

## Effect of length of albendazole treatment against *Trichuris trichiura* infection

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### Abstract

**Background** *Trichuris trichiura* is one of the most common soil-transmitted helminth that infects school-aged children. A single dose of albendazole has been shown to have wide variations in cure and egg reduction rates. Some studies have suggested that repeated doses of albendazole might increase its effectiveness.

**Objective** To compare the anti-trichuriasis effect of 400 mg albendazole taken daily for five consecutive days vs. seven consecutive days.

**Methods** A randomized open clinical trial was conducted from August to September 2009 on elementary school children at Jaring Halus in the North Sumatera Province. Stool specimens were collected before treatment and on days 7, 14, 21, and 28 after initiation of treatment, and examined by the *Kato Katz* method. Subjects were randomized into two groups. Group I received 400 mg albendazole daily for five consecutive days and Group II received 400 mg albendazole daily for seven consecutive days. Cure rates and egg reduction rates were compared using Chi-square and T-tests, respectively.

**Results** One hundred twenty-one children were enrolled, consisted of 61 children in Group I and 60 in Group II. For the first week after treatment ended, the cure rates in Group II was higher (86.7%) than in the Group I (39.3%) ( $P=0.001$ ), as well as in the second week after treatment ended (88.3% vs 68.9%,  $P=0.017$ ). However, after 3<sup>rd</sup> and 4<sup>th</sup> weeks, the cure rates were no longer significantly different. Egg reduction rate was also statistically higher in the Group II [20.3 (SD 23.77) %] compared to Group I [6.6 (SD 11.30) %].

**Conclusions** Albendazole for seven consecutive days is more effective in curing *Trichuris trichiura* infection in the 1<sup>st</sup> and 2<sup>nd</sup> weeks after treatment compared to that of five consecutive days, as well as in egg reduction rate, but the length of treatment does not influence the cure rate after the 3<sup>rd</sup> and 4<sup>th</sup> weeks.

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**Keywords:** albendazole, trichuriasis, single dose, repeated doses

Many species of helminths have been reported to cause infections in Indonesian populations. However, only some of these species are highly prevalent and widely distribute.<sup>1</sup> Trichuriasis, one of the most common soil-transmitted helminths (STH), compromises child health by disrupting growth, anemia, retarded cognitive development, and interfering with the immune response of the infected children.<sup>1-3</sup> Four antihelminthics are currently on the WHO model list of essential medicines for treatment and control of STH; those are albendazole, mebendazole, levamisole, and pyrantel pamoate.<sup>4</sup>

Albendazole is one of WHO-recommended antihelminthics for STH, including trichuriasis,<sup>3-6</sup> with a recommended single dose of 400 mg. A randomized controlled trial showed that albendazole single dosages of 400 mg, 800 mg, and 1200 mg revealed trichuris cure rates of 23%, 56%, and 67%, respectively. The corresponding egg reductions per gram of faeces were 96.8%, 99.3%, and 99.7%, respectively.<sup>7</sup> However, other data showed that increasing the dose of albendazole taken once daily did not always result in

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increased its efficacy, due to drug's antiparasitic action being dependent on prolonged contact time.<sup>8</sup>

The objective of this study was to compare the anti-trichuriasis effect of 400 mg albendazole taken daily for five consecutive days vs. seven consecutive days.

## Methods

A randomized open trial study was conducted between August to September 2009 in elementary school children at Secanggang, North Sumatera Province, Indonesia. Eligible participants were all children with stool examinations positive for trichuriasis, who had not taken antihelminthics for at least one month prior to the study, and whose parents provided an informed consent. We excluded children who refused to swallow the antihelminthic, refused to submit stool specimens after treatment, or had diarrhea. Participants were randomly assigned following a simple randomization procedure (using a random table) to one of two treatment groups. The first group received 400 mg albendazole once daily for five consecutive days, while the second group received 400 mg albendazole once daily for seven consecutive days.

Subjects collected stool specimens in provided plastic specimen bottles. Stool specimens were examined by the quantitative *Kato-Katz* method. Prior to treatment, participants underwent anthropometric assessments, and completed questionnaires on their socioeconomic and hygiene status. The albendazole regimen was given according to the group allocation. Participants chewed the tablets before swallowing with water while being observed by the investigators.

After the treatment regimens, subjects' stool specimens were re-examined on days 7, 14, 21, and 28. Infection intensity was determined according to WHO classification. All adverse reactions were recorded. Outcomes measured were cure rate and egg reduction rate. Cure rate reflected the percentage of egg-positive individuals who became negative after treatment. The reduction of mean eggs per gram (EPG) in stool was considered as egg reduction rate. Written informed consent was obtained from subjects' parents. This study was approved by the Medical Ethics Committee of the University of North Sumatra Medical School.

The primary analysis involved all patients who

were randomly assigned to a group. Cure rates and egg reduction rates of the two groups were compared using Chi-square and T-test, respectively. Differences were considered to be statistically significant for P values < 0.05.

## Results

During the study period, out of 435 children screened, we found 215 with STH infection. Ninety-one children did not return stool specimens for analysis, so 124 children were enrolled into this study and divided into two groups. Later, 3 subjects dropped out, leaving 61 children allocated to the first group, and 60 children to the second group (**Figure 1**).

The two treatment groups were balanced in terms of baseline characteristics (**Table 1**).

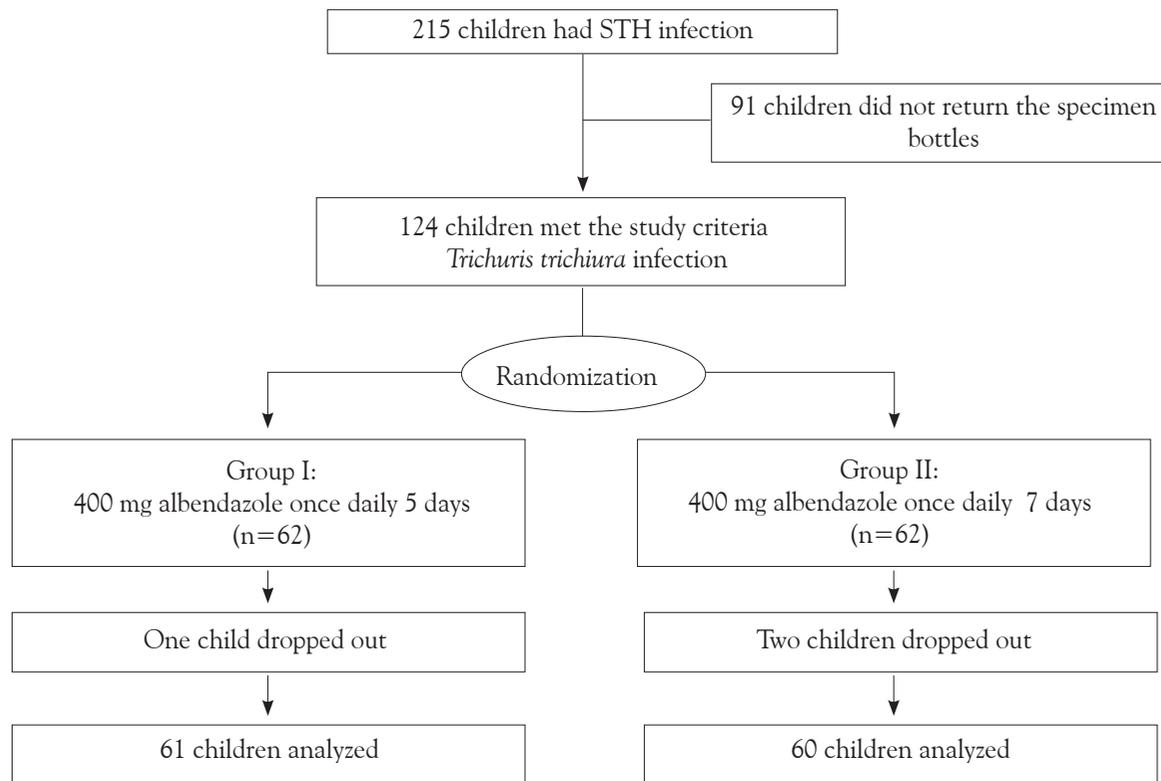
**Table 2** shows the cure rates of both groups over the 4 weeks after treatment was completed. Cure rates were significantly different between Group I and Group II with 39.3% vs 86.7%, respectively (P=0.001), in the first week after treatment, and 88.3% vs. 68.9%, respectively (P=0.017), in the second week after treatment. In the third and fourth weeks of observation there were no significant differences between the two groups (P=0.163 and P=0.365, respectively). Also, both regimens gave the highest cure rate at the fourth week, with 93.4% in Group I and 98.3% in Group II.

**Table 1.** Baseline characteristics of subjects

Characteristics	Received albendazole once daily	
	5 days (n=61)	7 days (n=60)
Age		
Mean (SD), years	9.5 (1.85)	9.6 (1.71)
Gender, n (%)		
Male	30 (51.7)	28 (48.2)
Female	31 (49.2)	32 (50.8)
Mean body weight (SD), kg	22.3 (5.53)	21.8 (4.18)
Mean body height (SD), cm	124.9 (9.88)	124.4 (8.96)
Trichuris eggs		
Range, eggs/g feces	46 – 6900	46 – 3036
Mean (SD), eggs/g feces	372.9 (962.60)	516.7 (624.99)
Egg counts, EPG		
Range	2 – 300	2 – 132
Mean (SD)	16.2 (41.85)	22.5 (27.17)

**Table 2.** The cure rates at the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> weeks after treatment

Albendazole administration	Group I		Group II		P value
	Cured n (%)	Not cured n (%)	Cured n (%)	Not cured n (%)	
1 <sup>st</sup> week	24 (39.3)	37 (60.7)	52 (86.7)	8 (13.3)	0.001
2 <sup>nd</sup> week	42 (68.9)	19 (31.1)	53 (88.3)	7 (11.7)	0.017
3 <sup>rd</sup> week	54 (88.5)	7 (11.5)	58 (96.7)	2 (3.3)	0.163
4 <sup>th</sup> week	57 (93.4)	4 (6.6)	59 (98.3)	1 (1.7)	0.365



**Figure 1.** Study profile

Egg reduction rates were noted in both groups. However, we found that the mean egg reduction in the Group II was higher than that of the Group I [20.3 (SD 23.77)% and 6.6 (SD 11.30)%; P=0.001, respectively].

Treatment adverse effects were recorded in both groups. In Group I nausea was found in 1 child (1.6%) and dizziness in 2 children (3.3%) while in Group II we found dizziness in 1 child (1.7%), dry mouth in 3 children (3%), and diarrhea in 1 child (1.7%).

## Discussion

The prevalence of trichuriasis in our study was 49%. In contrast, a previous study on primary school children in North Sumatera in the year of 2004 reported the prevalence to be 78.6%.<sup>2</sup>

Although albendazole is a broad spectrum antihelminthic drug that is widely used in a single oral dose to control intestinal nematodes, it is remarkably less effective in trichuriasis treatment than

in treatment of ascariasis or hookworm infections.<sup>9</sup> Single dose albendazole has been observed to be ineffective in most trichuriasis cases.<sup>10</sup> Multiple doses were needed to attain complete parasitological cures in all cases in a previous study.<sup>11</sup> Another study found that 3 consecutive daily doses of 400 mg albendazole was more effective in the treatment of trichuris infection.<sup>12</sup>

An increase in the duration of albendazole treatment from a single dose to five or seven doses, on consecutive days was shown to increase the efficacy of the treatment against trichuris infection.<sup>9</sup> Our results confirmed that albendazole treatment for seven consecutive days resulted in a significant reduction in the number of trichuris eggs being excreted. Also, a cure rate of 86.7% after 7 days of treatment in our study was markedly higher than the cure rate of 39.3% after 5 days of treatment. At the end of each week, the cure rate was higher in the 7-day treatment group, though not significantly different at weeks 3 and 4.

Worm infections impair child development by constraining growth, learning, and school attendance.<sup>13</sup> Worms feed on the host's gut contents, causing maldigestion and malabsorption, as well as a chronic inflammatory state that affects the appetite, leading to malnutrition.<sup>14</sup> Worm burden is a key indicator of morbidity in STH infections including trichuriasis. Another factor is the duration of infection, but such parameters are usually unknown.<sup>15</sup>

Another study performed in North Sumatera also shows that a single dose of albendazole has high efficacy against trichuriasis, reporting a 93.48% cure rate and a 99.69% egg reduction rate.<sup>2</sup> However, a Peruvian study reports a 58% cure rate and a 98.4% egg reduction rate.<sup>16</sup> A study reported a decreased prevalence of trichuriasis from 84% to 41.7% in 2002, and a 56.1% egg reduction rate in 2007.<sup>17</sup> Furthermore, in a systematic review, a single dose of albendazole was still recommended for all soil-transmitted helminthiasis.<sup>18</sup> The WHO reported that a single dose of albendazole still gave an acceptable egg reduction rate of about 80%.<sup>8</sup> Efficacy is still considered good if the cure rate is modest but accompanied with a high egg reduction rate. Egg reduction rate was relied on because it indicates a decreasing worm burden which would prevent further transmission.<sup>19</sup>

The effect of infection intensity is most pronounced in *T. trichiura* infection where a substantial

reduction in cure rate is seen in heavier infections. In a single dose albendazole trial, moderate and heavy cases usually had decreased cure and egg reduction rates.<sup>20</sup> A Thai study also reported a higher efficacy of a longer albendazole regimen, when analysis was based on intensity of infection.<sup>9</sup>

The only adverse effects detected in our subjects were nausea, dizziness, dry mouth, and diarrhea. The incidence of side effects reported in past studies on the use of albendazole for intestinal helminthiasis is very low, with only gastrointestinal side effects (all types of symptoms pooled) occurring with an overall frequency of just greater than 1%.<sup>20</sup> A study which used the longer regimen of up to 7 days reported an incidence of all side effect to be as much as 2.9%.<sup>19</sup>

A limitation of our study was that there was no blinding done, so the possibility of bias cannot be excluded. Also, trichuriasis diagnosis was done by a single *Kato-Katz* examination. The accuracy of this method in detecting STH infection is greatly influenced by day-to-day egg excretion rates.

In conclusion, albendazole for seven consecutive days is more effective in curing *Trichuris trichiura* infection in the 1<sup>st</sup> and 2<sup>nd</sup> weeks after treatment compared to that of five consecutive days, as well as in egg reduction rate, but the length of treatment does not influence the cure rate after the 3<sup>rd</sup> and 4<sup>th</sup> weeks.

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