



Comparison of Albendazole and Mebendazole on Soil-Transmitted Helminth Infections among School-Aged Children

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Abstract

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BACKGROUND: Anthelmintics, such as albendazole and mebendazole, are widely used to treat soil-transmitted helminths (STHs). With its extensive usage and administration along with other medical prescriptions, different environmental conditions, etc., some studies have reported unsatisfactory efficacy from albendazole to treat STHs.

AIM: To observe the efficacy of albendazole and mebendazole as a single dose in treating STH infections in elementary school children.

METHODS: An open randomized clinical trial was conducted in Batubara, North Sumatra, comparing the efficacy of albendazole and mebendazole. Samples were 6–12-year-old children infected with STHs based on Kato-Katz examination. A Chi-square test was performed to compare the cure rate and a t-test was done to compare the number of eggs per gram (EPG) feces in both groups.

RESULT: A total of 199 children from 426 met the study criteria. There was a significant difference ($p < 0.05$) in the cure rate of *Ascaris lumbricoides* infections at 87.5% and 31% for albendazole and mebendazole groups, respectively. The cure rate of *Trichuris trichiura* infection at 61.5% and 65.6% with albendazole and mebendazole, respectively, and there was no significant difference ($p > 0.05$). There was a significant reduction in the number of eggs of all STHs after the treatment either with albendazole or mebendazole.

CONCLUSION: Single-dose albendazole has better efficacy against *Ascaris lumbricoides* infection than mebendazole. Meanwhile, both albendazole and mebendazole have high efficacy in reducing the number of eggs.

Introduction

Soil-transmitted helminth (STH) infections are worm infections, which are transmitted through the soil, in the human intestines. Infections caused by worms are categorized into neglected tropical diseases (NTDs). They are groups of diseases with less attention from the community. Currently, the World Health Organization (WHO) focuses to handle NTDs. Three main groups of STHs that infect humans are roundworms (*Ascaris lumbricoides*), whipworms (*Trichuris trichiura*), and hookworms (*Ancylostoma duodenale* and *Necator americanus*) [1], [2].

Soil-transmitted helminth infections are commonly found in developing countries. Around one-third of the world's population are infected by at least one species of STHs. One billion people were estimated to be infected by *Ascaris lumbricoides*, whereas people with *T. trichiura* and hookworms infections were estimated to be at 800 and 740 million, respectively [3]. The infections are spread widely in tropical and subtropical countries. Climate is an important determinant in the transmission of infections; as worm larvae can grow in the soil with enough moisture and warm temperatures. Meanwhile, other determining factors can be poverty,

level of education, inadequate water supply and poor sanitation [4].

Pasaribu reported helminthiasis prevalence of 91.3% from the observation done in Suka village, Tigapanah, Karo Regency, North Sumatra [5]. In 2012, the North Sumatra provincial health service reported 32.3% helminthiasis prevalence, with species distribution as follows: 21% *Ascaris lumbricoides* 21%, *T. trichiura* 11%, and *Hookworm* 0%. This result was higher than the result obtained in the year 2011, at 28% [6]. The provided data have shown that helminthiasis cases are still high in school children, especially in North Sumatra.

Morbidity caused by STHs and schistosomiasis is generally associated with severe infections. There were 150 thousand death cases reported among 300 million people with severe helminthiasis every year. Besides that, several studies have shown that chronic STH infections caused malnutrition, stunting, intellectual development disorders (IDDs), and impaired cognitive functions. Furthermore, there was a huge impact on school attendance and achievement levels, as well as future economic productivity [7].

STHs are usually found as single infections or combinations of all three groups of STHs. Theoretically,

several broadspectrum anthelmintic drugs can eradicate worms with their advantages and disadvantages [8]. Albendazole and mebendazole are benzimidazole groups recommended by the WHO for the intervention in controlling STH infections. They have different chemical structures; hence, the differences in the pharmacokinetics [9]. Recent studies reported that STHs with albendazole treatment have an unsatisfactory cure rate and eggs reduction rate. This was suspected due to the emergence of parasites that had been resistant to the drug [10].

The study in Uganda reported unsatisfactory treatment of *T. trichiura*, where a repeated dose of albendazole was required to treat the infection [10]. Similarly, the research in Kenya also reported a low cure rate and eggs reduction for *T. trichiura* at 18.2% and 24.5%, respectively [11]. A systematic review published in 2007 reported a 28% cure rate for *T. trichiura* with a single dose of albendazole 400 mg treatment, being lower than that of mebendazole at 36% [12]. The cure rate for *Ascaris lumbricoides* and hookworms, however, was observed to be higher with albendazole. Worm infections caused by *T. trichiura* showed the highest cure rate with mebendazole in the study done by Speich *et al.* compared to other anthelmintics [13]. The study in Ethiopia with mebendazole as a single dose obtained 53.5% as the cure rate while the reduction in the number of eggs was satisfactory at 96.5% [14].

The efficacy study of a single dose mebendazole 500 mg done in six countries reported the reduction in eggs of *Ascaris lumbricoides*, hookworms, and *T. trichiura* at 97.6%, 79.6%, and 63.1%, respectively [15]. Another study conducted in China compared albendazole and mebendazole as single doses and observed a higher cure rate for *Trichuris trichiura* infections with mebendazole at 39.7% than albendazole (33.8%) [16].

Albendazole and mebendazole are larvicidal, ovicidal and vermifugal to *Ascaris lumbricoides*, *T. trichiura* and hookworms [17]. Albendazole works by binding to the β -tubulin of the parasites, inhibiting polymerization and interfering with glucose absorption. As a result, the nematodes are lacking energy which eventually kills the worms. While in mebendazole, the reproduction and survival of worms are disrupted by inhibiting the formation of cytoplasmic microtubules of worms. The damages on microtubules lead to the inhibition of organelle movement and interfere with the absorption and secretion functions, thereby, selectively and irreversibly inhibiting glucose uptake. This results in reduced glycogen storage and ATP formation which are required to survive and reproduce worms; ultimately causing the death of worms [17], [18].

The usage of albendazole in mass STHs treatments at endemic areas may cause drug resistance. Although albendazole is proven to be effective and safe in treating STHs, drug resistance should be paid close attention to because anthelmintic resistance cannot be simply resolved. There has not been a study in North Sumatra that directly compares the efficacy of

albendazole and mebendazole treatment as a single dose against STH infections. Therefore, this research was conducted to compare the efficacy of albendazole 400 mg and mebendazole 500 mg as a single dose to treat STH infections.

Methods

The study was an open randomized clinical trial that compared the efficacy of albendazole and mebendazole treatment as a single dose in treating STH infections. The research was conducted at primary schools in Talawi, Batubara regency, North Sumatra, from April 2021 to May 2021. Samples were schoolchildren with helminthiasis who met the inclusion and exclusion criteria. Student data was obtained from the school. Out of 449 children who were invited, 426 children fulfill the criteria. They were selected using consecutive sampling with simple randomization using a table with randomized numbers. Inclusion criteria were primary schoolchildren who resided within the same area with one or combined eggs of STHs (*A. lumbricoides*, *T. trichiura*, and hookworms) based on Kato-Katz analysis. Exclusion criteria were children who refused to drink anthelmintic drugs, did not return feces samples at the beginning and following examinations, and consumed other types of anthelmintics ≤ 1 month before the research or during the research. The parents or guardians of the children were invited to the school and informed about the study procedure including potential benefits and risks. Written informed consent was obtained from the parents or legal guardians and verbal assent from the participating children. This study has received approval from the Health Research Ethics Committee of the Faculty of Medicine, University of Sumatera Utara.

The study team collected subjects' characteristic data. Next feces samples were collected from the children and analyzed by using the Kato-Katz method. 19 Children who met the inclusion and exclusion criteria were chosen as samples, 199 children were positive for STH infection and they were divided into two groups using a simple randomization method. The first group received albendazole 400 mg as a single dose and the other group received mebendazole 500 mg as a single dose. After one month of drug administration, Kato-Katz analysis was repeated to determine the efficacy of treatment. Children who do not come to school during the collection of feces after one month, will be visited at their home to give the stool pot and take it back when it is filled. Data analysis was done using a computerized software system, Statistical Package for the Social Sciences for Windows (SPSS) version 19, 2010, with a 95% confidence interval (CI) and significance level of $P < 0.05$. Chi-square analysis was done to observe

the cure rate of STH infection after anthelmintic therapy and a *t*-test was conducted to know the difference in the intensity of worm eggs in the two groups based on the prior determined timeline.

Results

Basic chof research Samples

The study was conducted in Talawi, Batubara regency, North Sumatra. There were 3 from 32 primary schools selected randomly for the research. All 449 students in the selected primary schools agreed to have their feces examined and receive helminthiasis treatment. Twenty-three of the total children did not return the pot, meanwhile, 426 children were examined and 199 children were positive STH infections. They were divided into two groups randomly, where the first group consisted of 102 children who received albendazole 400 mg as a single dose and the other group with 97 children received mebendazole 500 mg as a single. The consort flow diagram for the overall procedures is shown in Figure 1.

Helminthiasis prevalence of primary schoolchildren in Talawi, Batubara Regency was 46.7% (199/426), with the infection rate of *A. lumbricoides* at 46.7% (93/199), *T. trichiura* at 89.4% (178/199), and hookworms at 5% (10/199). There were no differences in the basic characteristic data of research subjects in both groups before intervention; in which the average age was 9 years old, and the subjects had good nutritional status. From the observation, the highest STH infection was caused by *T. trichiura*. Among the research subjects, a single infection was caused by one type of helminths, while double or triple infections were caused by two or three types of worms, respectively. The highest double infection in this research was the combination of *A. lumbricoides* and *T. trichiura*. Based on the number of eggs per gram of feces, most of the children had a mild intensity of infections, although there were a few children with moderate intensity of STH infections. The basic characteristic data of samples are presented in Table 1.

The comparison of cure rate and intensity of infection

The cure rate of STH infections is dependent on the type of treatment given. Both drug regimens led

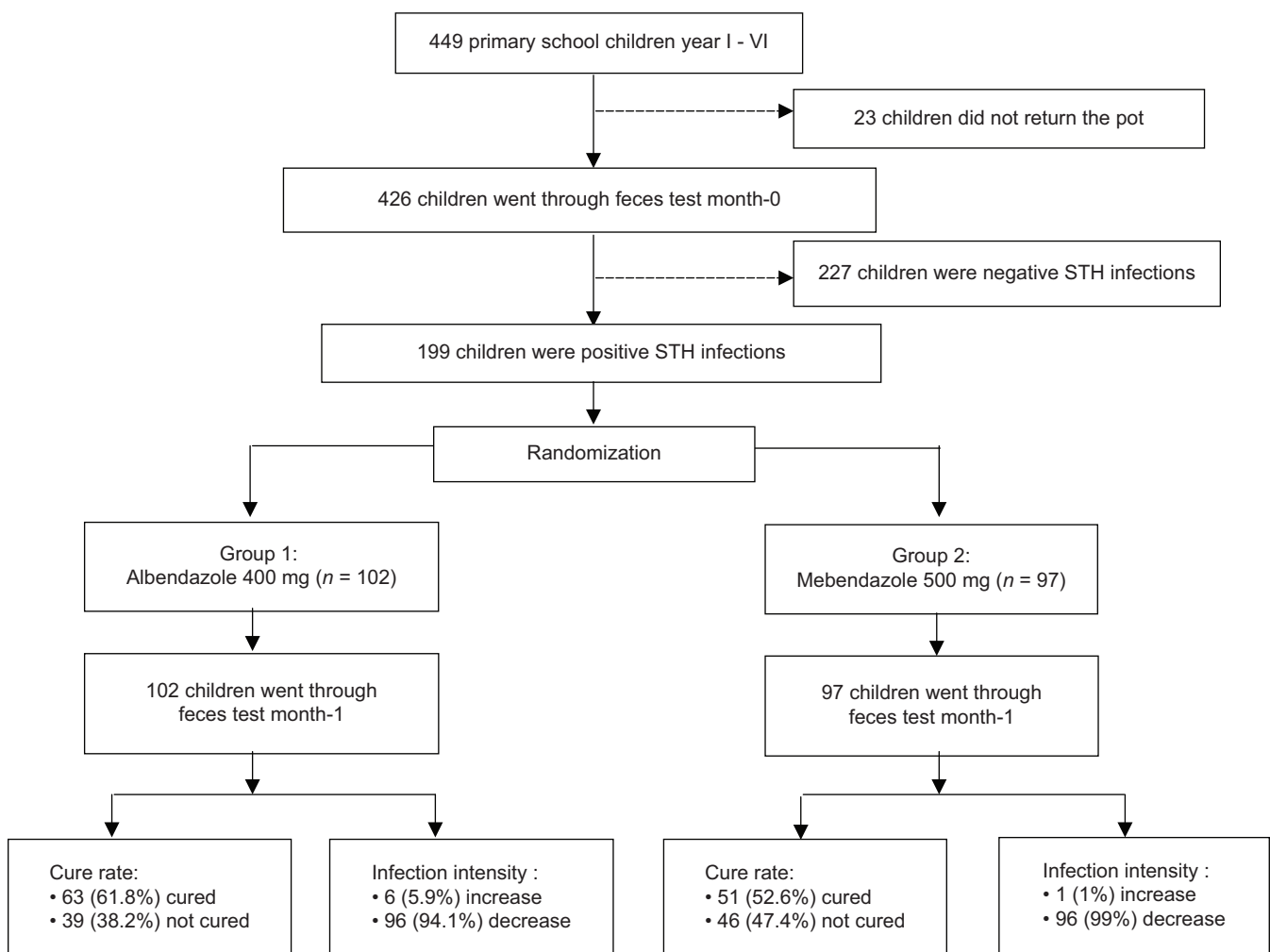


Figure 1: Consort flow diagram

Table 1: Basic characteristic of research samples

| Characteristic | Albendazole (n = 102), n (%) | Mebendazole (n = 97), n (%) |
|--------------------------------------------------|------------------------------|-----------------------------|
| Median age, years old (minimum–maximum) | 9 (6–12) | 9 (6–12) |
| Nutritional status | | |
| Malnutrition | 0 | 1 (1) |
| Poor nutrition | 39 (38.2) | 35 (36.1) |
| Good nutrition | 55 (53.9) | 51 (52.5) |
| Overweight | 7 (6.9) | 5 (5.2) |
| Obese | 1 (1.0) | 5 (5.2) |
| Gender | | |
| Male | 58 (56.9) | 47 (48.5) |
| Female | 44 (43.1) | 50 (51.5) |
| STH infections | | |
| Single infection | | |
| <i>A. lumbricoides</i> | 17 (16.7) | 4 (4.1) |
| <i>T. trichiura</i> | 38 (37.2) | 62 (63.9) |
| Double infection | | |
| <i>A. lumbricoides</i> + <i>T. trichiura</i> | 43 (42.2) | 25 (25.8) |
| <i>T. trichiura</i> +hookworm | 0 | 6 (6.2) |
| Triple infection | 4 (3.9) | 0 |
| Intensity of infection | | |
| <i>A. lumbricoides</i> | | |
| Mild | 54 (84.4) | 20 (69.0) |
| Moderate | 10 (15.6) | 9 (31.0) |
| <i>T. trichiura</i> | | |
| Mild | 69 (81.2) | 64 (68.8) |
| Moderate | 16 (18.8) | 29 (31.2) |
| Hookworm | | |
| Mild | 4 (100) | 6 (100) |
| Total eggs/gram feces, geometric mean EPG (± SD) | | |
| <i>A. lumbricoides</i> | 2.9 (0.64) | 3.2 (0.60) |
| <i>T. trichiura</i> | 2.4 (0.60) | 2.9 (0.50) |
| Hookworm | 1.6 (0.27) | 1.0 (0.19) |

STH: Soil-transmitted helminth, *A. lumbricoides*: *Ascaris lumbricoides*, *T. trichiura*: *Trichuris trichiura*, SD: Standard deviation, EPG: Eggs per gram.

to significantly different cure rates in *A. lumbricoides* infections with a $p < 0.05$ (Table 2).

Table 2: The comparison of cure rate after treatment

| STH infection | Albendazole (n = 102), n (%) | Mebendazole (n = 97), n (%) | p* |
|------------------------|------------------------------|-----------------------------|--------|
| Cure rate | | | |
| <i>A. lumbricoides</i> | 56 (87.5) | 9 (31.0) | <0.001 |
| <i>T. trichiura</i> | 52 (61.2) | 61 (65.6) | 0.649 |
| Hookworm | 4 (100) | 5 (83.3) | 1.000 |

*Chi-square test. STH: Soil-transmitted helminth, *A. lumbricoides*: *Ascaris lumbricoides*, *T. trichiura*: *Trichuris trichiura*.

The efficacy of treatment can be observed from the cure rate and reduction in total eggs of STHs. There was a significant reduction in STHs eggs in the two groups after the therapy for 1 month. The statistical analysis presented in Table 3 shows the reduction in eggs before and after treatment.

Table 3: Total worm eggs before and after treatment

| Jumlah telur STH | Sebelum pengobatan | Setelah pengobatan | p* |
|--------------------------------------------------|--------------------|--------------------|--------|
| Total eggs/gram feces, geometric mean EPG (± SD) | | | |
| Albendazole group | | | |
| <i>A. lumbricoides</i> | 3.5 (0.70) | 2.6 (0.41) | 0.023 |
| <i>T. trichiura</i> | 2.9 (0.52) | 2.4 (0.55) | <0.001 |
| Mebendazole groups | | | |
| <i>A. lumbricoides</i> | 3.5 (0.53) | 2.5 (0.49) | <0.001 |
| <i>T. trichiura</i> | 3.4 (0.40) | 2.4 (0.39) | <0.001 |

*Paired t-test. STH: Soil-transmitted helminth, *A. lumbricoides*: *Ascaris lumbricoides*, *T. trichiura*: *Trichuris trichiura*, SD: Standard deviation, EPG: Eggs per gram.

There were no side effects, such as anorexia, nausea, vomiting, diarrhea, dizziness, rash, and itching occurred during the research.

Discussion

Our study showed a 46.7% prevalence of helminthiasis in Batubara, North Sumatra. The result

is lower than the study done by Yunus in Medan with the prevalence of 73%, Dalimunthe in Karo year 2002 with the prevalence of 95.4% and Pasaribu in Karo year 2004 with the prevalence of 91.3% [5], [19], [20], [21]. Among three types of STHs, *T. trichiura* is often found in STH infection cases in human [2]. A lower prevalence in this research may be due to the helminthiasis control program held by the government since 2005 targeting preschoolers (1–4 years old) and primary schoolchildren (5–12 years old) [19].

In this study, the highest helminthiasis prevalence was due to *T. trichiura* at 89.4%, followed by *A. lumbricoides* and hookworms at the prevalence of 46.7% and 5%, respectively. Similar data were reported by Dalimunthe from the study done in Karo where the prevalence of *T. trichiura*, *A. lumbricoides* and hookworms was at 88.7%, 79.5%, and 3.1%, respectively [21]. *T. trichiura* infections are higher than the other types of nematodes because of the use of albendazole in the helminthiasis control program, where *T. trichiura* is less sensitive against single-dose albendazole [7], [19].

STH infections can be found as single or combined infections [22]. In this study, there were 37.2% double infections and 2% triple infections. The combination of *A. lumbricoides* and *T. trichiura* infections were found the highest. This is similar to the study previously done in Medan and Karo Regency [5], [20], [21]. The two types of nematodes are transmitted by having infective eggs swallowed [23]. There was a 5% of hookworm infection observed in the research. This is slightly higher than the previous study in Medan in 2008 with only 0.53% infection rate [20]. This may happen because the children where the research took place have different habits from the children in the city, such as being barefoot that can increase the risk of hookworm infections. This type of STH infects the host by penetrating infective larva through the skin.

Soil-transmitted infections are often found in children aged 5–15 years old. In this study, the average age of children with STH infections was around 9 years old. The prevalence of the infection was related to age, where the risk of infection decreased with the increase of age. Older children have different playing and activity patterns, as well as better personal hygiene and improved body immune than younger children [24].

Children with STH infections in this research had good nutritional status. This is, however, different from the study done in Medan by Yunus which correlated nutritional status with STH infections – children with STH infections suffered from poor nutrition to malnutrition [20]. The difference in the result may be influenced by other factors such as environmental, social, and economic status [25]. Based on the number of eggs per gram of feces, most subjects in this study had a mild degree of STH infections. Malnutrition cases usually occur in moderate to severe STH infection intensity. STH infections can affect the nutritional status of the hosts by causing anorexia, improving

the nutritional needs of the STHs, interfering with mucosal absorption in *A. lumbricoides* infections, and losing blood in *Ancylostoma duodenale* and *Necator americanus* infections [26].

A single-dose treatment in a single STH infection generally gives a good result, unlike combined infections. No satisfactory results have been obtained from the treatment given to combined infection cases. It has been a challenge to find one medicine with good efficacy toward all types of STHs, while most patients are not only found with single infections but combined infections of a few species. Today, there are several single-dose anthelmintic drugs with a broad spectrum, such as: albendazole, levamisole, mebendazole, and pyrantel pamoate, which can eradicate worms with their advantages and disadvantages [8].

A study in Medan reported the cure rate of albendazole compared with mebendazole for *A. lumbricoides* which were at 96.7% and 100%, respectively [27]. In this study, the cure rate obtained was 87.5% with albendazole and 31% with mebendazole. The cure rate of the infection differed significantly, which may be influenced by other factors i.e. worm susceptibility, drug-related variations, parasitic strains, the intensity of infections, host-specific factors, etc. [12]. One of the factors observed in this study was the average number of *A. lumbricoides* eggs where the mebendazole group had a higher number of eggs than the albendazole group. However, there may be other factors that affected the efficacy of medication that were not considered in this research.

As for *T. trichiura* infections, the cure rate obtained was 61.5% and 65.6% with albendazole and mebendazole, respectively. This is aligned with the study done by Anto and Nugraha which reported the efficacy of albendazole in *T. trichiura* infections was at 66.7%, as well as the study by Levecke *et al.* in six countries which reported a 63.1% cure rate [15], [28]. Steinmann *et al.* researched Yunnan, China that compared the efficacy of albendazole and mebendazole as a single dose [16]. They reported a low cure rate of *T. trichiura* infections, 33.8% with albendazole and 39.7% with mebendazole. The treatment of this STH type is generally more difficult than the others. The place where *T. trichiura* lives in the cecum makes this nematode more resistant against the anthelmintics administered. Moreover, the worms bury their heads in the intestinal walls [23].

The cure rate of hookworms in this study was satisfactory for both treatment groups at 100% and 83.3% in albendazole and mebendazole groups, respectively. The result is different from what has been reported in a previous study, where the efficacy was only 69.1% with albendazole and 31.0% with mebendazole [16]. This difference may be caused by the number of samples with hookworm infections being lower in this study.

After 1 month of treatment, there was no significant difference in the number of worm eggs in both

groups. However, there was a significant difference in the number of eggs before and after anthelmintic treatment. This means that both drugs can reduce the eggs of three STH types. The result is similar to the study in Ethiopia and North Sumatra that reported a significant decrease in several eggs with albendazole and mebendazole treatment [28], [29]. The direct reduction in eggs leads to lesser intensity of infection. This shows that both albendazole and mebendazole are ovicidal [30].

The side effects that may occur alongside albendazole and mebendazole consumption are usually mild and temporary such as nausea, vomiting, diarrhea, dizziness, drowsiness, headache, insomnia, and fatigue. Short-term drug administration does not usually have side effects [12], [19]. In this study, no side effects were observed after the drug administration. This is because anthelmintics are not well-absorbed in the digestive tract [12]. This study can become a source of information for the next research. What is lacking from this research is the observation of other factors, besides several eggs that influence the efficacy of helminthiasis treatment. The high and low cure rate of one treatment may be influenced by other factors besides the drug itself.

Conclusion

The treatment with albendazole as a single dose gave a better efficacy than mebendazole for the cure rate of *Ascaris lumbricoides* infections. Whereas for *Trichiuris trichiura* infections, neither albendazole nor mebendazole had a satisfactory result. There was no difference in the cure rate of hookworm infections in both treatment groups. If efficacy was observed from the reduction in the number of eggs, then both treatment groups gave good efficacy for all three types of soil-transmitted helminthes.

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Authors' Contributions

All authors conceived and designed the study. NH, ES and WW collected the data, conducted the

statistical analysis and interpretation of the findings. NH wrote the final manuscript. All authors read and approved the final version of this manuscript.

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