Efficacy of Albendazole and Mebendazole With or Without Levamisole for Ascariasis and Trichuriasis

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Abstract

BACKGROUND: Helminthiasis in school-aged children potentially causing physical growth and intellectual development retardation. Trichuriasis was the most common type of helminthiasis in children.

AIM: To investigated the efficacy and side effects of albendazole, albendazole combined with levamisole and mebendazole combined with levamisole for trichuriasis. The sample of this study were 180 elementary school students at Deli Serdang Regency State Elementary School, Medan, Indonesia. The study was conducted from April to June 2015.

RESULTS: The cure rate of helminthiasis on the 7th day was 81.7% after albendazole therapy, 88.3% after albendazole levamisole therapy, and 83.3% after mebendazole combined with levamisole therapy (p = 0.577). Cure rate on the 14th day was 88.3%, 95%, and 91.7% for albendazole, albendazole combined with levamisole, and mebendazole combined with levamisole therapy, respectively (p = 0.418). On the 21st day, the cure rate was 88.3%, 96.7%, and 91.7% (p = 0.230). Combination of albendazole and levamisole showed the highest cure rate, despite the statistically insignificant difference for all groups (p > 0.05). Combination of albendazole combined with levamisole showed better cure rate for mild trichuriasis (95.8%) than albendazole therapy (46.2%) and mebendazole combined with levamisole (83.3%) (p > 0.05).

CONCLUSION: Single-dose albendazole, a combination of albendazole and levamisole, and a combination of mebendazole and levamisole had similar efficacy in reducing egg count in helminthiasis. Combination of albendazole and levamisole showed better cure rate for mild trichuriasis and mixed infections. Side effects were similar in all treatment groups.

Introduction

Intestinal worm infection is still a major public health problem in Indonesia, especially in rural areas. In Indonesia and other developing countries, Ascaris lumbricoides, Trichuris trichiura, and hookworm are the most common intestinal parasites [1], [2]. World Health Organization (WHO) estimated that at least two billion people or nearly one-third of the world’s population had been infected with soil-transmitted helminths (STH) or helminthiasis [3]. About 300 million infected people suffered from severe illness, and about 400 million school-aged children worldwide had been infected [4], [5].

Many species of worms had been reported to cause infection in Indonesia. Trichuris trichiura, was resided in the human caecum, was the most common cause of helminthiasis and one of the most important intestinal nematodes in human [6], [7]. School-age children were frequently infected with helminthiasis, which potentially causing diarrhoea, nutritional deficiency, anaemia, growth disorders, and intellectual disturbance [8], [9].

Public health program to control helminthiasis was largely dependent on the administration of anti-helminthic drugs for elementary-school children [10]. Theoretically, there were several broad-spectrum anti-helminthic drugs such as albendazole, levamisole,
Results

There were 807 Deli Serdang elementary students; after the exclusion, we found 185 students with helminthiasis based on stool examination. Five of them had started therapy before the study. Therefore, they were excluded. The remaining 180 students were study subjects who undergone randomisation into three intervention groups (60 students in each group). The characteristics of the subjects can be seen in Table 1.

Table 1: Characteristics of Subjects

| Characteristics                  | First Group Albendazole | Second Group Albendazole + Levamisole | Third Group Mebendazole + Levamisole |
|----------------------------------|-------------------------|----------------------------------------|---------------------------------------|
| Age, years (mean ± SD)           | 9.2 ± 1.734             | 8.9 ± 1.540                            | 9.1 ± 1.567                           |
| Sex, n (%)                       | 36 (56.3)               | 28 (46.7)                              | 31 (51.7)                             |
| Male, n (%)                      | 25 (41.7)               | 32 (53.3)                              | 29 (48.3)                             |
| Female, n (%)                    | 11 (18.3)               | 14 (23.3)                              | 12 (20.0)                             |
| Parental occupation              |                         |                                        |                                       |
| Farmer                           | 11 (18.3)               | 45 (75)                                | 38 (63.3)                             |
| Civil servant                    | 41 (66.7)               | 17 (28.3)                              | 16 (26.6)                             |
| Entrepreneur                     | 10 (16.7)               | 1 (1.7)                                | 9 (15.0)                              |
| Parental education, n (%)        |                         |                                        |                                       |
| Uneducated                       | 1 (0.83)                | 7 (11.7)                               | 13 (22.4)                             |
| Elementary school                | 22 (36.7)               | 36 (60)                                | 25 (42)                               |
| Junior high school               | 46 (76.7)               | 38 (63.3)                              | 42 (73.3)                             |
| Senior high school               | 3 (5.0)                 | 39 (65)                                | 38 (65)                               |
| University                       | 8 (13.3)                | 6 (10)                                 | 2 (3.3)                               |

The most common helminthiasis was infection by Ascaris lumbricoides, followed by mixed infection by Ascaris lumbricoides with Trichuris trichiura, Trichuris trichuria only, and mixed infection by Ascaris lumbricoides with Trichuris trichuria and Enterobius vermicularis as seen in Table 2.

Table 2: Prevalence of helminthiasis

| Helminthiasis Etiology          | Numbers (%)             |
|---------------------------------|-------------------------|
| Ascaris lumbricoides            | 92 (51.1)               |
| Trichuris trichiura             | 37 (20.5)               |
| A. lumbricoides + T. trichiura  | 50 (27.7)               |
| A. lumbricoides + T. trichiura + Enterobius | 1 (0.56) |

Subjects with mild A. lumbricoides infection were 50 children (83.3%) in the first group, 39 students (65%) in the second group, and 46 students (76.7%) in the third group. Subjects with mild T. trichiura infection were 13 children (21.7%) in the first group, 24 children (40%) in the second group, and 24 children (40%) in the third group.

Table 3: Basic Characteristics of Research Based on Intensity of Infection

| Characteristics                  | First Group Albendazole | Second Group Albendazole + Levamisole | Third Group Mebendazole + Levamisole |
|----------------------------------|-------------------------|----------------------------------------|---------------------------------------|
| Helminthiasis Etiology           |                         |                                        |                                       |
| Ascaris lumbricoides             |                         |                                        |                                       |
| Mild                             | 50 (83.3)               | 39 (65)                                | 46 (76.7)                             |
| Moderate                         | 4 (6.7)                 | 2 (3.3)                                | 1 (1.7)                               |
| Trichuris trichiura              |                         |                                        |                                       |
| Mild                             | 13 (21.7)               | 24 (40)                                | 24 (40)                               |
| Moderate                         | 2 (3.3)                 | 2 (3.3)                                | 1 (1.7)                               |
The Statistical analysis did not show a significant reduction in egg count on the 7th day after therapy in all groups, whereas there was a significant reduction in the 14th and 21st day in all groups. Determination of egg reduction rate can be seen in Table 4.

### Table 4: Egg Reduction Rate on Day 7th, 14th, 21st

| Parasites | Anthelmintics | Mean (SD) | Mean (SD) | Mean (SD) | P value |
|-----------|---------------|-----------|-----------|-----------|---------|
| A. lumbricoides | Albendazole | 34.00 ± 165.64 | - | - | 0.651 |
| | Albendazole + Levamisole | 14.40 ± 111.54 | - | - | - |
| | Mebendazole + Levamisole | 34.80 ± 126.25 | - | - | - |
| T. trichiura | Albendazole | 33.60 ± 95.91 | 24.80 ± 81.23 | 20.40 ± 74.96 | 0.247 |
| | Albendazole + Levamisole | 20.00 ± 89.38 | 12.40 ± 73.47 | 7.60 ± 47.89 | - |
| | Mebendazole + Levamisole | 40.00 ± 122.66 | 18.80 ± 68.03 | 8.80 ± 29.63 | - |

The cure rate of helminthiasis on the 7th day was 81.7% after albendazole therapy, 88.3% after albendazole + levamisole therapy, and 83.3% after mebendazole + levamisole therapy (p = 0.577). Cure rate on the 14th day was 88.3%, 95%, and 91.7% for albendazole, albendazole + levamisole, and mebendazole + levamisole therapy, respectively (p = 0.418). On the 21th day, the cure rate was 88.3%, 96.7%, and 91.7% (p = 0.230). Combination of albendazole and levamisole showed the highest cure rate, despite the statistically insignificant difference for all groups (p > 0.05). Determination of cure rates analysis can be seen in Table 5.

### Table 5: The Cure Rates Analysis On Day 7th, 14th, 21th

| Recovery | Therapy | Recovered | Not Recovered | P |
|----------|---------|-----------|---------------|---|
| Albendazole (Day-7) | 49 | 81.7 | 11.8 | 0.577 |
| Albendazole + Levamisole (Day-7) | 53 | 88.3 | 7.11 | 0.7 |
| Mebendazole + Levamisole (Day-7) | 50 | 83.3 | 10.17 | 0.53 |
| Albendazole (Day-14) | 53 | 88.3 | 7.11 | 0.418 |
| Albendazole + Levamisole (Day-14) | 57 | 95.0 | 5.0 | - |
| Mebendazole + Levamisole (Day-14) | 55 | 91.7 | 5.8 | - |
| Albendazole (Day-21) | 53 | 88.3 | 7.11 | 0.230 |
| Albendazole + Levamisole (Day-21) | 58 | 96.7 | 2.33 | - |

Combination of albendazole combined with levamisole showed better cure rate for mild trichuriasis (95.8%) than albendazole therapy (46.2%) and mebendazole + levamisole (83.3%), p = 0.00. Determination of cure rate mild helminthiasis analysis can be seen in Table 6 and Table 7.

### Table 6: The Cure Rate of Mild Helminthiasis

| Parasite(s) | Treatment | Cured | Not Cured | P |
|-------------|-----------|-------|-----------|---|
| A. lumbricoides | Albendazole | 46 | 92 | 8 | 0.176 |
| | Albendazole + Levamisole | 39 | 100 | - | - |
| | Mebendazole + Levamisole | 42 | 91.3 | 4.8 | - |
| T. trichiura | Albendazole | 6 | 46.2 | 7 | 53.8 | 0.01 |
| | Albendazole + Levamisole | 23 | 95.8 | 1 | 4.2 | - |
| | Mebendazole + Levamisole | 20 | 83.3 | 4 | 16.7 | - |

The side effects during the treatment process in each group had been observed. Side effect observed in the albendazole group were 13.3%. Albendazole combined with Levamisole was 26.7%.

Observation data of side effect can be seen in Table 8.

### Table 8: Side Effects analysis

| Side Effect | Albendazole | Albendazole + Levamisole | Mebendazole + Levamisole |
|-------------|-------------|--------------------------|--------------------------|
| None | 52 (86.7) | 44 (73.3) | 48 (80.5) |
| Yes | 8 (13.3) | 16 (26.7) | 12 (20.0) |

### Discussion

Helminthiasis has still been a major health problem in Indonesia. A. lumbricoides, T. trichiura and hookworm (N. americanus and A. duodenale) were the most common etiology. WHO data on 2012 reported a high prevalence of helminthiasis in North Sumatera, i.e. 80% of school-aged children [18], [19].

Statistical analysis did not show a significant reduction in egg count on the 7th day after therapy in all groups, whereas there was a significant reduction in the 14th and 21st day in all groups. Even after the reduction in egg number at 14th and 21st day, we still found several T. trichiura eggs in subjects’ stool, indicating the difficulty in eradicating trichuriasis as mentioned in the literature [20]. A study by Saputri in 2010 found significant egg reduction rate in single-dose mebendazole and mebendazole with levamisole therapy for A. lumbricoides and T. trichiura infections [21]. The contradictive result was found by Sihite et al., (2014) and Knopp et al., (2010) study, which found no significant difference in the treatment with mebendazole, albendazole, and mebendazole with levamisole [22], [23].

Based on Table 5, the combination of albendazole and levamisole showed the highest cure rate, despite the statistically insignificant difference for all groups (p > 0.05). Therefore, this finding indicated the similar efficacy of albendazole, albendazole + levamisole, and mebendazole + levamisole therapy.

Based on Table 6, the combination of albendazole with levamisole showed better cure rate for mild trichuriasis (95.8%) than albendazole therapy (46.2%) and mebendazole combined with levamisole (83.3%), p = 0.01. We hypothesised that levamisole had enhanced efficacy than albendazole and mebendazole for mild trichuriasis. Previous studies
showed that a single dose of albendazole or mebendazole had 28% and 36% recovery rate, respectively [16, 23]. For mixed infection, albendazole combined with levamisole was more effective (cure rate 85.7%) than single albendazole (28.65%) or mebendazole combined with levamisole (66.7%), \( p = 0.079 \) that showed on Table 7. A study by Sihite et al., (2014) found no significant difference in the recovery of helminthiasis with mebendazole + levamisole or single mebendazole therapy [22]. Another study found no significant differences in the recovery rate of helminthiasis between mebendazole with or without levamisole therapy [21]. The most common side effects in all groups were nausea and diarrhoea. No serious side effects were observed in this study, and mild side effects had recovered by their own. Table 8 shows that there was no difference in side effects between intervention groups.

It can be concluded that single-dose albendazole, a combination of albendazole and levamisole, and the combination of mebendazole and levamisole had similar efficacy in reducing egg count in helminthiasis. Combination of albendazole and levamisole showed better cure rate for mild trichuriasis and mixed infections. Side effects were similar in all treatment groups.

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