

## The Effectiveness of Albendazole-Levamisole and Mebendazole-Levamisole on the Intensity of *Trichuris trichiura* Infection in Elementary School Children

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### ABSTRACT

**Background:** *Trichuris trichiura* worm infection is still a major public health problem in Indonesia, especially in peripheral areas. Until now, the search for antihelmintic combinations that have a high healing ability against *T. trichiura* infections and in the search for truly effective worming is still being done. Albendazole and Mebendazole single doses still show limited efficacy in the treatment of *T. trichiura* worms. The combination of Albendazole with Levamisol can increase effectiveness, but this combination still needs further investigation. Based on that fact, it is necessary to study the effectiveness comparison of the degree of infection intensity between the treatment of Albendazol-Levamisol and Mebendazol-Levamisol against *T. trichiura*.

**Subjects and Method:** A double blind randomized control trial was conducted at the State Elementary School in Medan, North Sumatera, from April to October 2019. A sample of 60 children was selected for this study. The dependent variable was the number of eggs decreased, the cure rate, and side effects. The independent variables were Albendazole 400 mg-Levamisol 50 mg/100 mg and Mebendazole 500 mg-Levamisol 50 mg/100 mg. The stools of elementary school children were examined using the Kato-Katz method to find eggs of *T. trichiura* infection. Data analysis was performed using the Chi square test.

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**Results:** Samples in the Albendazol-Levamisol and Mebendazol-Levamisol groups were 30 children, respectively. Children infected with *T. trichiura* consisted of 58 children of mild intensity (96.7%) and 2 children of moderate intensity (3.3%). On the results of stool examination, a significant difference in the number of eggs decreased in the two groups was obtained ( $p < 0.001$ ) and 96.7% was the cure rate for *T. trichiura* infection in the two groups of Albendazol-Levamisol and Mebendazol-Levamisol. In this study, there were no significant differences in side effects in the two treatment groups.

**Conclusion:** Treatment of *T. trichiura* infection with single doses of Albendazol-Levamisol and Mebendazol-Levamisol showed that there were significant differences in the Number of Decreased Eggs. Meanwhile, for the cure rate, there was no difference between the Albendazol-Levamisol and Mebendazol-Levamisol groups.

**Keywords:** *T. trichiura*, Albendazole-Levamisol, Mebendazole-Levamisol

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## BACKGROUND

Intestinal helminth disease is still a major public health problem in Indonesia, especially in rural areas. In Indonesia and in various developing countries, *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm are intestinal parasites of the nematode group that most often cause infections. An estimated 4.5 billion individuals are at risk of STH, of whom 1.2 billion may be infected with *A. lumbricoides*, nearly 800 million are infected with *T. trichiura*, and more than 700 million are infected with hookworms. More than 60% of children in Indonesia suffer from worm infections.

According to data from the North Sumatra Provincial Health Office, about 32% of North Sumatra's population suffers from worms, and about 87% of elementary school students in Deli Serdang suffer from worms. Many species of worms have been reported to cause infections in Indonesia. *T. trichiura* which lives in the human cecum is the most difficult cause of intestinal worms and one of the most important intestinal nematodes in humans. This helminthiasis is classified as a neglected disease, which is an infection that is lacking in attention and is chronic without causing clear clinical symptoms and the resulting impact is only seen in the long term. The *T. trichiura* worm is the most difficult to treat, which if usually infected by 2 other worms (*Ascaris lumbricoides* and hookworm) once taking medication immediately healed. However, *T. trichiura* has to take medicine three days in a row before it can show improvement (Beth Monkey al., 2006; Dent and Kazura, 2007; CDC, 2013).

In the management of infections, *T. trichiura* worm commonly used drug albendazol or mebendazol which can eradicate helminthiasis with each of the advantages and disadvantages. But in its implementation, it is still unsatisfactory in its treatment. Therefore in this study, it was used to see the

effectiveness comparison of the drug combination of the albendazole-levamisole group with mebendazole-levamisole against *T. trichiura* worm infections.

## SUBJECTS AND METHOD

### 1. Study Design

This was double blind randomized trial, which compared the effectiveness of Albendazol-Levamisole and Mebendazol-Levamisole dose alone against *Trichuris trichiura* infection.

The study was conducted at the Parasitology Laboratory of the Faculty of Medicine, Methodist University of Indonesia. To check the number of worm eggs in the stool before and after treatment, this is done by the Kato-Katz method.

### 2. Population dan Sample

The study population was elementary school children in Medan (Belawan and Tembung Districts) who were infected by *Trichuris trichiura*. Students selected as samples were children who tested positive for being infected by *Trichuris trichiura* based on the results of stool examinations in the laboratory by the Kato Katz method.

A sample of 60 children divided into two groups (Albendazol-Levamisole and Mebendazol-Levamisole) were selected for this study.

### 3. Study Variables

The dependent variable is the Number of Decreased Eggs (APJT) and the cure rate and side effects. The independent variables are Albendazol-Levamisole and Mebendazol-Levamisole.

## RESULTS

This study was conducted on students of public elementary schools in the city of Medan carried out starting in April and October 2019. The number of students was 251 people. Of the 216 students who returned the pots, 63 63 positive elementary school

students suffered from *Trichuris trichiura* infection through the Kato-katz examination. Of the 63 elementary school children, only 60 elementary school children met the study criteria, then randomly divided into 2 groups with group I (Albendazol 400 mg with single-

dose Levamisol one day), 60 children of elementary school and group II (Mebendazol 500 mg with a single dose of Levamisole one day) which is 60 children of elementary school students. The profile of the study can be seen in Figure 1.

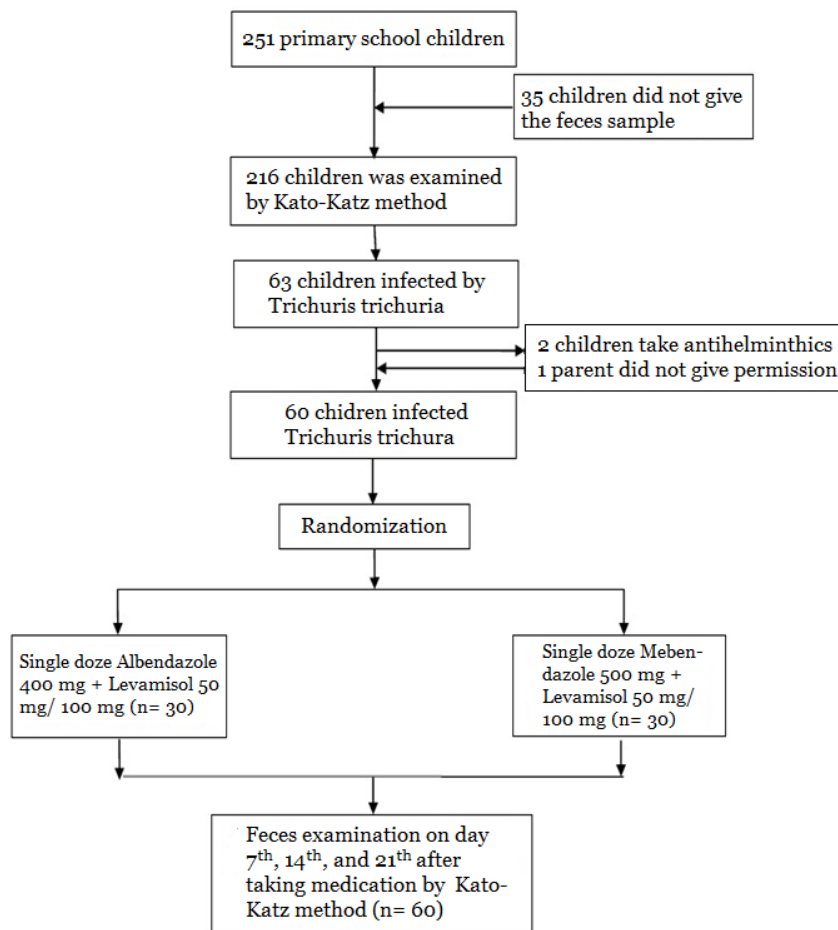


Figure 1. Study Profile

Table 1. Sample Characteristics

Characteristics	Albendazol-Levamisol n(%)	Mebendazol-Levamisol n(%)	p
<b>Gender</b>			
Male	16 (53.3)	14(46.7)	0.606
Female	14 (46.7)	16(53.3)	
<b>Infection Intensity</b>			
Mild	30 (100)	28 (93.3)	
Moderate	0 (0)	2 (6.7)	
<b>Nutritional Status</b>			
Poor	15 (50.0)	25 (83.3)	0.018
Good	15 (15.0)	5 (16.7)	

Table 1 shows that there were more male respondents than female respondents in the Albendazole-Levamisol group. Male respondents totaled 16 children (15.3%) and female respondents totaled 14 children (46.7%). Meanwhile, the number of males in the single-dose Mebendazole-Levamisol group was 14 children (46.7%) and women were 16 (53.3%).

The intensity of the infection is divided into mild and moderate infections. In *T. trichiura* infection the Albendazol-Levamisol combination drug group with a single dose of 30 children (100%) suffered from a mild in-

fection, while the Mebendazol-Levamisol single dose combination drug group had 29 children (96.7%) suffering from a mild infection and 1 child (3.3 %) have a moderate infection.

Nutritional status is divided into malnutrition and good nutrition. In the single-dose Albendazol-Levamisol group, there were 15 children (50%) who were undernourished, 15 children (50%) had good nutrition. Meanwhile, the single-dose Mebendazol-Levamisol group consisted of 25 children (83.3%) malnourished, and 5 children (16.7%) good nutrition.

**Table 2. Results of analysis of the number of STH eggs on Albendazol-Levamisol and Mebendazol-Levamisol on Day 21 After Treatment**

Intervention	n	Average Drop Rate of Eggs	SD	p
Albendazol-Levamisol	30	3.2	17.52	0.001
Mebendazol-Levamisol	30	12.0	65.72	

Table 2 shows that there were significant APJT differences in both groups for albendazole-levamisole (Mean= 3.2; SD = 17.52) and mebendazole-levamisole (Mean = 12; SD = 65.72) with p = 0.001 on the 21st day after treatment.

In table 3, observation of the 7<sup>th</sup> day, after the administration of a single dose of Albendazol-Levamisol combination, as many

as 2 children (6.7%) were not cured (6.7%) and Mebendazol-Levamisol was given as a single dose, children who did not recover were 2 children (6.7 %). On the 14<sup>th</sup> day of observation, after giving a single dose of Albendazol-Levamisol combination, 2 children (6.7%) were not recovered and 6.7 (single dose of Mebendazol-Levamisol) showed that 1 child (3.3%) did not recover .

**Table 3. The results of the analysis of single dose Albendazol-Levamisol and Mebendazol-Levamisol on the cure rate of STH infections on the 7<sup>th</sup>, 14<sup>th</sup> and 21<sup>st</sup> days**

Day	N cured	Cured proportion	p
<b>Day 7</b>			
Albendazol-Levamisol	28	93.3	1.000
Mebendazol-Levamisol	28	93.3	
<b>Day 14</b>			
Albendazol-Levamisol	28	93.3	0.584
Mebendazol-Levamisol	29	96.7	
<b>Day 21</b>			
Albendazol-Levamisol	29	96.7	1.000
Mebendazol-Levamisol	29	96.7	

At the observation of the 21<sup>st</sup> day after giving a single dose of Albendazol-Levamisol combination where the child who did not recover was as much as 1 (3.3%) and giving a single dose of Mebendazol-Levamisol combination where the child who did not recover was as much as 1 child (3.3%) (p= 1.000). The results of all observations showed that the comparison of *T. trichiura* infections with

mild to moderate intensity, from the two groups giving Albendazol 400 mg-Levamisol 50mg / 100mg and the combination of Mebendazol 500mg-Levamisol 50mg/100mg single dose did not show significant differences in cure rates.

Table 4 shows almost no difference between side effects in the two groups of drugs (p>0.050).

**Table 4. Side Effects of Albendazol-Levamisol and Mebendazol-Levamisol**

Characteristics	Side Effects		p
	Negative n(%)	Positive n(%)	
Albendazol-Levamisol	22 (73.3)	8 (26.7)	0.095
Mebendazol-Levamisol	27 (90.0)	3 (10.0)	

### DISCUSSION

Helminthiasis due to STH infection is still a major health problem for the people of Indonesia. *A. lumbricoides*, *T. trichiura* and hookworms (*N. americanus* and *A. Duodenale*) are the most common types of worms (Shumbejet al., 2015). WHO data (2012) shows that the area of North Sumatera is a relatively high degree of STH infection with a prevalence in the range of more than 80% for school-age children.

Comprehensive treatment through government programs in the field of health and individually against helminth infections has been carried out, but the incidence of infection with this disease is still high. Conversely, research by conducting health education and environmental interventions can reduce the number of worm infections in the community. It turns out that treatment alone without changes in Knowledge, Attitudes and Health Practices (PSP), can not reduce the reinfection rate of this worm infection (Strickland, 2000; Donkor and Lunberg, 2009).

On stool examination by the Kato-Katz method, a decrease in the number of eggs was seen in all groups of Albendazol-Levamisol, Mebendazol-Levamisol until the 21st

day. Statistical analysis with chi square on day 21 showed that the Albendazol-Levamisol and Mebendazol-Levamisol groups showed the effect of decreasing the number of eggs of different *Trichuris trichiura* (p <0.05). This is in contrast to study by Anto and Nugraha (2019), which found that APJT was not significant between Albendazol, Albendazol-Levamisol and Mebendazol-Levamisol in *T. Trichiura* infection on day 21 after treatment (p= 0.247).

Another study by Saputri (2010) showed that APJT was significant in the single dose Mebendazole group and Mebendazol-Levamisol both in *T. trichiura* infection after treatment. Whereas the study of Sihite, et al. (2014) showed that there was no significant difference in APJT in the single-dose Mebendazole group with the Mebendazol-Levamisol combination in STH infections. Study by Knopp, et al. (2010), states that there is no significant effect on APJT in the Albendazol and Mebendazol groups. In the 21st day study, the same cure rate was 96.7% (Table 3). Statistical analysis with chi square on day 21 of the Albendazol-Levamisol and Mebendazol-Levamisol groups did not show a significant difference with p= 1.000 for the cure rate (p>0.050).



All results showed that *T. trichiura* infection from the two groups of the drug Albendazol-Levamisol and Mebendazol-Levamisol showed no significant difference in AP (cure rate). This is similar to Julianto study (2017), which states that there is no significant difference in AP in the Albendazol, Albendazol-Levamisol and Mebendazol-Levamisol groups in *T. trichiura* infection  $p= 0.136$ .

Study conducted by Sihite et al. (2014) noted that there was no significant difference in cure rates for STH infections in the Mebendazol-Levamisol group compared to Mebendazol. According to Saputri in 2010, there was no significant difference in the cure rate.

Side effects found for the three groups after treatment were found by researchers only in the form of nausea and diarrhea. Comparison of side effects found in the Albendazol-Levamisol and Mebendazol-Levamisol groups were 26.7% and 10%, respectively (Table 4). This study used the 400mg Albendazol drug (Albendazol, PT. Indofarma), 500mg Mebendazole (Vermox 500®), Janssen-Cilag) and Levamisol (Askamex, Konimex). The results obtained showed that there were no links or sponsorship messages from the three drug trade names.

Helminthiasis due to STH infection is still a major health problem for elementary school children, especially in *T. trichiura*. In this study, it was found the most for mild-degree infection intensity. Use of Albendazole 400mg-Levamisol 50mg/ 100mg, Mebendazol 500mg-Levamisol 50/ 100mg and single dose Albendazol 400mg showed significant differences in terms of decreasing number of eggs in general after 21st day treatment.

As for the cure rate for STH infections, there were no significant differences between the two groups after 21st day treatment. In this study, side effects were found in the form of nausea and diarrhea in the comparison of the two treatment groups.

#### **AUTHOR CONTRIBUTION**

The contribution of researchers in this study is as main researcher and a member of this research who play a role in designing and drafting, providing socialization, collecting samples, conducting examinations, preparing reports, presentations and reports.

#### **CONFLICT OF INTEREST**

The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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