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EVALUATING THE EFFICACY OF ALBENDAZOLE AGAINST SOIL-TRANSMITTED HELMINTHIASIS AND SCHISTOSOMIASIS AMONG SCHOOL CHILDREN IN AKSUM, ADWA AND ADIET, NORTHERN ETHIOPIA

YEMANE TADESSE DESTA*[1] AND FEYISSA HAMDE KOFE[2]

[1]*Department of Biology & Biotechnology, College of Natural and Computational Sciences, Aksum University, Axum, Ethiopia.*

[2]*Department of Medicine, College of Health Sciences, Aksum University, Axum, Ethiopia.*

**Corresponding author: yemanetadesse@ymail.com*

ABSTRACT

Soil-transmitted helminth infections (STH) and schistosomiasis constitute major public health challenges among school-age children in sub-Saharan Africa. Chemotherapy with the Benzimidazole chemical family is one of the most effective strategies to lower the rates of morbidity and mortality. But now a day anthelmintic resistance in the treatment and control of human helminthes has been reported in different areas in Ethiopia. The objective of this study, therefore, is to assess the efficacy of albendazole (400 mg, manufactured by Khandeiwal Laboratories Pvt. Ltd) currently in use against soil-transmitted helminth infections among school children in many areas of Ethiopia. A total of 180 elementary school children were chosen using random sampling technique. Each student was instructed to submit fresh stool specimen. Formal ether concentration technique and Kato-Katz method were done at the study sites and Aksum University, laboratory of Department of Biology and Biotechnology. Among the total study children, 170 submitted fresh stool samples giving a response rate of 96.77%. The overall prevalence of helminth infection was 66.7 % (Adiet), 67.9% (Adwa) and 51.7% (Aksum). In all the study sites albendazole was effective against most soil-transmitted helminthes, with cure rate $\geq$ 85%, and egg reduction rate $\geq$90%. However, it was less effective against *Trichuris trichiura* with cure rate 58.5% and 57.9% at Adiet and Adwa, respectively. Therefore, due attention should be given with regard to treating helminth positive individuals together with intense environmental sanitation to curb the burden of helminth infection and alternative chemotherapy against *Trichuris trichiura* should be supplied to the study areas.

Keywords: albendazole, infection, parasitosis, schistosomiasis, soil-transmitted helminthes.

INTRODUCTION

Helminths have plagued humans since before the era of our earliest recorded history. The eggs of intestinal helminths can be found in the mummified feces of humans dating back thousands of years[1]. Soil-transmitted helminths are a group of parasitic nematode worms acquired through contact with parasite eggs or larvae in the warm and moist soil of the world's tropical and subtropical countries. As adult worms, the soil-transmitted helminthes live for years in the human gastrointestinal tract[2]. The high prevalence of these infections is closely correlated with poverty, poor environmental hygiene and impoverished health services[3]. WHO, estimates that almost 2 billion people are infected with one or more of soil-transmitted helminths, accounting for up to 40% of the global morbidity from infectious diseases exclusive of malaria. Of the 1-2 billion soil-transmitted helminths infection worldwide, approximately 300 million infections result in severe morbidity, which are associated with heaviest worm burdens[4,5].

In the vast majority of developing tropical and subtropical regions of the world, helminth infections particularly those caused by soil transmitted helminths (STHs) and schistosomes constitute major public health and developmental challenges. Infections caused by STHs – including hookworm

(*Necator americanus, Ancylostoma duodenale*), roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and schistosomes (*Schistosoma haematobium, Schistosoma mansoni*) are associated with poverty and underdevelopment and are most prevalent in the poorest communities of the developing world including almost all countries of the sub- Saharan Africa[3,6].

Estimates indicate that an about 4.5 billion individuals are at risk of STH infections and the global estimate of number of cases of *A. lumbricoides* is 807 million, *T. trichiura* 604 million, Hookworm (*N. americanus*; *A. duodenale*) 576 million, Schistosomiasis (*S.haematobium, S.mansoni* and *S.japonicum*) 207 million[1,2]. Although estimates of disability-adjusted life years (DALYs) lost due to these helminth infections portray a more accurate picture of the disease burden caused by the infections, the estimates of DALYs lost differ greatly from one source to another[6].

In Ethiopia, low economic standard, poor sanitation and ignorance of simple health promotion practices favor the wide distribution of intestinal helminths. Of all types of diseases in the country, helminthiasis is the second most common cause of outpatient morbidity next to malaria. Several studies in the country have also revealed that intestinal parasite infections are widely distributed with high prevalence rates**.** Children are the most affected group and serve both as source of infection and as victims, thus contributing to transmission of most parasitic infections within the community[7.]

Morbidity due to soil-transmitted helminthiasis is relatively easy to control with simple intervention measures[8]**.** The major means of controlling helminth infections is by the periodic administration of one of the five anthelmintic drugs recommended by the WHO. These include Mebendazole, Albendazole, Levamisole & Pyrantel for soil-transmitted helminths [9]. By providing single-dose anthelmintics on a regular basis to entire populations or high-risk groups, it is hoped to reduce both morbidity and transmission[10]**.** Among the anthelmintics, albendazole is one of the drugs which have a unique broad-spectrum activity[11]. A single oral dose of 400mg albendazole is highly effective against most of the soil-transmitted helminthes except for *Trichuris trichiura*[12, 13]**.**

The rapid spread of resistance to the major classes of veterinary anthelmintics should warn the medical world against the widespread use of anthelmintics for the control of helminths. Hence, the objective of this study is to assess the efficacy of albendazole currently in use against soil transmitted helminths in Axum, Adwa and Adiet, Northern Ethiopia.

MATERIALS AND METHODS:

The Study Area

The study was carried out in Adwa, Aksum and Adiet about which are 1000, 1024 and 1069km from Addis Ababa and 215, 240 and 285km from Mekelle respectively. The area has an elevation of about 1500-2100 m above sea level. According to the 2005.E.C censuses as the information gathered from the statistical center of the zone, the number of inhabitant is estimated to be above 80,000. Agriculture, government employee and small scale trading are means by which the local people earn their living. There are schools and health center in the town.

Study Population

School children were selected as the study population because school-age children typically have the highest intensity of worm infection of any age group. In addition, the most cost-effective way to deliver drugs regularly to children is through schools because schools offer a readily available, extensive and sustained infrastructure with a skilled workforce that is in close contact with the community[14]. Deworming has also an important impact on child development, physical fitness and working capacity[15]**.** The data collected from this age group can be used to assess not only whether soil-transmitted helminthiasis threaten the health of school-age children, but also as a reference for evaluating the need for community intervention[3]**.**

SAMPLE SIZE DETERMINATION

The required sample was calculated using the formula[16],

$$n = \frac{Z^2 P (1 - P)}{d^2}$$

Where, n is the sample size

Z = statistic for 95% level of confidence

d = precision, and

P = expected prevalence or proportion

Even though the prevalence of infection of soil-transmitted helminthes and schistosomiasis among school children in Axum and surrounding areas is not yet known, it is reported that in Southern part of Tigray to be about 45%[17]. Therefore, it is acceptable to take the prevalence of STHs among school children in the area to be 45% and estimation of effects with 95% confidence levels. Based on the above formula the sample size (n) would be 200. However, a minimum of 180 individuals were taken for the present study because of the inadequacy of the Kato materials.

STOOL COLLECTION AND EXAMINATION

After giving adequate instruction on how to provide stool samples, small pieces of plastic sheets were distributed to the study subjects to provide sizeable fresh stool specimens of their own. The specimens were processed using Kato technique employing a template delivering a plug of 41.7mg of stool and microscopically examined for eggs of intestinal helminthes[6]. The remaining stool specimens were also preserved in 10% formalin and examined using concentration method. The prepared slides were transported to Aksum University for microscopic examination, for further cross checking and quality control. Positive samples were rated as eggs per gram of stool in order to determine the intensity of infection. In this study, prevalence was estimated from the proportion of infection as compared with the total population examined. Intensity of infection was estimated from the number of eggs per gram of faeces (epg). Egg count for hookworm was performed within one hour of stool collection and Kato slide preparation. The slides were examined for other helminths in the laboratory within one week of stool collection. The number of eggs counted was multiplied by 24 to obtain the number of eggs per gram of faeces.

The school children, who were positive for at least one of the soil-transmitted helminth infections, were prepared for the treatment purpose. Following this, the students were informed the date of treatment through their school teachers and were treated with a 400 mg single dose albendazole. During the initiation for the treatment, all children were interviewed whether or not they received any antihelminthic drugs in the past three months and if they are aged between 6-15 years.

The day before and after drug treatment, a questionnaire containing closed and open-ended questions investigating side effects or any unusual reaction following albendazole treatment were administered to children who receive the treatment within 24 hours. Twenty-one days after treatment, faecal samples were collected for efficacy determination[18]. The egg reduction and cure rates of the drug were determined in terms of the percent of egg count reduction and cure rate. The intensity of infection was determined for parasites and quantified as egg per gram (epg) of faceas for each individual. Intensity of infection was compared using ANOVA.

RESULTS

A total of 180 school children with mean age 9.8 years were included in the study. Among the 180 school children from the three sites, only 170 properly submitted fresh stool samples (94.4 response rates). The majority of the students were Christian (90.8%) and Muslims (9.2%). 58 (32.2) school children out of 170 use streams or rivers as their water source and 127 of them had latrines and 101 (59.4%) of the participants wore shoes always.

Among the 60 students from Adiet, 57 properly submitted fresh stool samples (95% response rate) and the rest failed to produce samples and hence excluded from the study. Most (94.7%) of the participants from Adiet (Debregenet Elementary school) were Christians and 5.3% were Muslims. 45.9% of these school children use streams and rivers as their source of drinking water. Moreover 38.6% and 19.3% of the study participants do not have latrine and do not wear shoes at all respectively (Table 1).

Table 1. Socio-demographic characteristic of the study participants, Adiet (Debregenet Elementary School), North Ethiopia, Feb. 2012

Socio-demographic variables		Male (n=40)	Female (n=17)	Total
Religion	Muslim	2	1	3
	Christian	38	16	54
Water source	Pipe	17	5	22
	Well	7	3	10
	Stream	16	9	25
Availability of latrine	Yes	25	10	35
	No	15	7	22
Shoe wearing	Always	19	8	27
	Some times	13	6	19
	Not at all	8	3	11

From the 60 school children randomly selected in Mytsadk Elementary School (Adwa), only 53 produced fresh stool sample and the rest excluded from the study. Most (75.5%) of the participants from Mytsadk Elementary School were Christians and 24.5% were Muslims. 9.4% of these school children use streams and rivers as their source of drinking water. Moreover 18.9% of the study participants do not have latrine and 9.4% do not wear shoes at all (Table 2).

Table 2. Socio-demographic characteristic of the study participants, Adwa (Mytsadk Elementary School), North Ethiopia, Feb. 2012

Socio-demographic variables		Male (n=23)	Female (n=30)	Total
Religion	Muslim	6	7	13
	Christian	17	23	40
Water source	Pipe	19	23	42
	Well	2	4	6

	Stream	2	3	5
Availability of latrine	Yes	19	24	43
	No	4	6	10
Shoe wearing	Always	15	16	31
	Some times	4	12	16
	Not at all	4	2	6

All the 60 school children from Bazen Elementary School properly submitted fresh stool samples (100% response rate). All the participants (100%) from this school were Christians. 20% of these school children use streams and rivers as their source of drinking water. 18.3% of the participants do not have regular latrine in this study area and 6.67% of the participants do not wear shoes at all (Table 3).

Table 3. Socio-demographic characteristic of the study participants, Aksum (Bazen Elementary School), North Ethiopia, Feb. 2012.

Socio-demographic variables		Male (n=32)	Female (n=28)	Total
Religion	Muslim	0	0	0
	Christian	32	28	60
Water source	Pipe	28	20	48
	Well	2	4	6
	Stream	2	4	6
Availability of latrine	Yes	27	22	49
	No	5	6	11
Shoe wearing	Always	24	19	43
	Some times	6	7	13
	Not at all	2	2	4

Table 4.Pre-treatment helminth species prevalence in the study participants by age group, Adiet, Northern Ethiopia Mar. 2007

Age category	Total examined	Parasite species						
		Hw	Al	Tt	Schi	Fh	Tae	Ss
5-9	22	5	3	2	4	0	0	0
10-14	26	4	2	0	5	2	1	1
15-19	9	3	0	1	2	0	3	0
Total	57	12	5	3	11	2	4	1

Hw: hookworm, Al: Ascaris lumbricoides, Tt: Trichuris trichiura, Schi: Schistosoma species, Fh: Fasciola hepatica, Tae: Taenia species, Ss: Strongyloides stercolaris.

Direct microscopy was done to search for hookworms and the remaining stool samples were preserved using formalin-ether and examined by concentration method. The overall intestinal parasitosis among the study participants was 66.7% (38/57). 12 (21%) specimens were positive for hookworm, 5 (8.7%) were positive for *Ascaris lumbricoides*, 3 (5.3%) were positive for *Trichuris trichiura*, 11 (19.3%) were positive for *Schistosoma* species, 2 (3.5%) were positive for *Fasiola hepatical* and 4 (7%) and 1 (1.8%) samples were positive for *Taenia* species and *Strongyloides stercolaris* respectively. None of the sample showed mixed infection (Table 4).

Table 5. Pre-treatment helminth species prevalence in the study participants by age group, Adwa, Northern Ethiopia Mar. 2007

Age category	Total examined	Parasite species						
		Hw	Al	Tt	Schi	Fh	Tae	Ss
5-9	31	3	4	1	6	0	0	4
10-14	20	2	3	0	10	0	0	3
15-19	2	0	0	0	0	0	0	0
Total	53	5	7	1	16	0	0	7

Hw: hookworm, Al: Ascaris lumbricoides, Tt: Trichuris trichiura, Schi: Schistosoma species, Fh: Fasciola hepatica, Tae: Taenia species, Ss: Strongyloides stercolaris.

The overall helminth prevalence in the study area was 67.9%. Out of the 53 study children 5 (9.4%) were positive for hookworm species. 7 (13.2%) samples were also positive for *Ascaris lubricoides* and 1 (1.9%) were positive for *Trichuris trichiura* the largest infection (30.2%) was found for *Schistosoma species* (*Schistosoma haematobium* and *Schistosoma mansoni*). No positive samples for *Fasciola hepatica* and *Taenia species* found in the study. 7 (13.2%) samples were found positive for *Strongyloides stercolaris* (Table 5).

Table 6. Pre-treatment helminth species prevalence in the study participants by age group, Aksum, Northern Ethiopia Mar. 2007

Age category	Total examined	Parasite species						
		Hw	Al	Tt	Schi	Fh	Tae	Ss
5-9	38	0	2	0	7	4	1	0
10-14	20	0	5	0	8	4	3	0
15-19	2	0	0	0	1	0	0	0
Total	60	0	7	0	16	8	4	0

Hw: hookworm, Al: Ascaris lumbricoides, Tt: Trichuris trichiura, Schi: Schistosoma species, Fh: Fasciola hepatica, Tae: Taenia species, Ss: Strongyloides stercolaris.

31 out of the total 60 (51.7%) study children were infected by either of the helminth parasites. Only three helminth parasites, that is, *Ascaris lumbricoides* with 11.7% prevalence, *Schistosoma* species with 26.7% prevalence and *Faschiola hepatica* with 13.3% prevalence were detected in the study. However the samples were negative for most of the helminth parasites such as hookworm, *Trichuris trichiura, Taenia species* and *Strongyloides stercolaris* (Table 6).

Table 7. Summary of efficacy of albendazole on soil transmitted helminth infections in school children at each study Districts, Northern Ethiopia May 2011.

Parasite species	Debregenet Elementary school			Mytsadk Elementary school			Bazien Elementary school		
	P/P (%)	CR (%)	ERR (%)	P/P (%)	CR (%)	ERR (%)	P/P (%)	CR (%)	ERR (%)
Hookworm species	21.0/3.1	85.2	94.1	9.4/2.0	78.7	97.5	-	-	-
A. lumbricoides	8.7/1.1	87.4	100	13.2/1.2	90.9	100	11.7/0.9	92.3	98.5
T. trichiura	5.3/2.2	58.5	61.4	1.9/0.8	57.9	63.5	-	-	-
Schistosoma species	19.3/0.0	100	92.5	30.2/3.5	88.4	95.0	26.7/7.0	73.7	96.7
F.hepatica	3.5/0.3	91.4	98.0	-	-	-	13.3/0.7	94.7	87.5
Taenia species	7.0/1.0	85.7	91.0	-	-	-	-	-	-
S.stercolaris	1.8/0.0	100	98.3	13.2/0.3	97.7	100	-	-	-

P/P= Pre/post treatment prevalence; CR= Cure rate; ERR= Egg reduction rate

Significant reductions in prevalence of all seven worms were found in School children at Adiet in the post-treatment of albendazole (P<0.5). After a single dose of 400 mg albendazole the prevalence of Hookworm species fell from 21.0 pre-treatment to 3.1% post-treatment and *A.lumbricoides* from 8.7% pre-treatment prevalence to 1.1% post-treatment prevalence. The prevalence of *Trichuris trichiura* was 5.3 before treatment and 0.2% post-treatment. The prevalence of schistosoma species was also significantly reduced in the albendazole-treated groups from 19% pre-treatment prevalence to 0.0% post-treatment prevalence. The prevalence of *F.hepatica* and *Taenia* species was reduced from 3.5% and 7.0% to 0.3% and 1.0% respectively, and *S.stercolaris* has been disappeared after treatment (Table 7).

The prevalence of five worms, hookworm, *Ascaris lumbricoides*, Schistosoma species, *Trichuris trichiura*, and *S.stercolaris* was not that much high in the study population from Adwa. The highest prevalence in that area was Schistosoma species (*S.haematobium* and *S.mansoni*) with 30.2 which was reduced to 2.5 after treatment with a single dose of albendazole. But the rest two parasites, *F.hepatica* and *Taenia species*, were not found in the study area (Table 7).

In the third study site, Bazien Elementary School (Aksum), only three parasites are observed from the school children. These are *A.lumbricoides* with 11.9%, Schistosoma species 26.7% and *F.hepatica* 13.3% pre-treatment prevalence. Albendazole is effective against these parasites with cure rate >70% (Table 7).

Table 8. Assessment of post-treatment side effects experienced by the children at each study Districts, Northern Ethiopia June 2011

Study site	Lassitude	headache	dizziness,	abdominal distress	bloody diarrhea	limb pain	fever	pruritus	sweating
DES	1.75	-	3.77	-	-	-	3.5	-	-
MES	1.88	-	3.77	-	-	-	3.77	-	-
BES	1.66	-	-	-	-	-	1.66	-	-

DES= Debregenet Elementary School, MES= Mytsadk Elementary School, BES= Basien Elementary School.

The post-treatment side effects of albendazole have been assessed in the three study sites by distributing questionnaires to the study subjects. Only few school children, that is, experienced lassitude dizziness and fever after they take albendazole as a treatment (Table 8).

DISCUSSION

Soil-transmitted helminthic infection is one of the major health problems in Ethiopia. The knowledge of the prevalence and distribution of intestinal helminth infection has been gradually increasing. Various studies have been conducted on all intestinal parasites species or specifically on *Schistosoma mansoni, Ascaris lumbricoides and* hookworm infections in Ethiopia. In Tigray, a variety of surveys have been done[17].

However, prevalence studies in relation to evaluation of the efficacy of currently using antihelminthic chemotherapies are limited or none. The present study aimed at determining the prevalence and evaluating the efficacy of albendazole. The overall prevalence of intestinal helminth infections (66.7 from Adiet, 67.9 from Adwa and 51.7 from Aksum) in this study were relatively lower than previous reports on school children from Asendabo town, and Wondo-Genet area of SNNP region[19]. This difference could be explained by the different socio-demographic conditions of the people living in these areas that could in turn determine the distribution and prevalence of these geohelminthes.

Helminth species prevalence in the study population at Adiet District followed the same pattern to that reported from Western Oromia[20] whereby hookworm was the most prevalent (21.0%) followed by *Schistosoma* species (19.4%) and *Ascaris lumbricoides* (8.7%). On the other hand, a number of other studies have shown a different species prevalence pattern where *A.lumbricoides* and *Trichuris trichiura* were the predominant species in Waja, Northern Ethiopia[17]. This difference in helminth parasite species prevalence might be explained by altitude and soil type differences, which are known to influence species distribution of geohelminth parasites.

The fact that both schistosoma species and *Ascaris lumbricoides* are present at Adwa is in agreement with previous studies conducted elsewhere in the country. With regard to the prevalence of both hookworm species, our finding was in line with other study reports from southern Tigray[21]. Unlike some other studies that reported mixed infection by some of the helminth species in a single individual, no concurrent infection was detected in this study. This could possibly be explained by the fact that mixed infection is a rare incidence in Ethiopia[17] where only few people were identified harboring both species.

Only tree parasites, *A.lubricoides*, (11.7%), *Schistosoma* species (26.7%) and *F. hepatica* (13.3%) were identified from the stool of the study groups from Aksum. This law distribution of soil transmitted helminthes in that area could be related to the socio-demographic characteristics. That is, as the information collected using questionnaires, 80% of the study participants use modern pipes as their source of drinking water; 81.7 of the participants have latrine and about 95% of the students always wear shoes, which is relatively better than the other study sites[22].

Furthermore, the findings of this research indicated that albendazole exhibited considerable cure rates and egg reduction rates particularly against *A. lumbricoides* and hookworms. As reported by Hotez and others[1], Albendazole, Mebendazole, and Praziquantel were the antihelminthic drugs most commonly evaluated. Cure rates >80% and egg reduction rates >90% were recorded in most cases of helminthiasis using Praziquantel. Albendazole was very effective against *A. lumbricoides* and hookworm infections with majority of the studies recording cure rates >75%, but the efficacy of the drug was poor against *T. trichiura*. Our findings were also in line with this study indicating that the cure rates of albendazole in most of the helminthic infections in the three study sites are >85% and egg reduction rates >90%, however, relatively low cure rates of 58.5 (Adiet) and 57.9 (Adwa) were also observed for *T.trichiura* (Table 7).

This study indicated that a single oral dose of 400 mg of albendazole per kg of body weight was safe, showed no or only a few but transient side effects such as lassitude, dizziness and fever (Table 8), but resulted in high parasitological cure and egg reduction rates against most cases of helminth infections in the study areas.

In conclusion, this study identified the existence of soil-transmitted helminths in the study areas with *A.lumbricoides*, Schistosoma species and hookworms being the dominant once. Furthermore, relatively higher burden of helminth infection was seen in the study population in Adiet. In these areas albendazole with 400mg/kg single doze is effective against these soil-transmitted helminthes with higher cure rates and egg reduction rates except for *T.trichiura*. Besides its effectiveness against the soil-transmitted helminthes, albendazole did not show also any detrimental persistent side effects in the study subjects.

RECCOMMENDATIONS

This finding demonstrates that additional measures such as proper environmental sanitation and personal hygiene as well as vector control (for schistosomiasis) are needed to curb the observed soil-transmitted helmithiasis. Besides, treating

infected individuals is recommended. Although there is limited evidence from the study of a possible emergence of drug resistance, this may not be completely overruled. A number of previous studies have indicated that there are no drugs available that are highly effective against *T. trichiura* infection as single dose treatments and so do in our case. As a result of this, the need for alternative antihelminthics cannot be overstated. Because the possible emergence of drug resistance to the antihelminthic compounds used to control soil-transmitted helminth infections and schistosomiasis remains a matter of serious public health concern, the efficacy of combined antihelminthic treatments with differing modes of action was also recommended in these areas.

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