

Albendazole alone vs. albendazole and diethylcarbamazine combination therapy for trichuriasis

Windya Sari Nasution, Muhammad Ali, Ayodhia Pitaloka Pasaribu,
Syahril Pasaribu, Chairuddin P. Lubis

Abstract

Background *Trichuris trichiura* is one of the most common soil-transmitted helminths, estimated to infect 1 billion people worldwide. Several studies have compared the efficacies of albendazole and diethylcarbamazine, but the efficacy of a combination of these two drugs has been inconclusive.

Objective To assess the effectiveness of a single dose of albendazole compared to a combination of albendazole and diethylcarbamazine for trichuriasis treatment.

Methods A randomized, clinical open trial was conducted from June to September 2009 on elementary school children with trichuriasis from two villages in the North Sumatera Province. Stool specimens were collected at baseline and at days 7, 14, 21, and 28 after treatment, and examined by the *Kato Katz* method. Subjects were randomized into two groups. Group I received a single dose of albendazole (400 mg) and group II received albendazole (400 mg) plus diethylcarbamazine (6 mg/kg). Statistical analyses used were Chi square test for cure rates and *Wilcoxon* rank test for egg reduction rates.

Results One hundred eight children were enrolled and randomized into group I (53 children) and group II (55 children). The prevalence of *T. trichiura* infection was 54.7%. There were no significant differences ($P=0.52$) in the cure rate between groups I and II (66% and 60%, respectively) or in egg reduction rates at day 28 (54.5% and 60.07%, respectively, $P=0.10$).

Conclusion Albendazole alone and albendazole combined with diethylcarbamazine have similar efficacies for trichuriasis treatment, in terms of cure rates and egg reduction rates. [Paediatr Indones. 2014;54:109-13].

Keywords: albendazole, diethylcarbamazine, trichuriasis

Intestinal parasitic infections are a serious worldwide public health problem, including in Indonesia.¹ *Trichuris trichiura* is one of the most common soil-transmitted helminths, estimated to infect 1 billion people worldwide.^{2,3} Many of those infected live in warm, humid, tropical countries, and are often also infected with *Ascaris lumbricoides*.^{4,5} The prevalence in Asia is more than 50%, especially in rural areas with inadequate sanitation and poor hygiene.⁵

Albendazole is the most widely used drug for the control of soil-transmitted helminthiasis.^{6,7} It impairs glucose uptake in adult worms, resulting in immobilized intestinal parasites that slowly die.⁷ Albendazole is given orally as a single dose of 400 mg for children aged greater than 2 years and as a half dose for children ≤ 2 years.^{8,9} Diethylcarbamazine, a synthetic piperazine derivative, is the drug of choice for filariasis and is also used to eradicate *T. trichiura*.^{9,10}

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From the Department of Child Health, University of Sumatera Utara Medical School, H. Adam Malik Hospital, Medan, Indonesia.

Reprint requests to: Windya Sari Nasution, University of Sumatera Utara Medical School, H. Adam Malik Hospital, Jl. Bunga Lau No. 17, Medan 20136, Indonesia. Tel. +62-61-8361721/ +62-61-8365663. Fax. +62-61- 8361721. E-mail: windya_nst@yahoo.com.

According to the WHO recommendations, 5 to 6 mg/kg body weight may be given orally and combined with albendazole.¹⁰ The WHO recommends the following medications for soil-transmitted helminthiasis (STH): albendazole, mebendazole, levamisole, and pyrantel pamoate, with the drug of choice being albendazole and mebendazole for *T. trichiura*.¹¹

The aim of our study was to compare the efficacy of albendazole alone to that of combined albendazole and diethylcarbamazine for *T. trichiura* treatment.

Methods

A randomized clinical open trial was conducted from June to September 2009 in elementary school children in Karang Gading and Rintis Villages, Secanggang Subdistrict, Langkat District, North Sumatera Province. We gave stool containers to 300 elementary school-aged children and only 212 who returned the pots in which 108 were infected with *T. trichiura*. We included children who not recently been treated for helminthiasis, and agreed to participate in the study.

We excluded children who refused the medication, did not provide stool specimens, or had diarrhea.

Before enrollment, we explained the study methods, effect of *T. trichiura* infection and anthelmintic treatment to subjects and their parents. Prior to intervention, we recorded the age, gender, body height and weight, and severity of infection for all subjects. Stool specimens were collected in plastic containers and examined by *Kato-Katz* method. Written informed consent was obtained from subjects' parents.

Subjects were randomized into two groups. Group I (53 children) received a single dose of 400 mg albendazole alone and group II (55 children) received a single dose of albendazole and 6 mg/kg diethylcarbamazine. Stool specimens were collected at baseline, and at days 7, 14, 21 and 28 after treatment for follow up examinations. Subject categorized as cured if no egg is found in stool after albendazole or albendazole+diethylcarbamazine administration. All adverse reactions were recorded. This study was approved by the Medical Ethics Committee of the University of North Sumatra Medical School.

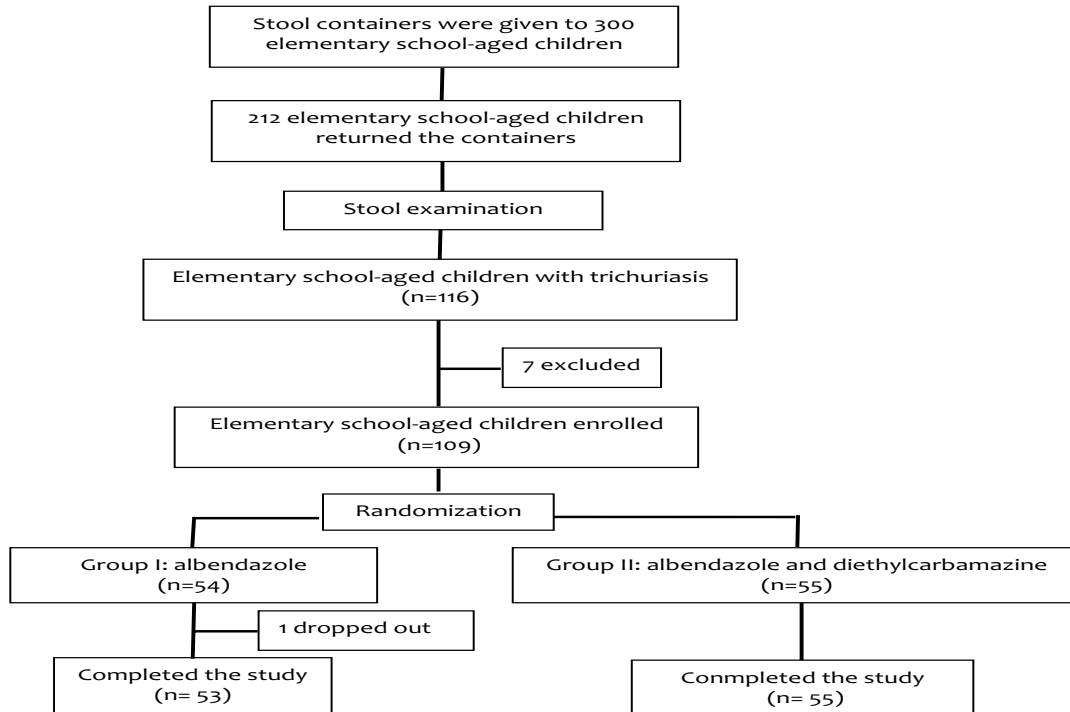


Figure 1. Study profile

We used SPSS version 14.0 to analyse the data. Statistical analyses were Chi square test for cure rates and Wilcoxon rank test for egg reduction rates. Results were considered to be significant for $P < 0.05$ with 95% confidence intervals (95% CI).

Results

Trichiuriasis was found in 54.7% (116/212) children. Of 116 children with thichuriasis, 7 were excluded (1 had diarrhea, 1 did not take the medicine, and 5 did not return the pot), and 1 dropped out from the study because parent refused to continue. A total of 108 subjects completed the study. The study profile is shown in **Figure 1**.

There was no significant difference in cure rates between the albendazole alone and albendazole plus diethylcarbamazine groups at 66% and 60%,

respectively ($P = 0.52$) (**Table 2**).

Egg counts from still specimens did not differ significantly between groups at days 7, 14, 21, and 28 after treatment ($P \geq 0.10$) (**Table 3**).

Discussion

Soil-transmitted helminthiasis is an infection caused by intestinal nematodes including *Ascaris lumbricoides*, *Trichuris trichiura*, and *Ancylostoma duodenale*.^{1,12} The hot and humid climate in tropical regions is suitable for these species to thrive.^{2,3} The prevalence of *T. trichiura* in North Sumatera in 1995 was 78.6%.¹² The Secanggang subdistrict is located in a coastal area with a high STH prevalence. We found that the STH prevalence in both primary schools of two villages had reached 54.5%, of which 93.9% were trichuriasis infections. More boys than girls had STH, probably

Table 1. Baseline characteristics of subjects

Characteristics	Group I (albendazole) (n=53)	Group II (albendazole+diethylcarbamazine) (n=55)
Gender, n (%)		
Females	22 (41.5)	23 (41.8)
Males	31 (58.5)	32 (58.2)
Mean age (SD), years	9.5 (1.72)	9.6 (1.71)
Mean weight (SD), kg	17.3 (4.61)	17.8 (4.83)
Mean height (SD), cm	122.7 (8.33)	124.8 (5.53)
Mean trichuris eggs counts, EPG* (SD)	208.3 (55.62)	204.1 (57.61)

*EPG=eggs per gram of stool

Table 2. Cure rates of trichuriasis at day 28 after treatment

	Group I (albendazole) (n=53)	Group II (albendazole+diethylcarbamazine) (n=55)	P value
Cured, n(%)	35 (66)	33 (60)	0.52
Not cured, n(%)	18 (34)	22 (40)	

Table 3. *T. trichiura* eggs counts at day 7 until day 28

Follow up of trichuriasis egg counts	EPG* (SD)			P value
	Group I (albendazole)	Group II (albendazole+diethylcarbamazine)	95% CI of differences	
Day 7	164.4(54.81)	172.2 (51.73)	-29.0 to 11.9	0.40
Day 14	119.2 (63.32)	121.6 (72.41)	-28.6 to 22.6	0.81
Day 21	68.1(64.13)	73.2 (71.32)	-29.6 to 17.7	0.61
Day 28	37.4 (54.50)	51.8 (60.07)	-27.9 to 15.9	0.10

*EPG=eggs per gram of stool

because boys play outdoors more often than girls, so they have more contact with soil.

T. trichiura as a soil-transmitted helminth is more difficult to control. We used the combination therapy of albendazole and diethylcarbamazine often used in the *Global Program Elimination of Lymphatic Filariasis* (GPELF) to assess their effect on *T. trichiura*.¹³ The WHO has categorized intensity of infection as mild infection (1-999 EPG), medium infection (1,000-9,999 EPG), and heavy infection ($\geq 10,000$ EPG).⁹ Based on these WHO criteria, our study subjects had mild infections. Before therapy, the mean intensity of eggs was similar in the two groups, with 208.3 (55.6) EPG in group I and 204.1 (57.6) EPG in group II.

We used the cure rates and reduction rates in the intensity of eggs (egg reduction rate, ERR) to determine the effectiveness of the single (albendazole) and combination (albendazole and diethylcarbamazine) therapies.¹ We found no significant difference in trichuriasis cure rates in the two groups. Intensity of trichuriasis eggs also did not differ significantly between groups, indicating that combination therapy was as effective as therapy single dose albendazole for treating trichuriasis. Studies on 400 mg albendazole for *T. trichiura* treatment have shown varied results.¹² A systematic review reported that albendazole reduced the prevalence of *T. trichiura* from 51.9% to 31.9%.¹⁴ However, a study in China reported that albendazole for *T. trichiura* infection had a low cure rate of 11.7%.¹⁵ A South African study using a single dose of 400 mg albendazole showed cure rates of 12.7% and 33.3% within six months after therapy, and recommended considering an alternative therapy for *T. trichiura*.¹⁶ Various results on albendazole against trichuriasis may due to small sample size, duration of therapy, or the severity of infection. However, large-scale anthelmintic therapy could give rise to resistant nematodes.¹ We used the combination of albendazole and diethylcarbamazine as an alternative therapy for *T. trichiura* infection.

A South India study showed a synergistic effect of combination therapy on STH, especially for *T. trichiura*.¹⁷ A Haiti study evaluated the effect of combination therapy with albendazole and placebo or diethylcarbamazine and found that the combination therapy was effective and well tolerated, with decreased prevalence and infection intensity. These studies concluded that the combination therapy

can be used in suppressing the infection due to *T. trichiura*.¹⁸

The WHO recommends that single dose albendazole therapy should be combined with diethylcarbamazine at a dose of 5 to 6 mg/kg.⁹ We observed that albendazole therapy alone was as effective as albendazole combined with diethylcarbamazine. However, it can be argued that there is the possibility of *T. trichuria* resistance after a single dose of albendazole, hence, combination therapy may be used as an alternative.¹³

None of our subjects experienced adverse effects after therapy. Generally, diethylcarbamazine in therapeutic doses does not cause side effects such as nausea, vomiting, dizziness, malaise, or swollen and painful joints.^{8,9}

In areas where people have poor hygiene, STH is a major public health problem.¹⁹ In Karang Gading and Rintis villages, low levels of hygiene were observed in individuals and in terms of environmental sanitation, resulting in children easily becoming infected with *T. trichiura*. Children with good hygiene, high levels of environmental sanitation, as well as parents or teachers providing education on these matters are at lower risk of STH.^{20,21}

In conclusion, combination therapy of albendazole plus diethylcarbamazine is as effective as single dose albendazole therapy against trichuriasis. Nonetheless, due to the possibility of anthelmintic resistance after a single dose of albendazole, we recommend using combination therapy as an alternative.

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