RANDOMIZED COMPARATIVE TRIAL OF TWO HIGH-DOSE ALBENDAZOLE REGIMENS FOR UNCOMPLICATED HUMAN STRONGYLOIDIASIS

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Abstract. A randomized trial study was conducted comparing the efficacy of two high-dose regimens of albendazole for the treatment of uncomplicated human strongyloidiasis. Agar plate culture (APC) was used as an evaluation technique for coprological diagnosis. All 115 subjects infected with *Strongyloides stercoralis* from 7 provinces in northeastern Thailand were divided randomly into two groups. Regimen-1 group received albendazole 800 mg/day twice daily for 3 consecutive days, and regimen-2 group received the same dose for 5 consecutive days. For each regimen, the same treatment was repeated once 7 days later. Stools were parasitologically examined at 14 days, and 10 days after the second course of treatment, respectively. A coprological cure rate of 87.9% (51/58) was obtained in the regimen-1 group, with 89.5% (51/57) in the regimen-2 group, which was not statistically significantly different ($P = 0.794$). The mild adverse effects were not statistically different between the two groups, at 8.6% and 8.8%, respectively ($P = 0.977$). We therefore suggest albendazole treatment using regimen 1 should be recommended. However, the use of new effective drugs should be considered, especially in hyperinfective strongyloidiasis.

INTRODUCTION

Strongyloidiasis, a serious threat to public health in tropical and subtropical areas, is an intestinal parasitic disease caused by *Strongyloides stercoralis* (Pearson, 2002). The prevalence of *S. stercoralis* in Thailand has been measured at 23.5% in the northeast (Jongsuksuntigul *et al*, 2003), and 24.5% in the north (Sukhavat *et al*, 1994). The clinical spectrum of strongyloidiasis varies from asymptomatic infection, to mild symptomatic abdominal and skin diseases, to fatal disseminated infection in immunosuppressed patients (Grove, 1996). Therefore, effective treatment is essential to prevent severe infection.

The efficacy of treating strongyloidiasis with albendazole has been inconsistent even when the same drug was used in similar regimens (Horton, 2000; Nontasut *et al,* 2005), for which several reasons have been proposed; one may be the differing sensitivity of methods used to assess treatment efficacy; different periods between treatments and follow-up examination may be another explanation, since incomplete treatment has frequently resulted in relapse.

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The current study compared the efficacy and drug safety of two high-repeated-dose regimens of albendazole for treating uncomplicated human strongyloidiasis. Agar plate culture (APC), the most sensitive coprological diagnosis technique, was used for assessment.

MATERIALS AND METHODS

A randomized comparative trial of uncomplicated strongyloidiasis was conducted in upper northeastern Thailand (Khon Kaen, Kalasin, Udon Thani, Loei, Nong Bualamphu, Nong Khai and Sakhon Nakhon), in 2002-2003. A total of 126 subjects infected with *S. stercoralis*, as diagnosed by APC technique, aged > 10 years, with no history of serious disease (*ie* renal, liver, or cardiovascular disease), with informed consent, were included in the study. They were weighed and histories were taken of drug allergy, pregnancy, breast feeding, or whether they had received any anthelmintic drug in the past 3 months, to elicit factors meeting the exclusion criteria, prior to drug administration. All participants were instructed to report any adverse drug reactions occurring post-treatment using a standard questionnaire. The final number of subjects in this study was 115 cases.

All 115 subjects were randomized using sequential allocation, and divided into two groups. Albendazole (Thailand Government Pharmaceutical Organization)

was administered orally at a dose of 800 mg/day after meals, twice daily. Group 1 (58 subjects) received albendazole for 3 consecutive days (regimen 1), whereas group 2 (57 subjects) received the same doses for 5 consecutive days (regimen 2). For each regimen, the same dose of albendazole was repeated once, 7 days later. Drug efficacy was evaluated by parasitological examination using APC technique (Intapan *et al,* 2005) at 14 days, and 10 days after the second course of treatment, respectively. Analysis of drug efficacy and its adverse effects was carried out by chi-square test using SPSS for windows version 9.0 (SPSS Inc, Chicago, Illinois, USA) to determine the significance levels among the two regimen groups. The Student's *t* test was used to compare means.

RESULTS

Of the 126 uncomplicated strongyloidiasis cases, 115 were enrolled in the trial, 11 subjects were excluded for medical reasons, and some were lost to follow-up. Seventy males (60.9%) and 45 females (39.1%) participated in the evaluation of the efficacy of two repeated high doses of albendazole. The baseline age, weight and sex of both groups were similar. The mean age was 47.6 ± 14.8 years and 46.1 ± 15.0 years (Student's *t*-test = 0.527, p = 0.599) for the regimen-1 and regimen-2 groups, respectively; the mean weight was 57.2 ± 9.7 kg and 58.4 ± 8.7 kg (Student's *t*-test = 0.664, p = 0.508) in the regimen-1 and regimen-2 groups, respectively. There was no significant gender difference between the groups (λ^2= 0.775, p = 0.379), as shown in Table 1.

Two high repeated doses of albendazole gave cure rates of 87.9% (51/58) and 89.5% (51/57), with no statistically significant difference (λ^2= 0.068, p = 0.794), in the regimen-1 and regimen-2 groups, respectively (Table 1). All subjects tolerated the drug well, with no serious side effects. Minimal adverse effects of albendazole, including constipation, abdominal discomfort, sleepiness, dizziness or malaise, occurred in 10/115 (8.7%) subjects with no statistically significant difference between the two groups (λ^2= 0.001, p = 0.977), as shown in Table 2. All symptoms were mild and transient, and subsided without medical treatment within one day.

DISCUSSION

The present study revealed no significant difference in efficacy between two high-dose regimens of albendazole for uncomplicated human strongyloidiasis. Neither increasing the high dose, extending the duration of treatment, or repeating treatment showed complete eradication. These results were similar to previous reports (Pitisuttithum *et al,* 1995; Toma *et al,* 2000; Nontasut *et al,* 2005). In addition, no

Table 1
Factors contributed in treatment outcome of two high doses regimens of albendazole in uncomplicated human strongyloidiasis.

Factors / Treatment outcome	Regimen-1 group	Regimen-2 group
No. of subjects (%)	58 (50.4)	57 (49.6)
Mean age ± SD; range (yr)[a]	47.6 ± 14.8; 12 – 74	46.1 ± 15.0; 12 - 73
Mean weight ± SD; range (kg)[b]	57.2 ± 9.7; 32 – 87	58.4 ± 8.7; 43 - 74
Sex[c]		
Male (%)	33 (47.1)	37 (52.9)
Female (%)	25 (55.6)	20 (44.4)
Albendazole regimens (800 mg/day twice daily)	for 3 days repeated 7 days later	for 5 days repeated 7 days later
Post-treatment follow-up	day 14	day 10
Cure rate (%)[d]	51 (87.9)	51 (89.5)

[a]p = 0.599; [b]p = 0.508; [c]p = 0.379 and [d]p = 0.794.

Table 2
Adverse effects of albendazole occurred in both regimen groups.

Symptoms	Regimen-1 group[a] No. (%)[c]	Regimen-2 group[b] No. (%)
Constipation	3 (5.2)	0
Abdominal discomfort	1 (1.7)	4 (7.0)
Sleepiness	0	1 (1.8)
Dizziness	1 (1.7)	0
Malaise	0	2 (3.6)

[a]5 of 58 (8.6%) has adverse effects; [b]5 of 57 (8.8%) has adverse effects; [c]p = 0.977 (regimen-1 group *vs* regimen-2 group).

statistically significant difference for adverse effects between the two regimens was shown. These results suggest that it is not useful to extend duration of treatment, so that using albendazole under regimen 1 is recommended. However, the use of new effective drugs should be considered *ie* ivermectin (Nontasut *et al,* 2005), especially in hyperinfective strongyloidiasis. Nontasut *et al* (2005) reported that treatment of human strongyloidiasis with ivermectin yielded a cure rate of 98.7%.

Ivermectin has proven highly effective against *S. stercoralis* (Grove, 1996; Toma *et al*, 2000; Nontasut *et al,* 2005). However, this drug is not available for the treatment of human strongyloidiasis in Thailand. Side effects were also indicated for the ivermectin-treated group, *ie*, anorexia, nausea, diarrhea, diffuse itching and drowsiness (12.7%), whereas the albendazole-treated group experienced nausea and diarrhea (5.7%) (Nontasut *et al,* 2005). The results showed that the side effects of albendazole were milder than those of ivermectin. Nevertheless, a regimen of albendazole 800 mg/day twice daily for 3 consecutive days yielded a reasonable cure rate and can be used in areas where ivermectin is unavailable.

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