *Trichuris* infection only 3.6% of cured children were reinfected again with *Trichuris*. However, in our study *Trichuris* infection should be considered as a continuing infection rather than reinfection because of the poor cure rate at the start. More than half of the *Trichuris* infected children reached their pre-treatment intensity at 4 months after treatment. Study by Albonico *et al* (1995) showed that by 6 months the intensities of infection were similar to pre-treatment levels. The finding of 4-monthly periodic treatment may be relevant for the planning of retreatment schedule in endemic areas.

Single-dose 400 mg albendazole gave a good cure rate and egg reduction rate in *Ascaris* and hookworm infection. However it was much less effective against *Trichuris* infection, although the egg reduction was significant. In endemic areas where transmission occurred continuously, periodic chemotherapy alongside other control measures is necessary to reduce the worm load in the community. Our findings suggest that 4-monthly targeted periodic treatment to the children with 400 mg single-dose albendazole in highly endemic areas can have some significant impact on the intensity of *Ascaris* and hookworm infection.

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