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Original Article

Albendazole versus combined pyrantel pamoate–mebendazole in the treatment of mixed infection of soil-transmitted helminthiasis

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ABSTRACT

Background Soil transmitted helminthiasis is still highly prevalent in Indonesia, especially in rural area and among poor socio-economic population. Helminthiasis is frequently found as a single or mixed infection. It is difficult to get a medication with better efficacy, low cost, and simple administration for all types of worms.

Objective The aim of this sudy was to compare the effectiveness of albendazole and pyrantel pamoate-mebendazole combination in treating soil-transmitted helminthiasis.

Methods A randomized clinical trial was performed in September until November 1995 on students of a primary school in Tanjung Anom Village whose stool examinations showed mixed infection of helminthiasis. Subjects were randomly allocated into two groups. The A group was treated with 400 mg oral albendazole as a single dose, while the B group was treated with the combination of pyrantel pamoate 10 mg/kg body weight as a single dose and mebendazole 100 mg twice a day for three consecutive days. Cure was considered if in the stool examination, no worm eggs were found. Statistical analysis was performed by Chi-square test with confidence interval of 95% and p value of < 0.05 was considered significant.

Results Out of 541 children, mixed infection of soil-transmitted helminthiasis was found in 374 children (69%). Three hundreds sixty-six children completed the study, consisted of 182 children in group A and 184 in group B. At 3 weeks after treatment, the cure rate in the A group was significantly better compared to that in B group.

Conclusions Albendazole was more effective than the combination of pyrantel pamoate - mebendazole for treating mixed infection of soil-transmitted helminthiasis. Besides the administration was simpler and caused minimal side effect. **[Paediatr Indones 2002;42:268-272].**

Keywords: *albendazole, pyrantel pamoate, mixed infection, soil-transmitted helminthiasis*

Soil-transmitted helminthiasis is still highly prevalent in Indonesia especially in rural area and in poor socioeconomic population.[1-4] It is frequently found as a single or mixed infection of *Ascariasis lumbricoides*, *Trichuris trichiura,* and hookworm, which may cause malnutrition, anemia, and defects in growth and intelligence.[4-8] However, since the infection often occurs without symptoms, it is considered to be harmless.[4,4] Economically, this disease also has a wide impact as expressed by Kosin that if all intestinal worms found in Indonesia measured in longitudinal axis, the length would reach 595,000 km or 108 times the distance of Sabang-Merauke and it would consume 333,200 kg of carbohydrate per day or 416,000 kg of rice.[3] Helminthiasis is often found in school-age children,[9-18] so that it may influence the intelligence level of children.[7]

Treatment of single infection of soil-transmitted helminthiasis usually produces a better result compared to that of mixed infection. It is difficult

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to find a medication with better effectiveness, low cost, and simple administration for all types of worms. In the Child Health Department, Medical School, University of North Sumatra, the standard treatment for mixed soil-transmitted helminthiasis is based on the study of Lubis *et al* (1977).[19] A combination of 10 mg/kg body weight of pyrantel pamoate administered in the morning as a single dose and mebendazole 100 mg twice a day for three consecutive days showed a good result. Recently, there is a progressive development of anthelmintic medications in which newer medications such as oxantel-pyrantel pamoate and mebendazole were found. Single dose of albendazole had better result in the treatment of mixed infection of soil-transmitted helminthiasis with more simple administration.[18,20] Albendazole is methyl-(6-propylthio-1-H-benzimidazole-2-yl) carbamate, a new derivative of benzimidazole that has higher anthelmintic activity. It has been proven to have larvicidal and ovicidal actions. This medication selectively inhibits the consumption of glucose by the intestine and the tissue of helminth. Consequently, elimination of glycogen reverse occurs in the parasite body causing decreased production of adenosine triphosphate (ATP). ATP is very important for reproduction and survival of worms.[6,21-24] The spectrum activity of albendazole is very wide including *Nematoda, Cestoda, Echinococcus* infection in human. Thus, albendazole is active against *Ascaris lumbricoides, Trichuris trichiura*, hookworm, *Taenia saginata*, *Taenia solium, Strongyloides stercoralis, Hymenolepis nana*, *Hymenolepis diminute* and also for *Echinococcus granulosus*. Albendazole is a safe anthelminthic agent, it only has a few and rare side effects including dry mouth, uncomfortable in epigastric area, nausea, weakness, and diarrhea. [20,21,25,26] Jagota (1986) studied the efficacy of albendazole for soil-transmitted helminthiasis with a single dose of 400 mg; feces was re-examined at third week after the administration of the agent. In this study, it was shown that the cure rate was 92.2% for *Ancylostoma duodenale*; 90.5% for *Trichuris trichiura* and 95.3% for *Ascaris lumbricoides*.[6]

The objective of this study was to compare the efficacy of albendazole and combined pyrantel pamoate-mebendazole in the treatment of mixed infection of soil-transmitted helminthiasis.

Methods

This study was carried out on schoolchildren in the 1st-6th grade of primary schools in Tanjung Anom Village, Pancur Batu Subdistrict, Deli Serdang District, North Sumatera, from September to November 1995. Parental consent was obtained. The inclusion criteria were clinically healthy children who did not get any anthelmintic agent for at least a month before the study and in the stool examination, two or more types of worm eggs or in combination with hookworm larvae were found. Children who irregularly consumed any anthelmintic agent were excluded. Sample estimation was calculated by using a hypothesis test for two proportion, [26] with a of 0.05 and power of 80% and the difference of expected cure proportion was 0.10. Subjects needed for each group were 165 children.

This was a randomized clinical trial using a parallel design.[26] Subjects were randomly assigned by using a randomized numerical table. Children in the A group received a single dose of albendazole 400 mg orally, while the B group got a standard treatment consisting of pyrantel-pamoate 10 mg/kg body weight as a single dose per oral combined with mebendazole 100 mg twice a day per oral for three consecutive days. On the first day, mebendazole was consumed 30 minutes after administrating pyrantel-pamoate to avoid probable migration effect of any worms. The medications were taken in the morning supervised by the investigators and in the afternoon, the subjects took the medications accompanied by their parents. The side effects of the medications were monitored by the investigators every day for 7 consecutive days.

The stool was examined for worm eggs by using Kato Katz's method and for hookworm larvae by Harada Mori's modified method.[27] The stool was examined for three times, first before the administration of anthelmintic agents, and at the 14th day and the 21st day after taking the medications. Stool examination was carried out at the Parasitology Department of Medical School, University of North Sumatra, by a senior parasitologist. Cure was considered if in the stool examination, there were no worm eggs found.

Subjects who neither taking the medication completely nor having complete stool examinations were not included in the analysis. Children who had severe side effects such as diarrhea, vomiting, abdominal spasm, and others were dropped out from the study. Statistical analysis was carried out by X^2 test with the significance level of $p < 0.05$.

Results

Of 541 schoolchildren whose stools were examined, 469 (87%) subjects were positive for eggs and larvae of intestinal worms. Of these positive samples, 374 (69%) were mixed infections and 95 (18%) were single infection. Most of the infections were caused by *Trichuris trichiura* which was found in 369 children (79%), followed by hookworm in 283 children (60%), and *Ascaris lumbricoides* in 123 children (26%).

Three hundred and seventy four children with mixed infection were randomly allocated into 2 groups. Each group consisted of 187 subjects. The mean age of the subjects was 10 years (range 6.4-15.l) in the A group and 9.8 years (range 6.3-14.7) in the B group. Sex distribution in both groups was not different, namely in the ratio of 97 (51.9%): 94 (50.2%) for male and 90 (48.1%):93 (49.8%) for female. In general, the nutritional status of the subjects was good (A group: 75.9%; B group: 66.9%); 42 (22.5%) children in the A group and 58 (31%) in the B group had moderate nutritional status. While those suffered from malnutrition were only 3 (1.6%) children in the A group and 4 (2.1%) children in the B group. Parasite infestations for both groups included the combination of *Ascaris lumbricoides* and hookworm; *Ascaris lumbricoides* and *Trichuris trichiura*; hookworm and *Trichuris trichiura*. The proportion of parasite infection in both groups was equal, except for the combined infection of hookworm and *Trichuris trichiura* which was found more in the B group, while the combination of *Ascaris lumbricoides*, hookworm, and *Trichuris trichiura* was more in the A group **(Table 1).** Five children (3%) in the A group were excluded because they did not take the medications completely. While in the B group, 3 (2%) children were excluded because their stool specimens were not available.

TABLE 1. DISTRIBUTION OF PARASITES INFESTATION IN BOTH GROUPS

TYPES OF PARASITES INFESTATION	A GROUP N=187	B GROUP N=187
AL+HW	3 (1.6%)	2 (1.1%)
AL+TT	46 (24.6%)	45 (24.1%)
HW+TT	57 (30.5%)	94 (50.2%)
AL+HW+TT	81(43.3%)	46 (24.6%)

AL= *Ascaris lumbricoides;* HW= hookworm; TT= *Trichuris trichiura*

TABLE 2. DISTRIBUTION OF CURE RATE IN BOTH GROUPS AT 2 WEEKS AND 3 WEEKS AFTER ANTHELMINTHICS ADMINISTRATION

TREATMENT GROUP	RESULTS		TOTAL	p
	Cured	Not cured		
At 2 weeks after taking medications				df =1; X^2=1.34; p=0.247
Group A	106	76	182	
Group B	118	66	184	
Total	224	142	366	
At 3 weeks after taking medications				df =1; X^2=5.97; p=0.015
Group A	163	19	182	
Group B	148	36	184	
Total	311	55	366	

We found the side effect of headache in 1 child of the A group and 1 child in the B group, while 2 children in the B group got side effect of diarrhea. The side effects occurred in 0.5 % of children in the A group and 1.6% of the B group. These side effects occurred on the first day and disappeared on the second day.

Stool examinations at two weeks after administrating the medications revealed the results of treatment in the both regimens were not significantly different. On the other hand, stool reexamination at three weeks after the treatment showed the cure rate in the A group was better than that of the B group ($p < 0.05$) (**Table 2**).

Discussion

Kosin's study (1989) indicated that albendazole 400 mg in single dose could produce 96 % cure rate for ascariasis, 96 % for ancylostomiasis and 70 % for trichuriasis. He concluded that albendazole was an ideal medication for a mass treatment of intestinal worm.[23] The study of Mebendi *et al* (1985) in Zaire regarding the use of albendazole and pyrantel pamoate for the treatment of soil-transmitted helminthiasis found that albendazole 400 mg in single dose was effective with the cure rate ranged from 99.3% to 100% and it had wider spectrum so that it could be used for a mass therapy for combined infestation.[24]

Lubis *et al*[19] (1977) reported their study at the Child Health Department, Medical School, University of North Sumatra using a single dose of pyrantel pamoate 10 mg/kg body weight combined with mebendazole 100 mg twice a day for three consecutive days, for mixed infection of soil-transmitted helminthiasis. They showed that on the eleventh days, the cure rate was of 100% for hookworm, 69.4% for ascariasis and this figure increased to 100% in the second evaluation, while the cure rate for trichuriasis was 52.38% and then raised to 82.30% in the second evaluation. Our study showed that the result of treatment for mixed infection of soil-transmitted helminthiasis on the 21st day after taking albendazole was better significantly compared to that of the combined pyrantel pamoate-mebendazole regimen.

In conclusion, albendazole is more effective than the combination of pyrantel pamoate-mebendazole in the treatment of mixed infection of soil-transmitted helminthiasis. Its administration is simpler and has minimal side effects.

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