

Treatment of intestinal helminthiasis: mebendazole only or mebendazole-pyrantel pamoate?

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Abstract

Background Although intestinal helminthiasis causes high morbidity and has a negative impact on children's growth and development, the efficacy of anthelmintics for multiple helminthiasis in mass treatment is still doubtful.

Objective To compare the efficacy of single dose mebendazole and a combination of pyrantel pamoate and mebendazole for the treatment of multiple infections due to *Ascaris lumbricoides*, hookworm, and *Trichuris trichiura*.

Methods Subjects were elementary school students in Suka Village, Tiga Panah subdistrict, North Sumatera. They were randomized to either receive mebendazole (M Group) or mebendazole-pyrantel pamoate group (MP Group). Stool examinations were performed on each subjects on day 7, 14, 21, and 28 after treatment. Analyses were performed by using chi-squared and Mann-Whitney U tests.

Results The prevalence of intestinal helminthiasis was 95.4%. *T. trichiura* (88.7%) was the most common cause of infection followed by *A. lumbricoides* (79.5%), and hookworm (3.1%). Two hundred thirty nine (76.8%) children had multiple infections. Although the egg reduction rate of intestinal helminthiasis in the combination group was faster than that of the mebendazole group, there was no significant difference in the cure rate of both groups.

Conclusion A single dose of mebendazole is preferred for mass treatment of multiple intestinal helminthiasis infections. [Paediatr Indones 2007;47:216-220].

Keywords: helminthiasis, mebendazol, pyrantel pamoate, *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm

Intestinal helminthiasis remains a public health problem, especially in tropical and subtropical developing countries. More than one billion of the world's population including at least 400 million school-age children are chronically infected with intestinal helminthiasis.¹ In 1992 the prevalence of intestinal helminthiasis in Indonesia was still high with ascariasis (70–90%), trichuriasis (80–95%), and hookworm infection (30–59%).² The high prevalence of helminthiasis is caused by multiple factors, i.e., economical status, education, and poor environmental hygiene and sanitation.^{1,3} *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworm are the three most common causes of helminthiasis affecting children in developing countries. This disease causes high morbidity and contributes to malnutrition, vitamin A deficiency, and anemia, and has a negative impact on general health and children's development.⁴ Treating ascariasis is almost not a problem because a

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single dose anthelmintic therapy gives satisfying result. However, treatment of other helminths such as *Trichuris trichiura* and hookworm often gives disappointing results.

Several anthelmintics in varying regimens have been tried to eradicate those parasites with various results. One of the most frequently used anthelmintics is a single dose pyrantel pamoate 10 mg/kg followed by mebendazole 100 mg twice daily for 3 consecutive days.⁵ This method is neither practical nor convenient especially for mass treatment. Ideally, anthelmintics should satisfy the needs of the majority of patients, including simple regimen, easy to administer, low cost, minimal side effect, high therapeutic effect, and effective to all parasite stadia.^{1,3} Recently, a single dose 500 mg mebendazole is used an alternative treatment.^{6,7} However, study on the effectiveness of two or more anthelmintics for intestinal helminthiasis in mass treatment is still rare, especially for multiple or mixed helminthiasis. Therefore, this study aimed to investigate the effectiveness of two different anthelmintics for multiple helminthiasis infection.

Methods

This randomized double blind clinical trial was conducted in primary schools from September to October 2002, in Suka village Tiga Panah subdistrict, Karo district, North Sumatera. Stool of all students (grades I to VI) was collected in plastic bottles. Stool was then examined using Kato-Katz technique in the Department of Child Health, Medical School, North Sumatra University.

We included all students of the primary schools who had more than one species of intestinal helminths in their stools, but had not taken anthelmintic for one month prior to the study. They must be otherwise healthy on doctor's examination and gave parental consent. Participants were then randomized to either receive oral single dose pyrantel pamoate 10 mg/kg followed by mebendazole 100 mg twice daily for 3 consecutive days (PM Group), or single dose mebendazole 500 mg only (M Group). Using the same method, stool examinations were repeated on 7th, 14th, 21st, and 28th day after treatment to determine egg reduction rate and cure rate. A complete cure was defined as no egg detected on a single Kato-Katz smear

technique one to four weeks after treatment. Side effects of the anthelmintics were observed and recorded.

Data of students who could not complete the study, those who failed to consume the anthelmintic regularly, and those who had severe side effects of the anthelmintics were excluded from analysis. We used chi-squared test to compare the effectiveness of treatment between the two groups. To assess the eggs reduction rate we used Mann-Whitney U test. All data were processed by SPSS version 11.0 for windows.

Results

Stool specimens were initially examined from a total of 326 subjects, 311 (95.4%) were found to be positive for helminth infection. Trichuriasis had the highest prevalence (88.7%), followed by ascariasis (79.5%), and hook worm infection (3.1%). Seventy-two (23.2%) of the test specimen had single and 239 (79.8%) had multiple infection (**Table 1**).

Of 239 students with multiple helminthiasis, 140 specimens were randomly taken and randomized into PM or M group, so there were 70 students in each group. At the end of the study, there was 1 student in PM group and 5 students in M group who could not finish the study because of sick, moved to another school, or no stools obtained at examination time. The characteristics of the subjects in both groups are shown in **Table 2**; both groups were essentially comparable.

Egg reduction rate of helminths in both PM and M group are shown in **Table 3**. On day 7 after treatment, there was a significant difference of egg reduction rate of *Trichuris* 92.6% in the PM group, and

Table 1. Prevalence and variation of intestinal helminth in 326 subjects

| Intestinal helminth infections | Total | % |
|---|-------|------|
| Type of infection: | | |
| <i>A. lumbricoides</i> | 259 | 79.5 |
| <i>T. trichiura</i> | 289 | 88.7 |
| Hookworm | 10 | 3.1 |
| Single infection: | | |
| <i>A. lumbricoides</i> | 21 | 6.5 |
| <i>T. trichiura</i> | 51 | 15.6 |
| Multiple infection: | | |
| <i>A. lumbricoides</i> + <i>T. trichiura</i> | 229 | 70.2 |
| <i>A. lumbricoides</i> + Hookworm | 1 | 0.3 |
| <i>T. trichiura</i> + Hookworm | 1 | 0.3 |
| <i>A. lumbricoides</i> + <i>T. trichiura</i> + Hookworm | 8 | 2.5 |

Table 2. Baseline characteristics of PM Group and M Group

| Characteristic | Combination Group | Mebendazole Group |
|----------------------------|-------------------|-------------------|
| Sex | | |
| Boy | 40 | 28 |
| Girl | 29 | 37 |
| Body weight, kg, mean (SD) | 27.2 (6.41) | 27.8 (6.53) |
| Age, yr, mean (SD) | 10.6 (1.76) | 10.5 (1.89) |

79.3% in M group (P=0.042), but there were no significant difference in eggs reduction rate of *Ascaris*. On day 14, 21, and 28 after treatment, there were no significant difference in egg reduction rate of *Trichuris* and *Ascaris* in both PM and M group.

The cure rate of helminths in both PM and M groups are shown in **Table 4**. On day 7 after treatment, there was a significant difference of the cure rate of *Ascaris* and *Trichuris* in both PM and M groups. The cure rate of *Ascaris* in the PM group was 92.8% and in M group was 76.9% (P=0.01). The cure rate of *Trichuris* in PM group was 88.4% and in M group was 73.6% (P=0.03). On the 14th, 21st, and 28th day after treatment, no significant difference of the cure rate of *Trichuris* and *Ascaris* was found in both PM and M group. The prevalence of hookworm infection was only 3.1% and not considered for further analysis.

Discussion

The prevalence of intestinal helminthiasis in this study was similar to that of previous studies. Study of 348 elementary school students in Jakarta reported that prevalences of *A. lumbricoides*, *T. trichiura*, and hookworm were 85.1%, 92%, and 2.1%, respectively.⁷ Similar results were reported by other studies in

Table 3. Mean of egg reduction rate (ERR) from the 1st week until 4th week after treatment

| Week | PM (%) N = 69 | M (%) N = 65 | P |
|----------------------|------------------|-----------------|-------|
| 1 st : AL | 98.4 | 98.3 | >0.05 |
| TT | 92.6 | 79.3 | 0.04 |
| HW | 100 | 100 | |
| 2 nd : AL | 100 | 99.9 | >0.05 |
| TT | 97.2 | 94.9 | |
| 3 rd : AL | 100 | 99.9 | |
| TT | 98 | 98.1 | |
| 4 th : AL | 100 | 99.9 | |
| TT | 97.9 | 98.1 | |

Table 4. Mean of cure rate (CR) from 1st week until 4th week after treatment

| Week | Combination group (%) N = 69 | Mebendazol group (%) N = 65 | P |
|----------------------|---------------------------------|--------------------------------|-------|
| 1 st : AL | 92.8 | 76.9 | 0.01 |
| TT | 88.4 | 73.8 | 0.03 |
| HW | 100 | 100 | |
| 2 nd : AL | 100 | 96.9 | >0.05 |
| TT | 91.3 | 86.2 | |
| 3 rd : AL | 100 | 96.9 | |
| TT | 92.8 | 89.2 | |
| 4 th : AL | 100 | 96.9 | |
| TT | 94.2 | 92.3 | |

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

Indonesia.^{2,8} In Malaysia, the prevalence of *A. lumbricoides*, *T. trichiura*, and hookworm were 62.9%, 91.7%, and 28.8% respectively.⁹ Merid et al¹⁰ in Ethiopia, Clewes et al¹¹ in Bangladesh, Albonico et al¹² in Zanzibar, Oyewole et al¹³ in Nigeria, Watkins¹⁴ in Guatemala, and Smith et al¹⁵ in Honduras reported similar prevalence of intestinal helminthiasis. However some studies reported lower prevalence of helminthiasis. Some studies had lower prevalence of helminthiasis both in Indonesia,^{16,17} and in Guinea.¹⁸

High prevalence of ascariasis and trichuriasis in this study probably due to poor personal hygiene and the condition of study location is high in humidity and agriculture surrounding. On the other hand, the low prevalence of ascariasis and trichuriasis in some studies are probably caused by frequent participation of subjects.¹⁹

Not all studies reported the prevalence of multiple infections. In this study, 70.2% of children had both ascariasis and trichuriasis simultaneously. Similar results were reported by many studies.^{7,8,20-23} The reason for this is unclear, but it may be explained by the similar route of infection for the two parasites.¹⁵

In our study at the end of stool examination, the egg reduction rate (ERR) of *Ascaris lumbricoides* and *Trichuris trichiura* were 100% and 97.9% in combination group and 99.9% and 98.1% in mebendazole group. Legesse et al²⁴ used mebendazole 2 x 100 mg for 3 consecutive days and obtained ERR of 99.8 and 92.3% for *A. lumbricoides* and *T. trichiura*. Abidin and Rassad⁷ used single dose mebendazole 500 mg and found that the ERR was 99.8% and 89.7% for *A. lumbricoides* and *T. trichiura*, respectively. Abadi⁶ used single dose mebendazole 500 mg and found that ERR

was 99.0% and 92.8% for *A. lumbricoides* and *T. trichiura*. Jongsuksuntigul et al²⁵ also used single dose mebendazole 500 mg and found the ERR 100% and 89.9% for *A. lumbricoides* and *T. trichiura*.

There was significant difference in the cure rate (CR) in the 7th day of stool examination, in which combination was greater than mebendazole group. But at the end of the stool examination, there was no significant difference between the two groups. CR of combination group were 100% and 94.2% for *A. lumbricoides* and *T. trichiura*, respectively, while in mebendazole group were 96.9% and 92.3% for *A. lumbricoides* and *T. trichiura*, respectively. It suggests that combination of pyrantel pamoate-mebendazole eliminates intestinal helminth faster than does single dose mebendazole. The very high CR of ascariasis in this study was similar with other studies.^{7,26-28} However the CR of trichuriasis in this study was higher than that in other studies. Abidin and Rassad⁷ used single dose mebendazole 500 mg in trichuriasis obtained only a 41.7% CR. Purnomo et al²⁶ found only 12.4% CR using pyrantel pamoate, that was similar to that found Albonico et al¹² using mebendazole. The high CR for trichuriasis in this study is possibly related to the fact that our subjects had never included in the trial so that compliance was better.

Some studies had reported the side effect of antihelmintic especially mebendazole. Abidin⁷ reported 3.8% of erratic migration of ascaris as side effect of mebendazole.⁷ Purnomo et al²⁶ suggested that mebendazole was not widely used in Indonesia, mainly because it stimulates erratic migration of *A. lumbricoides*. The basic principle was to combine a rapid acting, worm neurotoxic agent to mebendazole in order to quickly paralyze *Ascaris*. Kan and Chua²⁹ suggested that the combination of mebendazole and levamisole had decreased the possibility of erratic migration of ascaris in mixed infection. Some experts recommend to use mebendazole in mass treatment because it is given as a single dose, it has a large spectrum property, safe, and easy to administer without considering body weight.^{6,7} Unfortunately, mebendazole is more expensive than other antihelmintics. No side effect was found in our study.

In conclusion, treating intestinal helminthiasis by combination of single dose pyrantel pamoate 10 mg/kg body weight followed by mebendazole 2x100 mg for 3

consecutive days eliminates intestinal helminth faster compared to that by single dose 500 mg mebendazole only. However there is no significant difference of cure rate of intestinal helminthiasis between both combination and single dose mebendazole, suggesting that a single dose of mebendazole is preferred for mass treatment of multiple helminth infections.

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