

## Randomized Trial of Albendazole with Combination of Pyrantel Pamoate - Mebendazole in Treatment of Mixed Helminthiasis in Children

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**ABSTRACT** This study aimed to compare the effectiveness of albendazole and pyrantel pamoate-mebendazole combination for the treatment of mixed infection of soil transmitted helminthiasis. Subjects were students of primary school in Tanjung Anom village, North Sumatra. The study was performed from September until November 1995. Patients were randomized into two groups; Group A received 400 mg/oral albendazole in single dose while group B received a combination of pyrantel pamoate 10 mg/kgBW as a single dose and mebendazole 2 x 100 mg in three consecutive days. From 541 children examined, mixed soil transmitted helminthiasis was found in 374 children (69%). Analysis was performed on 182 children in Group A and 184 in Group B. Comparison between two groups, cure rate at 3 weeks after treatment proved to be significantly different ( $p < 0.05$ ). We conclude that albendazole was more effective than combination of pyrantel pamoate - mebendazole for the treatment of mixed infection of soil transmitted helminthiasis. Administration more simple and have minimal side effect. [**Paediatr Indones 1999; 39:163-171**]

### Introduction

Soil transmitted helminthiasis still highly prevalent in Indonesia, especially in rural area and in poor socio-economic families.<sup>1-4</sup> It is frequently found as a single or mixed infection of *Ascariasis lumbricoides*, *Trichuris trichiura* and hookworms, which may

cause malnutrition, anemia, and defects in growth and intelligence.<sup>4-8</sup> Economically, it also has a wide impact.<sup>3</sup> Helminthiasis is often found in school-age children,<sup>9-18</sup> so that it has an effect on intelligence level.<sup>7</sup> Treatment of single soil transmitted helminthiasis generally produce good result; however treatment for mixed infection is still a problem. In the Child Health Department of Medical Faculty of University of North Sumatra, the standard treatment for mixed soil transmitted helminthiasis is based on the study of Lubis et al.<sup>19</sup> Recently, newer anthelmintics are proved to give a good result for treatment of combined helminthiasis infection with simple method of administration.<sup>18,23</sup>

Albendazole is a methyl-(6-propylthio-1-H-benzimidazole-2-yl) carbamate which is a new derivative of benzimidazole with a higher anthelmintic activity. It has been proved to have larvicidal and ovicidal effects. This medication selectively worked to inhibit consumption of glucose by the intestine and tissue of the worm in which larvae may be survive. Consequently, elimination of glycogen reverse occurs in parasite body that caused the decrease in production of adenosine triphosphate (ATP), a substance which is very important for reproduction and survival of the worms.<sup>6,20,21,27-29</sup> Albendazole has a wide spectrum and has been known to be effective in the treatment of Nematoda, Cestoda, and Echinococcus infestations in human. Thus, albendazole is active for *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm, *Taenia saginata*, and *solium*, *Strongyloides stercoralis*, *Hymenolepis nana*, *diminuta* and also for *Echinococcus granulosus*. Furthermore, albendazole is a safe anthelmintic.<sup>20,22-24</sup> The objective of this study was to compare the effectiveness of albendazole and a combination of pyrantel pamoate and mebendazole in the treatment of mixed infestation of soil transmitted helminthiasis in school children.

## Methods

This was a randomized clinical trial,<sup>24,25</sup> using a parallel design without matching. This study was carried out on all the Primary School Children of Tanjung Anom Village of Pancur Batu Subregency of Deli Serdang, North Sumatra, from September to November 1995. By using type I error of 0.05 and power of 0.90, 165 subjects per group were required. The inclusion criteria were: 1. healthy child, 2. at last in one month did not take any anthelmintics agent, 3. stool examination showed two or more types of worm eggs and hookworm larvae. Patients who failed to comply the study protocol, those who failed to present themselves on days 14 or 21, and those who showed severe side effects such as diarrhea, vomiting, abdominal spasm were excluded from the study. Sample estimation was determined by using formula for hypothesis testing for two proportions.<sup>24</sup>

Parental informed consent was obtained from all study subjects. Subjects were randomized by using random number table, to either received a single oral 400 mg albendazole (Group A), or a combination of a single oral 10 mg/kgBW pyrantel-pamoate

and 2 x 100 mg mebendazole 2x100 mg for three consecutive days in which at the first day, this medication was taken 30 minutes after pyrantel-pamoate to avoid probable migration effect of any worm (Group B). The subjects took the anthelmintics in the presence of the author in the morning, and then in the afternoon, they took the medication with their parents. The side effects of the medications were monitored by the authors every day for 7 consecutive days.<sup>20,24</sup>

The stool was examined by using Kato Katz's method<sup>26</sup> The number of worm eggs was counted every day, and examination of hookworm larvae was performed by modified Harada Mori's method.<sup>27</sup> The stool was examined three times, i.e., first before the treatment, and then at the 14th and the 21th day after treatment. This examination was carried out at the Parasitology Department of Medical Faculty of University of North Sumatera by a senior parasitologist. A subject was considered to be cured when no eggs were found on the third stool examination.<sup>28,29</sup>

The nutritional status was determined by mentioned weights for the heights and compared with NCHS in terms of age and sex. Based on comparison, the status level of nutrition were divided into the following:

Good	>90.0% median NCHS
Moderate	70.1%-90.0% median NCHS
Low	60.1%-70.0% median NCHS
Under nutrition	<60.0% median NCHS

Analysis of data included sex, age, weight, height, parents occupation and education, side effect of the anthelmintics. Statistical analysis was carried out by  $X^2$  test with the level of significance  $p < 0.05$ .

## Results

Of over 541 school children examined, in 469 (87%) children eggs or larvae of intestinal worms were found. Of these 469 subjects, 374 showed a combined infection and 95 as a single infection. Of the 469 children with helminthiasis, *Trichuris trichiura* was the most frequently found, i.e. in 369 children (79%), followed by hookworm in 283 children (60%) and *Ascaris lumbricoides* of 123 children (26%).

Table 3 shows that the most of the parents were workers, farmers, or fishermen, i.e. 55%. Of this 297 parents, the most included as farmers (282), followed by workers of 13 and 2 fishermen. Most parents only had a primary school education; there were still some parents who never got formal education (Table 2).

Table 1. Occupation of parents, in Tanjung Anom Village Primary School Children

Types of occupation	Total	Percentage (%)
Worker/Farmer/Fisherman	297	55
Businessman	128	24
Civil Employees/Army	43	8
Others:	73	13
Total	541	100

Table 2. Education levels of the parents of the study subjects

Education level	Mothers	%	Fathers	%
Unschooling/Not graduated of PS	19	3	26	5
Primary school (PS)	368	68	260	48
Junior high school (JHS)	109	20	150	27
Senior high school (SHS)	41	8	103	19
University	4	1	2	1
Total	541	100	541	100

The 374 students with combined worm infestation, 187 were included in Group A who received a single oral 400 mg albendazole and 187 belonged to Group B who received a combination of pyrantel pamoate 10 mg/kg BW in single dose and 2x100 mg oral mebendazole orally for three consecutive days.

Table 3 shows the clinical characteristics of both groups. The mean age of this study was 10 (range 6.4-15.1) years in Group A and 9.8 (range 6.3-14.7) years in Group B. Sex in the both groups was not different, namely in ration of 97 (51.9%): 94 (50.2%) for male and 90 (48.1%): 93 (49.8%) for female. In general, the nutritinal status of those children was good, 75.9% in Group A and 66.9% in Group B. While those who suffered from malnutrition was only 3 children in Group A and 4 children in Group B.

Parasite infestation for the both groups included the combined *Ascaris lumbricoides* and hookworm; *Ascaris lumbricoides* and *Trichuris trichiura*; hookworm and *Trichuris*

*trichiura*. The proportion of parasite infection in the both group was almost the same except of the combined infection of Hookworm and *Trichuris trichiura* and the amount was more in Group B while the amount of *Ascaris lumbricoides*, Hookworm and *Trichuris trichiura* was more in Group B.

The side effects seen were headache of 1 case in each of A and B group, and 2 cases with diarrhea at Group B (Table 3). The side effect in Group A of 0.5% and 1.6% at B group. These side effects occurred on the first day and disappeared on the second day (Table 3).

Table 5. Clinical characteristics and laboratory at the individual groups of treatment

Characteristics	Group A N=187	Group B N=187
Age (year)		
▪ Mean (SD)	10 (2.1)	9.8(1.9)
▪ Range	6.4-15.1	6.3-14.7
Sex		
▪ Male	97 (51.9%)	94 (50.2%)
▪ Female	90 (48.1%)	93 (49.8%)
Nutritional status		
▪ Good	142 (75.9%)	125 (66.9%)
▪ Moderate	42 (22.5%)	58 (31.0%)
Low	3 (1.6%)	4 (2.1%)
Bad	-	-
Parasitic infestation		
▪ 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%)
Side effects		
▪ Diarrhea	-	2 (1.1%)
▪ Headache	1 (0.5%)	1 (0.5%)

Note: AL = *Ascaris lumbricoides*; HW= Hookworm; TT = *Trichuris trichiura*

Five children (3%) in Group A were excluded because they did not take the anthelmintic, in Group B, 3 (2%) were excluded because no stool examination was performed after treatment.

The results of treatment in the both regimens were depicted in Tables 6 and 7. It shows that there was no significantly difference between the cure rates in both groups 2 weeks after treatment; i.e. 58.2% in Group A and 64.1% in Group B (Table 4). However, 3 weeks after treatment the cure rate of Group A was higher than that of Group B (89.6% vs 80.4%) as shown in Table 5.

Table 4. Results of treatment after 2 weeks

Treatment Group	Outcome		Total
	Cured	Not Cured	
A	106 (58.2%)	76 (41.8%)	182
B	118 (64.1%)	66 (38.9)	184
Total	182	184	366

df=1,  $\chi^2=0.2943$ , p=0.2477

Table 5. Results of treatment after 3 weeks

Treatment Group	Outcome		Total
	Cured	Not Cured	
A	163 (89.6%)	19 (10.4%)	182
B	148 (80.4%)	36 (19.6%)	184
Total	182	184	366

df=1,  $\chi^2=0.0216$ , p=0.0145

## Discussion

Kosin et al. find albendazole in single dosage of 400 mg could produced 96% cure rate for sscariasis, 96% for ancylostomiasis and 70% for trichuriasis. It could be said that albendazole is an ideal medication for mass treatment of intestinal worm.<sup>28</sup> The study of Mebendi et al in Zaire used albendazole and pyrantel pamoate. They found that 400 mg albendazole in single dosage was effective for soil transmitted helminthiasis with the cure rate ranged from 99.3% to 100.0%, so that it could be used for mass therapy for combined worm infestations.<sup>29</sup>

The study of Lubis<sup>19</sup> based on the clinical experience in the Department Child Health, Medical School, University of North Sumatera used a single dose of 10 mg/kgBW pyrantel pamoate and 2x100 mg mebendazole for three consecutive days for mixed infection of soil transmitted helminthiasis. At eleventh day, it could be shown that the cure rate was of 100% for hookworm, 69.4% for ascariasis and these figures reached 100% in the second evaluation while the cure rate of trichuriasis was 52.4% and then reached 82.3% after the second evaluation.<sup>19</sup>

In this study, it was shown that treatment for the mixed infection of soil transmitted helminthiasis between albendazole and pyrantel pamoate-mebendazole regimen produced a significant result on the 21st day. It is concluded that albendazole is more effective than a combination of pyrantel pamoate and mebendazole in the treatment of mixed infestation of soil transmitted soil helminthiasis. The single dose is definitely more simple, and it has only minimal side effects.

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