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The Effect of Albendazole Administration and Iron-Folic Acid Supplementation on Hemoglobin Level in Primary Schoolchildren with Soil-transmitted Helminth Infections

Willhans Wijaya, Ayodhia Pitaloka Pasaribu*, Erwin Suteno, Nirmala Husin, Syahril Pasaribu

Department of Child Health, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Abstract

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***Correspondence:** Ayodhia Pitaloka Pasaribu, Jln. Tridharma No. 110 Kampus USU, E-mail: ayodhia@usu.ac.id
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BACKGROUND: Soil-transmitted helminth (STH) infections were the highest infection in children aged 5–15 years old. They lead to iron deficiency anemia and folic acid deficiency. One of the strategies to treat the issues is anthelmintic administration with iron-folic acid supplementation.

AIM: This study aims to evaluate the effectiveness of single-dose albendazole and albendazole with iron-folic acid supplementation on hemoglobin (Hb) levels in children with STHs.

METHODS: This was an open-label randomized clinical trial conducted in Batubara Regency from September to November 2018. Subjects were primary schoolchildren with STH infections. They were grouped into albendazole and albendazole with iron-folic acid supplementation groups. The data were analyzed by independent t-test and Mann–Whitney U-test.

RESULTS: From 139 children, 72 children received albendazole single dose and 67 children received albendazole with 30 mg iron and 250 µg folic acid weekly for 3 months. The median of baseline hemoglobin level was 12.2 gr/dL, whereas after intervention was 12.7 gr/dL. The hemoglobin level increases did not differ significantly between the two groups ($p > 0.05$). However, clinical improvement was observed.

CONCLUSION: Iron-folic acid supplementation in addition to albendazole did not show any benefit for primary schoolchildren with STH infection in Batubara Regency, North Sumatera, Indonesia.

Introduction

Soil-transmitted helminths (STHs) are groups of nematode worms which cause infections in humans through contacts with soil that contain worm eggs or larvae. In general, STH infections are caused by roundworms (*Ascaris lumbricoides*), whipworms (*Trichuris trichiura*), threadworms (*Strongyloides stercoralis*), and hookworms (*Ancylostoma duodenale* and *Necator americanus*) [1], [2], [3], [4].

The research done by Pasaribu (2004) in Suka Village, TigaPanah district, Karo Regency, North Sumatera, Indonesia, showed that the prevalence of helminthiasis in schoolchildren was 91.3% [5]. The performance accountability report of North Sumatera government health agency (2012) stated that the prevalence of STH infections in primary schoolchildren was 32.3%, with the distribution of *A. lumbricoides* and *T. trichiura* and hookworms species at 21%, 11%, and 0%, respectively [6]. Another study done by Jiero *et al.* (2015) in Medan, Belawan, North Sumatera in two primary schools showed 65.4% prevalence of STH infections [7]. The provided data have shown that

helminthiasis cases are still high in schoolchildren, especially in North Sumatera.

STH infections mainly occur in children living in slums where sanitation is inadequate, population is dense, education levels are low, and health facilities are lacking. World Bank stated STH infections as the most found cases of infections in children aged 5–15 years old [8]. The long-term effects of STH infections can affect nutritional status in children, performance in schools, and long-term cognitive development. Iron status is assumed to be the intermediary for the occurrence of those effects. Hookworm and whipworm infections are related to iron deficiency anemia which lead to the decrease of physical activity and work productivity. Besides that, STH infections also cause micronutrient deficiencies, one of them is folic acid [8], [9].

Hookworm infection is the main cause of anemia and iron deficiency in children. They depend on several factors such as the species and quantity of worms, the length of infections, iron deposits in the body, food intake and absorption, and the physiology of iron needs. Mild hookworm infection may cause anemia in individuals with low iron intake and stores in the body. *A. duodenale* infection is less common but it causes

higher blood loss than *N. americanus* infection. Adult worms attach to host's intestinal mucosa and ingest food from there. This is the main cause of blood loss from the intestines that lead to iron deficiency and anemia. Besides the habit of feeding on blood, hookworms also release anti-clotting factor that makes blood excreted continuously. *A. duodenale* causes 2–10 times more blood loss compared to *N. americanus* [10], [11].

A. lumbricoides worm infection is known to affect the nutritional status in infected children. However, the mechanism of anemia is not known clearly. The research done by Osazuwa *et al.* (2011) in Nigeria showed a significant correlation between *A. lumbricoides* infection and anemia [11]. Around 1 billion of school-age children in the world were estimated to be infected with at least one type of STH. While, around 600 million of pre-schools and schoolchildren were estimated to suffer from anemia. Half of those cases were caused by iron deficiency [12].

Iron supplementation aims to prevent anemia and treat iron deficiency before iron deficiency anemia occurs. The strategy for supplementation and food intake to increase iron stores is recommended in the population with risks of anemia and iron deficiency. Once a week iron and folic acid supplementation effectively increases iron stores [13], [14]. Besides that, the WHO recommends deworming strategy, in which anthelmintic is given to control the morbidity due to STH infections in high-risk populations. Anthelmintic drugs intervened to control STH infections are albendazole, mebendazole, levamisole, and pyrantel pamoate [15]. The study in India by Bhoite and Iyer (2012) showed that the supplementation of iron and folic acid in deworming program to schoolchildren led to effective hemoglobin increases [16].

This study aims to compare the efficacy of anthelmintic drug administration, which is albendazole due to its work mechanisms as larvicidal, ovicidal, and vermicide [17], followed by the supplementation of iron plus folic acid to increase Hb levels in schoolchildren with STH infections.

Methods

This study was an open-label randomized clinical trial conducted in SD Negeri 014734 Labuhan Ruku, SD Negeri 014740 Pahang, and SD Negeri 010157 Sei Muka in Talawi, Batubara Regency, North Sumatra. The study was done from September to November 2018. Samples that met inclusion and exclusion criteria were selected by simple random sampling. Inclusion criteria were schoolchildren in primary education level I–VI, with one or combined STH infections such as *A. lumbricoides*, *T. trichiura*, *A. duodenale*, or *N. americanus* based on Kato-Katz

analysis, no consumption of other anthelmintic drugs in ≤ 1 month and iron and folic acid in the past 3 months before the study. Exclusion criteria were all children who did not follow the study procedures such as blood sampling and feces collection and have been previously diagnosed, or through anamnesis and physical examination, with chronic diseases.

All parents and guardians were informed about the study and consent was received before joining the study. Feces were collected and examined by Kato-Katz method. Children with positive results of helminthiasis were divided into two groups and Hb level test was done to the children. The first group received albendazole 400 mg as a single dose, while the second group received albendazole 400 mg together with weekly administration of iron 30 mg and folic acid 250 μg for 3 months. Feces and Hb level tests were repeated after 3 months. Hb level was measured using HemoCue Hb 301.

Data analysis

Data analysis was done using computerized system SPSS version 22, with 95% confidence interval (CI) and significance level of $p < 0.05$. Data from both groups were analyzed using Chi-square and Mann-Whitney analyses to compare STH infections and Hb levels, respectively.

Ethical considerations

This study was approved by Health Research Ethics Committee, Medical Faculty, Universitas Sumatera Utara (No.01/TGL/KEPK FK USU-RSUP HAM/2018).

Results

Characteristic data of research subjects

In this study, feces examination was done to 384 children from primary education level I to VI. Based on the inclusion and exclusion criteria, 139 children with STH infections were involved in this research and they were divided into two groups. The first group consisted of 72 children and they received albendazole 400 mg tablet therapy as a single dose, whereas the second group consisted of 67 children who received albendazole 400 mg tablet therapy with weekly supplementation of iron 30 mg and folic acid 250 μg for 3 months. The consort flow diagram for the overall procedures is shown in Figure 1.

Most STH infections found were *T. trichiura* type of worms. STH infection mostly occurred in children at the age of 5–13 years old, with more male children

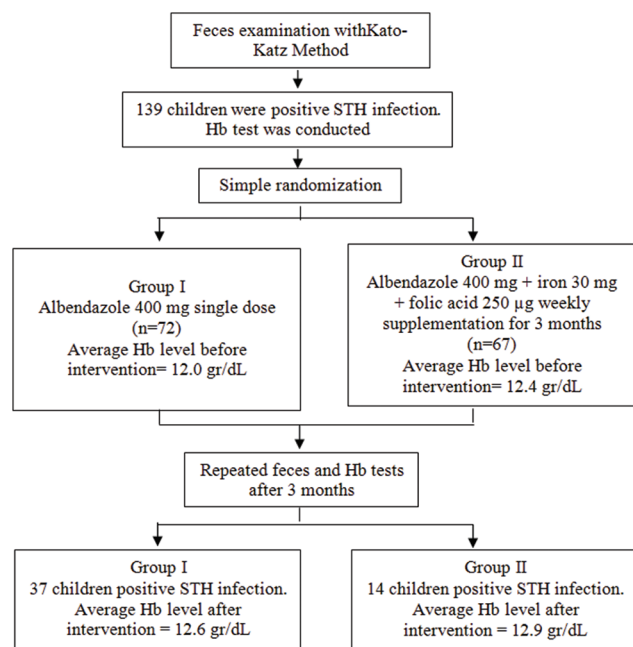


Figure 1: Consort flow diagram

than female's in both groups, where 56.9% of male and 43.1% of female in Group I while 53.7% of male and 46.3% of female in Group II. The average age of the two groups was 9 years old. The majority of children with STH infections were recorded to have good nutritional status. The distribution of subject characteristics data is shown in Table 1.

Table 1: Subject characteristics data distribution

Characteristic	Group I (n = 72)	Group II (n = 67)
Gender, n (%)		
Male	41 (56.9)	36 (53.7)
Female	31 (43.1)	31 (46.3)
Age, years old Median (range)	9 (5–13)	9 (6–12)
Weight, kg Median (range)	22 (14–61)	22 (17–39)
Height, cm Average (SD)	123.3 (10.8)	124.9 (8.9)
Nutritional status, n (%)		
Undernutrition	24 (33.3)	10 (14.9)
Good nutrition	40 (55.6)	53 (79.1)
Overnutrition	8 (11.1)	4 (6.0)
STH infections, n (%)		
<i>A. lumbricoides</i>	20 (27.8)	11 (16.4)
<i>T. trichiura</i>	65 (90.3)	57 (85.1)
Hookworm	0 (0)	1 (1.5)
Eggs/gram feces, epg		
Geometric mean (SD)		
<i>A. lumbricoides</i>	2395.5 (5.87)	95.5 (13.73)
<i>T. trichiura</i>	282.0 (4.24)	107.6 (2.31)
Hookworm	0 (0)	648 (648)
Hemoglobin level before intervention, gr/dL	12.0 (10.1–13.2)	12.4 (9.9–15.1)
Median (range)		

Comparison of soil-transmitted helminth infections before and after intervention

The prevalence of helminthiasis in this study conducted in Talawi, Batubara Regency, North Sumatra, was 36.2% (139/384). The most found worm infections were *T. trichiura* at 31.8% (122/384) followed by *A. lumbricoides* and hookworm at 8.1% (31/384) and 0.5% (1/384), respectively. The intensity of *A. lumbricoides* and *T. trichiura* worm infections was mild to moderate, while hookworm infection was at mild intensity.

There were 123 children with single STH infections while 16 children had two types of worm infections. The overall prevalence of STH infections dropped after albendazole therapy to 13.3% (51/384) with *A. lumbricoides* and *T. trichiura* infections become 1.3% (5/384) and 12.8% (49/384), respectively. There was an increase of hookworm infection prevalence to 0.5% (2/384). These data are presented in Table 2. The prevalence was decreased in both groups after the intervention for both *A. lumbricoides* and *T. trichiura* infections. There were no significant differences statistically in both groups after the intervention.

Table 2: The comparison of STH infections before and after intervention

Variable	Before albendazole administration n (%)	After albendazole administration n (%)
STH infection,		
<i>A. lumbricoides</i>	31 (8.1)	5 (1.3)
<i>T. trichiura</i>	122 (31.8)	49 (12.8)
Hookworm	1 (0.3)	2 (0.5)
Intensity of <i>A. lumbricoides</i> infection		
Mild	24 (6.3)	3 (0.8)
Moderate	7 (1.8)	2 (0.5)
Intensity of <i>T. trichiura</i> infection		
Mild	107 (27.9)	47 (12.2)
Moderate	15 (3.9)	2 (0.5)
Intensity of hookworm infection		
Mild	1 (0.3)	2 (0.5)
Moderate	0 (0)	0 (0)
STH single infections	123 (32)	47 (12.2)
Infections with two types of worms	16 (4.2)	4 (1)

Hb level differences after albendazole and iron-folic acid supplementation

The average Hb levels of all children before intervention in this study were 12.2 gr/dL and after intervention were 12.7 gr/dL. The differences between pre- and post-treatment in both groups were statistically significant ($p < 0.05$). However, there were no significant differences ($p < 0.05$) in Hb level increases between the groups with single dose of albendazole and the group with albendazole and iron-folic acid supplementation treatment (Table 3).

Table 3: Hb level in both research groups

Variable	Group I	Group II	P
Hb level before intervention, gr/dL	12.0 (10.1–13.2)	12.4 (9.9–15.1)	0.020*
Median (range)			
Hb level after intervention, gr/dL	12.6 (10.3–13.6)	12.9 (11.5–14.8)	0.010*
Median (range)			
Hb level increases, gr/dL	0.5 (-0.5–2.2)	0.3 (-2.3–3.3)	0.650 ^a
Median (range)			

^aMann-Whitney U-test

Discussion

STH infection is one of the major health problems in developing countries, especially in regions with warm and moist climate where the sanitation and hygiene are poor [18]. Indonesia is one of the countries with tropical climate where STH is suitably developed. The prevalence of STH infection in this study done in

Talawi, Batubara Regency, North Sumatra, was 36.2%. This result was lower than the previous studies done by Jiero *et al.* (2015) in Medan, Belawan, North Sumatra and Pasaribu (2019) in Suka Village, TigaPanah district, Karo Regency, North Sumatra, with 57.24% sample population positive for one or more STH infections. There were 67.91% of children with single infection, 30.97% with double infections, and 1.12% with triple infections [19]. The low prevalence may be due to the helminthiasis control program done by the government targeting pre-schools (1–4 years old) and school-age (5–12 years old) children [20].

This study shows STH infection occurred in children at the age of 5–13 years old. This result was not far different from the previous research done by Jiero *et al.* (2015) in Belawan that reported cases in children aged 7–13 years old (7), while another study done in Suka Village by Pasaribu (2004) and Pasaribu (2019) showed that children of 5–10 years old had the highest prevalence [5],[19].

There were more male children than female with STH infection cases. A study done by Annisa *et al.* (2018) in Palembang showed more female children (51.7%) with STH infections [21]. The differences in STH infections between male and female were not influenced by gender but lack of personal hygiene factor in children [22].

According to Ahmed *et al.* (2012) and Cabada *et al.* (2015), STH infections were correlated to the decrease of appetite and food intake which lead to the decrease of growth, poor physical health, and cognitive functions and even malnutrition in children [23,24]. In this study, a big portion of children with STH infections had good nutritional status. This result aligns with the previous study done by Maharani *et al.* (2015) in Padang where most children with STH infections had good nutritional status and there were no relationships between STH infections and nutritional status observed from body height and weight aspects [25]. However, a research conducted by Simarmata *et al.* (2015) in Kabanjahe, North Sumatra, showed that most children (70%) with STH infections had malnutrition [26]. Several other studies showed a complex relationship between nutritional status and STH infections which are influenced by many factors such as environment, social, and economy status. Moreover, this study showed that most cases were mild degree of infections, while there was a research done showing malnutrition was correlated to moderate and severe STH intensity [27].

The most found worm infections were *T. trichiura* at 31.8% (122/384) followed by *A. lumbricoides* and hookworm at 8.1% (31/384) and 0.5% (1/384), respectively. The previous studies done by Jiero *et al.* (2015) in Medan Belawan, Pasaribu (2004) and Pasaribu (2019) in Karo Regency showed *A. lumbricoides* as the highest infections found [5], [7], [19]. This difference may be due to the treatment for *T. trichiura* infections require repeated doses of albendazole [4], [28], [29]. Although

albendazole is a broad-spectrum anthelmintic drug taken orally as a single dose to control intestinal worms, the treatment for *T. trichiura* infections is less effective than to *A. lumbricoides* and hookworm infections [29]. The study done by Sungkar *et al.* (2019) showed that the consumption of albendazole for 3 consecutive days was effective to control STH infections [28].

Hb level increase in this study showed no significant differences statistically between the groups that received albendazole as a single dose and albendazole with iron-folic acid supplementation. However, the study done by Bhoite and Iyer (2012) showed that the supplementation of iron and folic acid in deworming program to schoolchildren led to effective hemoglobin increases [16]. These differences were possible because the subjects with anemia in this research were very few and the majority of STH infections were mild.

Conclusion

In this study, iron-folic acid supplementation in addition to albendazole did not show any benefit for primary schoolchildren with STH infection in Batubara Regency, North Sumatera, Indonesia. Hb levels increase after the administration of albendazole either with or without the supplementation of iron and folic acid. Further research with a larger sample size is needed to observe the supplementation of iron-folic acid in children with STH infections.

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