

Mebendazole vs. mebendazole-pyrantel pamoate for soil-transmitted helminthiasis infection in children

Fereza Amelia, Muhammad Ali, Syahril Pasaribu

Abstract

Background Soil-transmitted helminthiasis (STH) is the most common infection in developing countries. Although it causes high morbidity, it is still difficult to find the efficacy dose of antihelmintics for its treatment.

Objective To determine the efficacy of mebendazole and mebendazole-pyrantel pamoate in treating STH infection in children.

Methods We conducted a randomized open-label controlled trial from July to September 2009 in Secanggang, Langkat District, North Sumatera Province, Indonesia, on primary school-aged children. Before the intervention, data on age, sex, nutritional status, and STH infection status were collected. The children were randomized into two groups. Children in group I received a single dose of 500 mg mebendazole while they in group II received a single dose of 500 mg of mebendazole combined with 10 mg/kgBW of pyrantel pamoate. We examined subjects' stool specimens on days 7, 14, 21, and 28 after treatment to determine cure rates and egg reductions. Statistical analyses were performed by Chi square and student's T-test with 95% confidence intervals and P values of < 0.05 considered to be significant.

Results We found that the cure rates were 95.4%, 78.5%, and 89.3% for *Ascaris lumbricoides*, *Trichuris trichiura*, and mixed (*A. lumbricoides* and *T. trichiura*) infections, respectively, in the mebendazole group. The cure rates were 98.5%, 89.2%, and 90.2% for *A. lumbricoides*, *T. trichiura*, and mixed infections, respectively, in the mebendazole-pyrantel pamoate group. Although the cure rate results were not significantly different between the 2 treatment groups, the total eggs per gram (EPG) was significantly lower for both *A. lumbricoides* and *T. trichiura* infections ($P=0.001$ and $P=0.002$, respectively) in the combination therapy group than in the mebendazole alone group.

Conclusion Mebendazole in combination with pyrantel pamoate has higher efficacy than mebendazole alone in terms of faster egg reduction rates. However, the cure rates of these two antihelmintics regimens are similar. [Paediatr Indones. 2013;53:209-13.].

Keywords: mebendazole, pyrantel pamoate, soil transmitted helminth, children.

Helminth infections caused by soil-transmitted helminths (STH) and schistosomes are among the most prevalent afflictions of humans who live in areas of poverty in the developing world.¹ Approximately one-third of the world's population is infected with one or more helminth species which live in the gastrointestinal tract. Common helminth species are *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm), as well as *Ancylostoma duodenale*, and *Necator americanus* (hookworms).²⁻⁴ Soil-transmitted helminths infections are considered to be an enduring public health problem in Indonesia, although national-level data is incomplete. Surveys over the 1970–1980 period in South-East Asia region revealed prevalences of more than 70% for *Ascaris* and *Trichuris* infections.⁵ Preschool-aged children account for 10%–20% of the 2 billion people worldwide who are infected with soil-transmitted helminths.⁶ School-aged children in

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

Reprint requests to: Fereza Amelia, Department of Child Health, University of North Sumatera/ H. Adam Malik Hospital. Jl. Bunga Lau No.17 Medan 20136 . Tel +62-618-361-721, +62-618-365-663, Fax. +62-618-361-721. E-mail: doc_fea@yahoo.com

developing countries suffer the worst consequences from this condition,⁷ as STH infection may manifest as diarrhea, abdominal pain, poor weight gain, malnutrition, anemia, and poor intelligence.⁸

Several antihelmintics of various regimens have been tried in order to eradicate these parasites, but with varying results. Four antihelmintics are currently on WHO model list of essential medicines for the treatment and control of STH, these are albendazole, mebendazole, levamisole, and pyrantel pamoate.⁹ Mebendazole acts by interfering with carbohydrate metabolism and inhibiting polymerization of microtubules. Pyrantel pamoate has depolarizing effects that causes the dysfunction of the synaptic transmission in helminth's body and neuromuscular blockade development with further helminth's muscles paralysis.⁵

Previous studies state that both drugs have been found to be equally effective against enterobiasis. Pyrantel pamoate is recommended as the drug of choice in cases of multiple parasitic infections excluding *T. trichiura* and *S. stercoralis* whereas those with one or both of these in addition to others should be treated with mebendazole. A systematic review and meta-analysis reveals that single-dose of mebendazole and pyrantel pamoate pose a high cure rates against *A. lumbricoides*.

The aim of this study was to determine the efficacies of mebendazole alone compared to mebendazole combined with pyrantel pamoate for treating STH infection in children.

Methods

We conducted a randomized open-label controlled trial from July to September 2009 in Secanggang, Langkat District, North Sumatera Province. Subjects were primary school-aged children infected with STH who had not received treatment for helminthiasis for at least one month prior to the study. Children who refused to take the medication or provide stool specimens, as well as children with diarrhea, cough, or fever were excluded. Informed consent was obtained from parents or guardians. Sample size was calculated and 65 children in each group were required. Helminthiasis diagnosed based on any of helminth species finding in the stool examination. Before

giving the treatment for each group, we examined the stool, to look for the egg reduction, and compare it before and after treatment. This study was approved by the Ethics Committee of the University of North Sumatera Medical School.

Prior to enrollment, we explained the study methods, the effects of STH infection and antihelmintic treatment to the subjects and their parents. Before intervention, data on subjects' ages, sex, nutritional status, and STH infection status were collected. The children were divided into two groups by simple randomization using a random number table. Children in group I received a single dose of 500 mg mebendazole while they in group II also received a single dose of 500 mg mebendazole combined with 10mg/kg BW pyrantel pamoate. We examined subjects' stool specimens on days 7, 14, 21, and 28 after treatment to determine egg reductions and cure rates. Egg reduction was defined as the decrease in total eggs per gram (EPG) from the first to the fourth week after treatment. Eggs per gram is the amount of eggs per slide multiplied by 23. A complete cure was defined as no eggs detected on stool examination from the first to the fourth week after treatment.

Chi-square and independent T-test were used for statistical analyses, with a significance level of $P < 0.05$ with 95% confidence intervals (95% CI). All data were processed with SPSS version 14.0 for Windows.

Results

Initially we screened 500 students, of whom 212 did not provide stool specimens. We performed stool examinations (using Kato-Katz technique) on 288 primary school-aged children, and found 130 with STH infections. We enrolled and randomly assigned them to one of two groups. **Figure 1** shows the study profile.

Of the 130 children, there were 33 males and 32 females in the mebendazole alone group and 36 males and 29 females in the combination group. The mean subjects' ages were 9.6 (SD 1.99) years in the mebendazole group and 9 (SD 9.0) years in combination group. Fifty six children (44.6%) were found with *A. lumbricoides* infection, 23 children (16.1%) with *T. Trichiura*, and 51 children (39.3%) with mixed infection. The baseline characteristics

Table 1. Baseline characteristics of subjects

Characteristics	Group I (mebendazole) (n=65)	Group II (combination) (n=65)
Gender, n (%)		
Females	33 (50.7)	36 (55.3)
Males	32 (49.3)	29 (44.7)
Mean age (SD), years	9.6 (1.99)	9.0 (2.83)
Mean weight (SD), kg	22.7 (6.78)	20.5 (3.54)
Mean height (SD), cm	131 (9.72)	113 (14.80)
Nutritional status, n (%)		
Severely malnourished	2 (3)	5 (7.7)
Moderately malnourished	18 (27.6)	4 (6.1)
Mildly malnourished	31 (47.6)	24 (37)
Well-nourished	14 (21.8)	30 (46.2)
Overweight	0	1 (1.5)
Obese	0	1 (1.5)
Mean total eggs per gram (SD)		
<i>Ascaris lumbricoides</i>	1,160.4 (59.8)	1,011.9 (58.6)
<i>Trichuris trichiura</i>	131.9 (12.7)	118.1 (10.6)

of subjects were similar between the two groups (Table 1).

We found no significant difference in cure rates between groups. In the mebendazole alone group, the cure rates were 95.4% and 78.5% for *A. lumbricoides* and *T. trichiura* infections, respectively. In the mebendazole-pyrantel pamoate group, the cure rates were 98.5% and 89.2% for *A. lumbricoides* and *T. trichiura* infections, respectively. Similarly, in the mixed infection patients, cure rates were not significantly different between the mebendazole alone and the combination therapy groups (89.3% and 90.2%, respectively) (Table 2).

Table 3 shows the egg reduction rate for the two groups. There were significant differences on the 28th day after treatment for both groups, the total EPG reduced faster on mebendazole-pyrantel pamoate combination group.

Table 2. Cure rates by group for two STH species

Parasites	Anthelmintics regimens	Cure rate, %	P value
<i>A. lumbricoides</i>	mebendazole	95.4	0.081
	mebendazole + pyrantel pamoate	98.5	
<i>T. trichiura</i>	mebendazole	78.5	0.067
	mebendazole + pyrantel pamoate	89.2	
<i>Mixed A. lumbricoides</i> <i>+ T. trichiura</i>	mebendazole	89.3	0.063
	mebendazole + pyrantel pamoate	90.2	

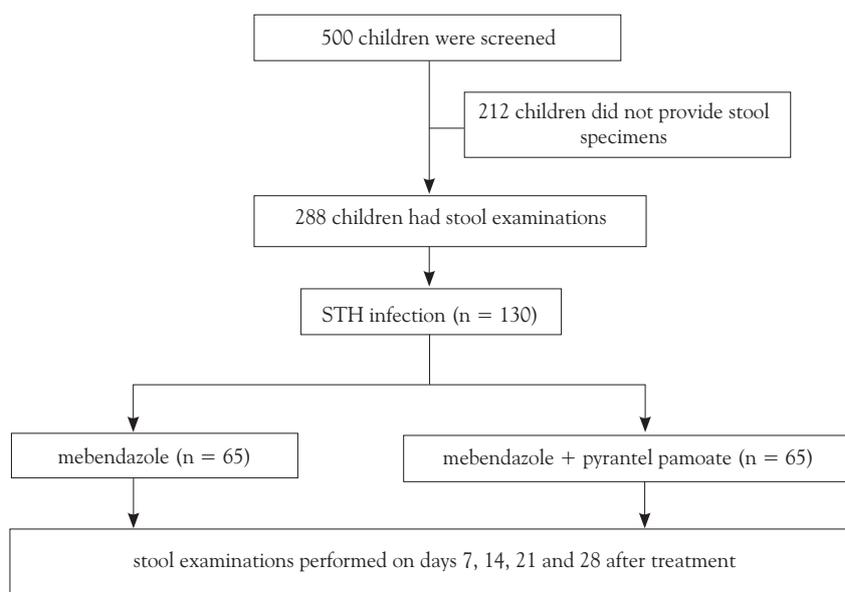


Figure 1. Study profile

Table 3. Egg reduction rate at the 1st week and 4th week

Parasites	Anthelmintics regimen	Total eggs per gram			P value
		Mean (SD) 7 th day	Mean (SD) 28 th day	95% CI reduction	
<i>A. lumbricoides</i>	mebendazole	871.4 (52.2)	30.2 (5.8)	0.36-2.58	0.001
	mebendazole + pyrantel pamoate	92.4 (7.3)	9.1 (0.8)	0.46-1.59	
<i>T. trichiura</i>	mebendazole	472.3 (50.4)	10.8 (1.9)	0.35-2.57	0.002
	mebendazole + pyrantel pamoate	93.1 (9.3)	3.6 (1.2)	0.46-1.50	

Discussion

Factors influencing the STH prevalence rate are hygiene, sanitation, socioeconomic level, knowledge, educational level and environmental differences. In North Sumatera in 1995, the prevalence of STH was about 57–90%.¹⁰ In villages, even though the pattern of STH transmission is generally similar, different lifestyles may affect helminthiasis transmission, as shown by differing prevalences between areas.¹¹

We found that the prevalence of STH infection in Secanggang, Kabupaten Langkat, North Sumatera Province was 45.1%. Our study involved 130 subjects with *A. lumbricoides* infection (44.6%), *T. trichiura* infection (16.1%), and mixed infection (*A. lumbricoides* and *T. trichiura*) (39.3%), but no subjects had hookworm infection.

Several anthelmintics in varying regimens have been tried to eradicate those parasites with various results.⁹ Medications recommended by WHO for reducing morbidity due to STH include albendazole, levamisole, mebendazole, and pyrantel pamoate.^{9,12} World Health Organization mebendazole recommended dosages are as follows: 500 mg in a single dose for ascariasis, or 100 mg twice daily for 3 days, or 500 mg in a single dose for trichuriasis and hookworm infections. WHO also recommended dosages of 400 mg albendazole in a single dose, 2.5 mg/kg body weight for levamisole, and 10 mg/kg body weight for pyrantel.¹²

We found that mebendazole combined with pyrantel pamoate had better efficacy in treating STH infections in children. In our subjects, total EPG reduced faster in the mebendazole-pyrantel pamoate group than in the mebendazole group, but there was no significant difference in the cure rate at the 28th day after treatment.

Our findings were in agreement with a previous

study in 2007, in Suka Village, Tiga Panah Subdistrict, Kabupaten Karo, North Sumatera Province. In this clinical trial, a combination of a single dose of 10 mg/kg body weight pyrantel pamoate followed by 100 mg mebendazole twice a day for three consecutive days eliminated intestinal helminths faster than a single dose of 500 mg mebendazole alone, but there was no significant difference in cure rate from intestinal helminthiasis between the combination and single dose mebendazole groups.¹³

A 1995 clinical trial in Tanjung Anom Village, Pancur Batu Subdistrict, Kabupaten Deli Serdang, North Sumatera Province showed that 400 mg single dose albendazole orally had higher efficacy than 10 mg/kg body weight pyrantel pamoate as a single oral dose combined with 100 mg mebendazole twice a day orally for three consecutive days.¹⁴

Adverse effects from mebendazole therapy that were occasionally reported were transient gastrointestinal discomfort and headaches. Mild gastrointestinal disturbance, headaches, dizziness, drowsiness, insomnia, and rash have been occasionally reported during pyrantel pamoate treatment.^{15,16} Vomiting was found in five children in the combination group, and in two children in the mebendazole group in our study. No other adverse effects were noted.

In conclusion, mebendazole in combination with pyrantel pamoate has higher efficacy than mebendazole alone in terms of faster egg reduction rates, however, the cure rates of these two anthelmintics regimens are similar.

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