Responses to Albendazole Treatment for Hookworm Infection in Ethnic Thai and Immigrant in West-central Thailand

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Ethnic Thai and immigrant schoolchildren and villagers of Bo-ong, a village in Pilok sub-district, Thong Pha Phum District, Kanchanaburi Province, western Thailand, were investigated for helminth infections in September 2003 and July 2004. Among the 143 schoolchildren, total cumulative hookworm prevalence in both surveys was 58.7%, with 47.6% for Thais and 63.4% for immigrants, while among the 183 villagers, it was 69.4% (Thais: 60.6%; immigrants: 75.0%). The efficacy of 400 mg single-dose albendazole among different hookworm-infected racial/ethnic groups was analyzed 21 days' post-treatment. Kato-Katz and polyethylene tube cultivation methods were used for stool examination. Among the 211 hookworm-positive cases in both surveys, only 82 cases from the last survey were followed up. By Kato-Katz technique, for the schoolchildren and villagers combined, the cure rate tended to be higher among the immigrants (65.0%) than the Thais (54.6%) ($p = 0.445$). By Sasa's modified Harada-Mori culture technique, the cure rates also differed by racial grouping, and were higher (46.3%) among the immigrants and lower (27.8%) among the Thais ($p = 0.269$). However, similar egg reduction rates were found for the two racial groups, at 96.0 and 92.6%, respectively. In addition, a higher intensity of hookworm infection tolerated albendazole therapy, lower cure rates were obtained in moderate-to-heavy infections (56.3%) and higher rates for light infections (63.6%) among the total population. There were no significant differences in drug efficacy among the 2 ethnic groups of Thai and immigrants ($p > 0.05$) in Kanchanaburi Province, Thailand.

Key words —— hookworm, albendazole, Thailand, Kanchanaburi, ethnic groups

INTRODUCTION

Hookworm infection is a major soil-transmitted helminthiasis that causes health problems among the population, particularly children in poor communities in developing countries. In Thailand, overall nationwide hookworm infection decreased from 40.6% in 1982, to 11.4% in 2001.[1, 2] However, the prevalence was higher in southern Thailand than other parts of the country, where the prevalence in 14 southern provinces in 1989 was 68.8%.[3] Consequently, in other parts of the country, especially in remote areas, prevalence remains high.[4, 5]

Albendazole, a benzimidazole anthelminthic, has been widely used in large-scale treatment programs for intestinal nematode infections, including hookworm, with a recommended 400 mg single dose. Studies have shown high variability in drug efficacy for hookworm and *Trichuris* infections in different regions. In Africa, where hookworm infection is caused by *Necator americanus*, a single-dose treatment with albendazole was effective, with 78.8%[6] and 56.8%[7] cure rates in over 1000 pupils in a number of primary schools 3 weeks' post-treatment. In China, albendazole is highly effective, with a 95.4% cure rate against hookworm infection caused by *N. americanus* and *Ancylostoma duodenale* (*N. americanus*: *A. duodenale* ratio = 1 : 0.7) in adult populations in Hunan Province, when assessed by Kato-Katz technique 14 days' post-treatment.[8] In ancylostomiasis hookworm, a high cure rate (92.2%) was obtained in 480 patients aged 2–60 years,[9] while an 87.2% cure rate was reported in children aged 2–15 years.[10] In Kanchanaburi Province, western Thailand, a number of neighboring minority ethnic populations have mi-

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grated and settled along the Thai-Myanmar border over several decades. This study aimed to evaluate the effective differences in treatment against hookworm infections for two main groups, immigrant and ethnic Thai schoolchildren and villagers in a remote area of western Thailand, using single-dose albendazole.

MATERIALS AND METHODS

Characterization of the Study Areas and Population —— The study was carried out in Bo-ong, a village in Pilok Subdistrict, Thong Pha Phum District, Kanchanaburi Province, west-central Thailand. The village is located southwest of the water basin of Vajiralongkorn Dam, close to the Thai-Myanmar border. It is a rural highland surrounded by perennial water, and to the west, by heavy forest, and a partial plain area. Communication to and from nearby villages and the district centers is limited to boat or foot. There are approximately 800 residents, 70% of whom are immigrants. The majority of the immigrants are Karen (90%), and the rest are Mon, Karang, Myanmar, and Laos. Between ethnic Thai and immigrant group, there are no obvious differences of ethnical characteristics, food and cooking habits or occupational activities. However, the immigrant group earned lower income and is laborious worker. There is no local health station; the health service for the villagers is at Thong Pha Phum District Hospital. The climate of the area is tropical with hot, rainy, and dry seasons. The main occupations are rice and cassava agriculture, and fishing. No house in the village had electricity or piped water. The village water supply was in a precarious condition, available via direct piping from the mountain to the village temple, where the residents needed to convey it independently. The water volume during the dry season was inadequate. Houses in the village were built of wood, roofed with corrugated iron sheeting or thatch. A small number of houses had toilet facilities. The community had a branch of the municipal primary school, but no building or rooms for classes, so that the temple's multi-purposes open hall was arranged into classrooms.

Parasitological Examination and Follow-up —— The study was approved by the ethics committee of the Faculty of Tropical Medicine, Mahidol University and informed consent was obtained from the subjects. The studied subjects were schoolchildren of the village primary school and villagers aged > 5 years. Two parasitological surveys of both schoolchildren and villagers were carried out in September 2003 and July 2004. Stool boxes were distributed through the teachers to the schoolchildren, and the village leader to the villagers. All stool samples were examined by Kato-Katz technique[11] and the level of intensity followed the World Health Organization (WHO) classification.[12] All cases of helminthic infection were treated with albendazole 400 mg single dose, except those with *Trichuris* infection, who received it for 3 consecutive days. Follow-up treatment was performed only at the last survey, in July 2004, 21 days' post-medication, when the stool containers were distributed, and the feces of treated patients collected and re-examined by Kato-Katz technique. Sasa's modified polyethylene tube cultivation technique was used for samples of pre-treated hookworm-positive cases, to detect filariform larvae.[13, 14] Only hookworm-infected cases were assessed for the curative efficacy of albendazole. The egg-reduction rate (the ratio of egg-count per gram of feces reduced from pre-treatment to post-treated levels) was also analyzed. Mixed hookworm- and *Trichuris*-infected cases were excluded from the cure analysis.

Statistical Analysis —— Two groups of the examined population, schoolchildren and villagers, were constituted by race—ethnic Thais and immigrants. Hookworm prevalence and cure rates after treatment were used for comparison among the two population groups. Associations among category variables were tested by Fisher' exact test.

RESULTS

Parasitic Infections in the Schoolchildren

The school had a total of 162 students (70 males; 92 females). Of these, 47 were Thais and 115 immigrants; 88.3% (143/162) of the schoolchildren participated in stool examinations during the study period. The stool examination results are shown in Table 1. Prevalence is expressed as cumulative positives for helminth eggs in both surveys. The overall prevalence of all 3 kinds of soil-transmitted helminthic infections was 62.9%; it was higher in immigrant schoolchildren (66.3%) than Thais (54.8%). The higher pattern of prevalence among immigrants was seen in all types of helminthic infection. Hookworm was the most

Table 1. Stool Results for Primary School Children and Villagers Aged 5–78 Years in Bo-ong, Pilok Subdistrict, Thong Pha Phum District, Kanchanaburi Province, in September 2003 and July 2004, by Kato-Katz Technique

	Number Examined	STH[c)] (%)	Hookworm (%)	*Trichuris* (%)	*Ascaris* (%)	*Taenia* (%)
Schoolchildren						
Thai	42	23 (54.8)	20 (47.6)[d)]	4 (9.5)	1 (2.4)	0
Immigrant	101	67 (66.3)	64 (63.4)[d)]	13 (12.9)	2 (2.0)	2 (2.0)
Total	143[a)]	90 (62.9)	84 (58.7)	17 (11.9)	3 (2.1)	2 (1.4)
Villagers						
Thai	71	43 (60.6)	43 (60.6)[e)]	1 (1.4)	0	1 (1.4)
Immigrant	112	85 (75.9)	84 (75.0)[e)]	14 (12.5)	6 (5.4)	5 (4.5)
Total	183[b)]	128 (69.9)	127 (69.4)	15 (8.2)	6 (3.3)	6 (3.3)

a) Males 61, Females 82, *b*) Males 92, Females 87, Not specified 4, *c*) STH = Soil-transmitted helminths, *d*) $p = 0.095$, *e*) $p = 0.048$.

common parasite, occurring in 58.7% of the examined students, with 63.4% in immigrants and 47.6% in Thais. No significant difference was found between the Thai and immigrant groups for hookworm infection, $p = 0.095$. *Trichuris* infection was moderate, with 11.9% overall prevalence, and 12.9% in immigrants and 9.5% in Thais. *Ascaris* was a minor infection, in approximately 2% of cases. *Taenia* eggs were found in 2.0% of immigrants, *i.e.*, in two immigrant boys. A small number of schoolchildren had mixed infections with 2 or 3 kinds of helminths. Among the mixed infections, almost all cases were immigrant children; the most common combination of helminths was hookworm and *Trichuris*. One immigrant boy in grade 1 had triple mixed infections with hookworm, *Trichuris* and *Ascaris* (Data not shown).

Parasitic Infections in the Villagers

A total of 183 villagers (92 males; 87 females; 4 not specified) were enrolled for stool examination during the study. Approximately 60% (112) were immigrants and the rest, 40% (71), were Thais. They had similar infection rates to the schoolchildren, and the cumulative positive rates for each parasitic infection among the immigrants were higher than among the Thais. These included soil-transmitted helminths (STH) 75.9% and 60.6%; hookworm 75.0% and 60.6%; *Trichuris* 12.5% and 1.4%; *Ascaris* 5.4% and 0%; and *Taenia* 4.5% and 1.4%, respectively (Table 1). Hookworm infection was the most prominent in both immigrants and Thais, with an overall prevalence of 69.4%, which almost equaled that of STH (69.9%). There was a slight significant difference in hookworm infection among the Thai and immigrant villager groups, $p = 0.048$. Analysis of the combination of schoolchildren and villagers showed a significant difference in hookworm infection between these two groups, $p = 0.015$.

Treatment Efficacy

A total of 211 hookworm-positive cases of both surveys, 52 villagers and 30 schoolchildren of the last survey, were enrolled for albendazole therapy at 400 mg single dose and follow-up drug efficacy were assessed at 21 days' post-treatment. Most of the hookworm-infected cases (66; 80.5%) (22 schoolchildren and 44 villagers) in the 82 follow-up cohort had light-intensity infections. No heavy infection was found in the schoolchildren, and only one was found in each of the Thai and immigrant villager groups. Moderate infection was found in 2 Thai and 6 immigrant schoolchildren; and 3 each of Thai and immigrant villagers (Fig. 1). The average number of eggs per gram (NEPG) of feces in each intensity class is shown in Table 3. The stool results after albendazole administration are shown in Table 2. The immigrant villagers showed a higher response to albendazole by Kato-Katz technique and tended to had a higher cure rate (72.2%) than the Thais (56.3%), $p = 0.340$. The schoolchildren showed a similar trend, higher (54.2%) for immigrants than Thais (50.0%), $p = 0.999$. However, the cure rates in the two groups of villagers plus schoolchildren, immigrants (65.0%) and Thais (54.6%) did not differ significantly ($p = 0.445$).

Seventy-two stool samples from 82 follow-up patients were deemed sufficient for stool culture. Cure rate assessed by coproculture was generally lower than by Kato-Katz technique. However, similar result patterns were obtained; the immigrants, either schoolchildren or villagers, showed better responses to albendazole treatment than the Thais.

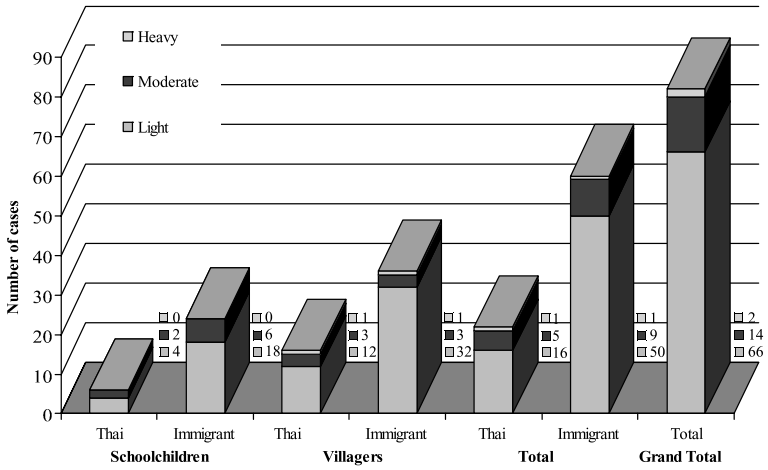

Fig. 1. Hookworm-infected Cases of Thai and Immigrant Schoolchildren and Villagers, Grouped by Intensity Class of Infection
Light: < 2000 EPG, Moderate: 2000–7000 EPG, Heavy: > 7000 EPG. EPG = egg per gram of feces.

Table 2. Efficacy of Albendazole 400 mg Single Dose Against Hookworm Infection in Primary School Children and Villagers Aged > 10 Years in Bo-ong, Pilok Subdistrict, Thong Pha Phum District, Kanchanaburi Province, in September 2003 and July 2004, by Kato-Katz and Culture Techniques

	Kato-Katz		Culture	
	No. treated	No. cured (%)	No. treated	No. cured (%)
Schoolchildren				
Thai	6	3 (50.0)[a)]	6	2 (33.3)
Immigrant	24	13 (54.2)[a)]	23	10 (43.5)
Total	30	16 (53.3)	29	12 (41.4)
Villagers				
Thai	16	9 (56.3)[b)]	12	3 (25.0)
Immigrant	36	26 (72.2)[b)]	31	15 (48.4)
Total	52	35 (67.3)	43	18 (41.9)
Schoolchildren plus Villagers				
Thai	22	12 (54.6)[c)]	18	5 (27.8)[d)]
Immigrant	60	39 (65.0)[c)]	54	25 (46.3)[d)]
Total	82	51 (62.2)	72	30 (41.7)

a) $p = 0.999$, *b*) $p = 0.340$, *c*) $p = 0.445$, *d*) $p = 0.269$.

The cure rates for immigrant schoolchildren and villagers were 43.5 and 48.4%, respectively, whereas those of the Thais were 33.3 and 25.0%. The overall cure rate for the studied population, assessed by fecal culture, was 41.7%. There was no significant difference in the cure rate for the immigrants (46.3%) and Thais (27.8%) ($p = 0.269$; Table 2).

Cases with light-intensity infections had better responses to drug therapy, and a higher cure rate (63.6%) was obtained than the moderate-plus-heavy infections (56.3%). Consequently, the immigrants responded well, with 66.0% in light and 60.0% in moderate-plus-heavy infections, whereas the Thais responded more poorly, with 56.3% in light and 50.0% in moderate-plus-heavy infections. The overall cure rate in the studied population was 62.2% (Table 3).

Albendazole induced a high-percentage reduction in egg count (93.9%). The 2 groups of study subjects showed similar egg-reduction rates (ERR), at 96.0% for Thais and 92.6% for immigrants. Lower ERR for either Thais (84.1%) or immigrants (80.4%) were obtained for light-intensity infections than for moderate-plus-heavy infections (98%; Table 3).

Table 3. Cure and Egg Reduction Rates (ERR) for Hookworm Infection Obtained after Albendazole Treatment, by Intensity of Infection

(a) In Thais and Immigrants (Schoolchildren plus villagers)

Intensity	Thais				
	Pre-Treatment		Post-Treatment		
	No. of cases	EPG (Range)	No. cured (%)	EPG (Range)	ERR (%)
Light	16	597 (40–1880)	9 (56.3)	95 (0–480)	84.1
Moderate plus Heavy	6	6447 (2080–18440)	3 (50.0)	67 (0–280)	98.9
Total	22	2193 (40–18440)	12 (54.6)	87 (0–480)	96.0
Intensity	Immigrants				
	Pre-Treatment		Post-Treatment		
	No. of cases	EPG (Range)	No. cured (%)	EPG (Range)	ERR (%)
Light	50	493 (40–1960)	33 (66.0)	97 (0–1520)	80.4
Moderate plus Heavy	10	4708 (2200–13880)	6 (60.0)	48 (0–360)	98.1
Total	60	1195 (40–13880)	39 (65.0)	89 (0–1520)	92.6

(b) In the Studied Populations (Thais and Immigrants) of Schoolchildren (30) plus Villagers (52)

Intensity	Thais and immigrants				
	Pre-Treatment		Post-Treatment		
	No. of cases	EPG (Range)	No. cured (%)	EPG (Range)	ERR (%)
Light	66	518 (40–1960)	42 (63.6)	96 (0–1520)	81.4
Moderate plus Heavy	16	5360 (2080–18440)	9 (56.3)	55 (0–360)	98.9
Total	82	1463 (40–18440)	51 (62.2)	88 (0–1520)	93.9

EPG: eggs per gram of feces.

DISCUSSION

Soil-transmitted helminthiases, particular hookworm infection, are still highly prevalent in Thailand. More than 50% of the studied population, either schoolchildren or villagers, were infected (Table 1), and the immigrant group had higher prevalence than the Thais. At baseline, these two groups of patients showed a significant difference in hookworm prevalence which is the main infection under study. After treatment with albendazole, the cure rates tended to be higher among the immigrants than the Thais, but were found to have no significant difference. The significant difference in hookworm prevalence shifted to an insignificant difference after albendazole therapy. However, our data indicated no association between hookworm infection and race. Nontasut *et al.* studies the treatment of trichuriasis with mebendazole and found insignificantly different cure rates among two groups of patients, Thais and Karen, residing in different regions of Thailand.[15] Unfortunately, this study reported no statistical analysis of prevalence prior treatment in these two host groups.

To assess the efficacy of drug treatment, the type of diagnostic test is an important factor. The coproculture method is designed to diagnose nematode infections like hookworm, where the parasites give rise to a larval stage that dwells in the soil. This method can detect larvae even in very light infections. Marwi[16] compared Katz's modified Kato's thick-smear method with Harada-Mori culture for detecting hookworm infection and found a 78.8% recovery rate for the former and 85.8% for the latter in 354 known hookworm-egg-positive stool samples. Our results for hookworm infection recovery after albendazole treatment agreed with the above report. A higher recovery rate for hookworm larvae by culture method was found than for hookworm eggs by Kato-Katz technique. On the other hand, a lower cure rate was obtained by culture method than by Kato-Katz technique.

The initial intensity class of infection influences drug efficacy; cure rates declined with increasing intensity of infection. Nontasut *et al.*[17] reported cure rates varied from 66.6, 64.3, and 50.0% in light, moderate, and heavy hookworm infections, respectively, with a 64.6% total cure rate for primary

schoolchildren with an average age of 10 years. Similarly, in adult patients, a cure rate of 75.0% with NEPG < 5000, and 50.0% with NEPG > 5000 were recorded by Viravan *et al*.[18] Our cure-rate results agreed well with those investigators.

Albendazole produced substantial reductions in hookworm egg loads. A similar high ERR of 96.6% was obtained in 29 aborigine (Orang Asli) hookworm-infected patients 1–13 years old, and 94.5% of 32 residents of rubber and oil-palm estates in Malaysia.[19, 20] Moreover, Sitthichareonchai *et al*.[21] reported equal ERR (96.0%) in patients with different NEPG of < 1000 and > 10000. Our results, by contrast, showed higher ERR in NEPG > 2000 (98.5%) than in NEPG < 2000 (81.5%).

A wide variety of results have been obtained for drug efficacy of anthelminthics in hookworm infection. A number of factors could reflect variations in drug efficacy; we demonstrated type of diagnostic test and initial intensity class of infection. Although different ethnic/racial populations showed some different responses to albendazole, no significant differences were found in drug efficacy among the 2 ethnic groups, Thai and immigrant populations in Kanchanaburi Province, Thailand.

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