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The Evaluation of Pre and Post Treatment Assessment of Albendazole among School Children in Ogun State, Nigeria

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Abstract **Original Research Article**

Background: Soil-transmitted helminths (STHs) are common in tropical and subtropical countries especially in areas with poor sanitation and restricted access to clean water sources and impact approximately 2 billion people worldwide, with school-age children being the most afflicted. *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworms (*Necator americanus* and *Ancylostoma duodenale*) collectively cause a significant global disease burden. The benzimidazole anthelmintics, mebendazole and albendazole, are commonly used to eradicate these infections. This study assessed the drug efficacy of albendazole in the treatment of STH infestations in school children.

Methods: Faecal egg counts (FEC) were determined using the Kato-Katz, Mac-Master Chamber, and formol-ether concentrations techniques, among 1103 elementary school students, ages 4 to 15 and efficacy was evaluated by the Cure Rate (CR) and the Faecal Egg Count Reduction (FECR).

Results: The cure rate (CR) of single dose albendazole treatment was observed for *T.* trichiura (99.3%), Hookworm (99.1%) and *A. lumbricoides* (98.1%).

Conclusion: A standard single-dose of Albendazole has a satisfactory efficacy against STHs among the school children in the study areas.

Keywords: Anthelminthics, Albendazole, helminths, school children, treatment, cure rate(CR)

Introduction

Soil transmitted helminths (STH) refer to the intestinal worms infecting humans that are transmissible through faecal contaminated soil. World Health Organization (WHO) classifies Soil-transmitted helminth (STH) infections as a neglected tropical disease, with estimated 1.5 billion people affected globally(1). Four main species associated with human helminthiases are *Ascaris lumbricoides*, *Trichuris trichiura* and hookworms-*Ancylostoma duodenale* and *Necator americanus*(2).

In sub-Saharan Africa, the estimated prevalence of moderate-to-heavy intensity infection exceeds the 2% target threshold (3) among children aged 5-14 years between Jan 1, 2000, and Dec 31, 2018 (4).

Large-scale delivery and periodic distribution and administration, of safe, quality-assured medicines, either alone or in combination to entire population groups also known as preventive chemotherapy is one of the main strategies employed by WHO to control soil transmitted helminths (5-8). Current aims of control programs are focused on reducing infection intensity and transmission potential, primarily to reduce morbidity and avoid mortality rather than eradication of the disease (9).

Of the anthelminthics the most widely used for the control of STH is the benzimidazole (BZ) drug, i.e., albendazole (ALB) and mebendazole (10-12). While both show broad-spectrum anthelmintic activity, for hookworms a single dose of ALB is more effective than mebendazole (13-16). These medications are used not only to treat symptomatic soil-transmitted helminth infections but also to avoid morbidity in children residing in endemic areas on a wide scale. The global community is becoming more aware of the significance of soil-transmitted helminth infections due to statistics demonstrating improvements in child health and education following deworming, as well as the burden of disease linked to these diseases. Efforts to create and test alternative control techniques have been spurred by worries about the sustainability of periodic deworming with benzimidazole anthelmintics and the emergence of resistance (17).

Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by diminishing its energy production, ultimately leading to immobilization and death of the parasite (18). It acts by binding tubulin in parasitic worms which it does with greater avidity than the tubulin in mammalian cells. The well documented occurrence of resistance to anthelmintics in nematode populations of livestock (19), highlights the potential for frequent treatments used in chemotherapy programs to select drug resistant worms. Such an eventuality threatens the success of treatment programs in humans, both at individual and community levels.

Materials and Methods

Ethics

Ethical approvals were obtained from the Committees of the following institutions and establishments: Ogun State Health Research Ethics Committee (OGHREC); Universal Basic Education Board; and Ministry of Education, Science and Technology.

Study Area and sites: The study area was spread around the three senatorial zones namely Ogun- East, Ogun -Central and Ogun- West made of 20 local governments in total most especially their core rural area where social amenities is lacking.

Study design: Community based cross-sectional study design was employed in primary schools' children in senatorial zones of Ogun State between ages of 4 - 15 whose parental consents was obtained from their guardians/ parents to partake in the research without manifestations compatible with malaria in the past 14 days.

Study approach: The primary school was selected randomly most especially those that are based in the rural areas. The cross-sectional in primary school students was chosen.

Study Population: Children aged 4- 15 years old with no history of sickness and not on anti-malaria, anti-helmintic drug and not on iron supplementation for the past 6 weeks were included in the study.

Selective Criteria

(1) Inclusion criteria.

The participants must not have taken any anti-helminths drugs medication in past six weeks and should be enrolled in school through-out this period and schools must base in the rural area of the local government

(2) Exclusion Criteria

The students on anti-helminths drugs less than three weeks or about to transfer to another school in less than six weeks.

Data collection

Structured questionnaire was administered to the participants and all the necessary information was well taken.

Sample collection

Fresh stool sample into sterile plastic universal bottle was well labelled for identification and processing.

Sample Transport

Stool / Fecal samples transported under cold environment using ice-park inside transport box to the laboratory for processing.

Sample Storage

Stool sample was aliquatily divided into two, one is stored at 10% formol saline while the other sample was frozen for other studies.

Sample Processing

Methods

Stool samples were collected from a total of 1103 primary school pupils with ages ranging between 4 and 15 years. Samples were processed using formol-ether concentrations, Kato-Katz and Mac-Master techniques to confirm intestinal helminths infection as described in a previous study (20).

Statistical package for social Sciences (SPSS) Version was used for analysis of the data.

Determination of efficacy of albendazole (400mg) against STH

Students that were positive to helminths microscopically using Mc-Master technique and formol ether concentration (FEC) were treated by administered 400mg of Albendazole. However, 14-21 days after treatment their stool sample was taken for microscopy analysis again for albendazole efficacy determinant. The parasite counts were done on the stool analysis for pre and post administration of Albendazole 400mg to the students who participated in the research.

Result and Discussions

Soil transmitted helminths (STH) infection is a major health problem in tropical countries such as Nigeria. Albendazole is an effective and widely used anthelmintic agent to treat STH. The strategy for STH control in endemic areas focuses on morbidity control through large scale administration of anthelminthics to at-risk populations, especially school-age children (21-23). In this study, we show the effectiveness of single dose albendazole (400mg) in reducing the prevalence of STH. Prior to the intervention we found that the prevalence of the three types of worms was very high, especially among school-aged children. The efficacy of albendazole was evaluated against ascariasis, trichuriasis and hookworm infections at 400mg single dose**. Albendazole** is a broad-spectrum anthelmintic with activity against several **nematodes** and flat worms and work by binding the β-subunit of tubulin which inhibits microtubule formation, interrupts glucose transport and results in depletion of glycogen **works** by keeping the worm from absorbing sugar (glucose), so that the worm loses energy and dies

The strategy for STH control in endemic areas focuses on morbidity control through large scale administration of single dose anthelminthics to at-risk populations, especially school-age children. In this study, we show the effectiveness of single dose albendazole in reducing the prevalence of STH similar to previous studies (24-25).

Table 1 Cure Rate (CR) from treatment of soil-transmitted helminths with single dose of albendazole

	Ascaris		**Hookworm**		***T. trichuiria***	
Location	**N**	**Cure rate (%)**	**N**	**Cure rate (%)**	**N**	**Cure rate (%)**
Senatorial districts						
Ogun East	133	97.7	21	99.3	16	99.1
Ogun Central	117	98.7	16	99.0	16	99.4
Ogun West	104	98.3	20	99.2	4	100.0
Age						
4-9	121	98.0	16	99.1	11	99.6
10-15	233	98.3	41	99.2	24	99.4
Sex						
Male	177	97.7	34	98.5	17	99.4
Female	177	98.6	23	99.5	18	99.5
Pre-intervention						
Low	298	98.3	50	84.5	24	72.7
Moderate	54	72.2	-		-	
TOTAL	**352**	**98.1**	**50**	**99.1**	**-**	**99.0**

The cure rate (CR) The cure rate (CR) of albendazole was expressed in **Table 1**. The highest cure was observed for *T. trichiura* (99.3), Hookworm (99.1) and *A. lumbricoides* (98.1) which is similar to a previous study (26) but contrary to *T. trichiura* which is less than 90%Cure Rate. When age group was considered, the CRs varied across the different trials, age classes and pre-intervention faecal egg count (FEC) levels. The differences in CRs between each senatorial districts were not significantly different, the *T. trichiura* CRs of (100%) for the trials in Ogun West, while Hookworm had highest cure rate in Ogun East (99.3%), *A. lumbricoides* had (98.7) in Ogun Central.

The CRs increased over the two age classes (*A. lumbricoides*: 98.0 to 98.3; also, Hookworm 99.1 to 99.2%), but *T. trichiura*: decries from 99.6 to 99.4%). For each of the three STH, most especially *A. lumbricoides*, there was a decline in the CR with increasing levels of infection intensities at the pre-intervention survey most especially (99.3 to 97.4%) although is less pronounced, but not observed in Hookworm and *T. trichiura* because both don't have moderate and high infection rate in the study area

This study found a significant difference between pre and post intervention egg counts (mean count) ($p = 0.001$) thereby indicating that the drugs are most effective in either reducing the egg production or eliminating the parasite itself in the case of Ascariasis and Hookworm

infection.

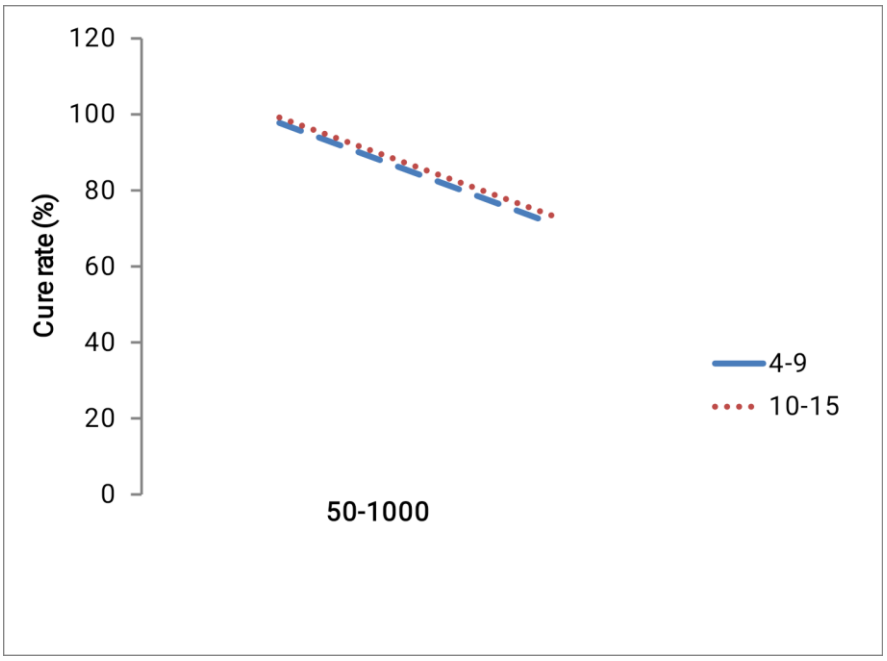

Figure 1.0 Relationship between Cure Rate and Age Range of the participant in pre-intervention

When the differences in CR were considered between age and pre-intervention FEC as illustrated in Figure 1, most especially age group (4-9) and (10-15) which shown no differences. The variability in the CR of the three parasites was not considered because Hookworm and *T. trichiura* fecal egg count shown only low infection rate unlike *A. lumbricoides* that shown low and medium infection rate as result of parasite count i.e Faecal egg count (FEC). The pre-intervention FEC was probably the most important as it had a considerable effect on the CR of *A. lumbricoides.* The decline in the CR was observed with increasing levels of infection intensities at the pre-intervention survey. The drop was observed for *A. lumbricoides* between (98.3%) to (72.2%), while Hookworm and *T. trichiura* cannot be considered due to low infection rate only.

The impact of pre-intervention FEC on the CR of *A. lumbricoides* was shown no significant differences between older pupils than younger ones, but *Hookworm* and *T. trichiura* cannot be considered due to the absence of moderate infection rate, therefore age is not a determining factor for determine the cure rate of albendazole.

The cure rate of 98.1%, against ascariasis obtained with 400mg of albendazole in the present study is slightly lower than study done in Bolivia in 1993 with a cure rate of 100, while that of hookworm (99.1%) which is similar to earlier studies (26,27) but higher than Bolivia (91.7). However, when *T. trichiura* was considered the CR of our study was (99.0%) but higher than observed by Saleha *et al* (26), while that of Bolivia was 59.7 and contradicting other authors (25, 28-29) which may due to low or light infection rate of *T. trichiura* in the study area compared to other authors which recorded heavy infection rate.

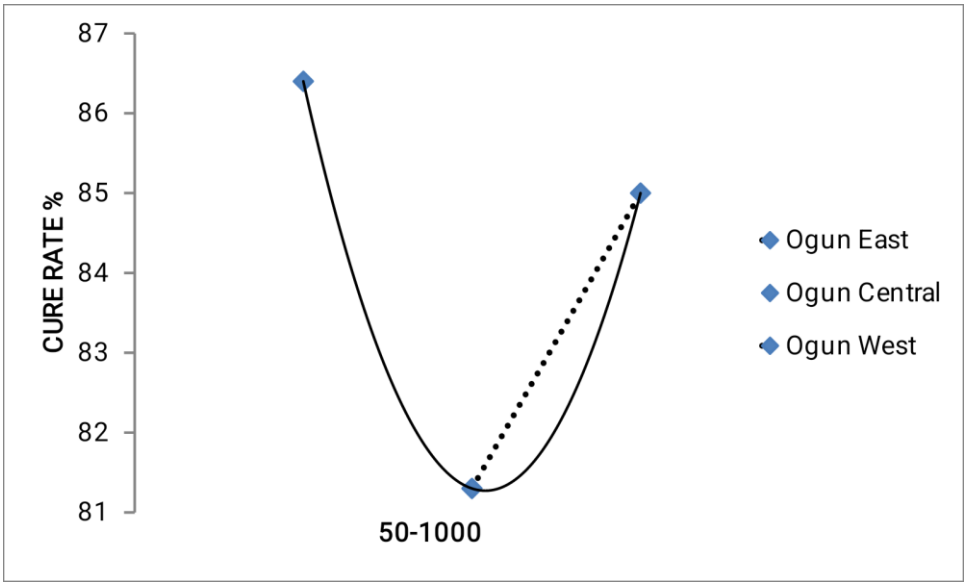

Figure 2. Relationship between Cure Rate at the different Senatorial zones of Ogun State

Adequate cure rates and egg reduction rates above 98.7% were found with a single dose of albendazole for *A. lumbricoides* infection, Hookworm 99.3% and *T. trichiura* 100%, respectively which may be due low and medium infection rate in the study area.

When senatorial districts were considered the differences in CRs between trials were most pronounced for *A. lumbricoides* in Ogun Central between 72.2 to 98.7 but in Ogun East and Ogun West STH cure rate most especially *Hookworm* and *T. trichiura* shown low infection faecal egg count rate, therefore their cure rate cannot be compared excepts in *A. lumbricoides* which is not significant, as displayed in Figure 2.

Table 2. Fecal egg count reduction (FECR) across different senatorial zones, age, gender and post-intervention intensities.

	Ascaris				**Hookworm**				***T. trichiura***			
	N	**FECR (1) (%)**	**FECR (2) (%)**	**FECR (3) (%)**	**N**	**FECR (1) (%)**	**FECR (2) (%)**	**FECR (3) (%)**	**N**	**FECR (1) (%)**	**FECR (2) (%)**	**FECR (3) (%)**
Districts												
Ogun East	132	98	-5.6	98.5	21	-13.5	-106.6	76.4	16	-21.5	-195.5	57
Ogun Central	117	84	46	99	16	-8.0	-32.7	70.3	14	-19.7	-140.3	47.1
Ogun East	105	91	33	98.7	20	-10.2	-66.4	74.4	4	-19.4	-144.5	-88
Age (years)												
4-9	122	93	24	98.6	16	-12.5	-88.7	58.9	16	-19.9	-155.7	27.3
10-15	232	92	37	98.9	41	-10.4	-71.2	79.6	1	-20	-156.8	46.5

									8			
Sex												
Male	178	94	19	98.8	34	-12	-84.84	78.9	11	-19.8	-157.9	39.2
Female	176	91	32	98.8	23	-9.9	-65.9	68.2	23	-19.8	-153.9	41.1
Pre-intervention												
Low	298	93.1	98.2	95.4	50	-34	-89.1	-94.5	24	-70.0	-81.2	72.1
Moderate	54	100.0	100.0	100.0								

FECR (1): group based and arithmetic mean; FECR (2): group based and geometric mean; FECR (3): individual based and arithmetic

Comparative formulae for assessment of FECR

The pre-intervention fecal egg count (FEC) for the different STH ranged from 50 to 50,000 egg per gram EPG for *A. lumbricoides* (arithmetic mean =6877 EPG), from 50 to 23,200 EPG for *T. trichiura* (arithmetic mean =824 EPG) and from 50 to 13,800 EPG for hookworm (arithmetic mean = 650 EPG) but according to the report, infection rate in the study area involves both low and medium which is between 50 to1,000 and 1001- 5,000 for *A.lumbricoides* while that of *Hookworm* and *T trichiura* had low or light infection rate.

The data in Table 1.0 show that there was considerable variation in the arithmetic means of the FEC from the trial groups in the 3 senatorial districts of the three STH species.

The FEC reduction rate calculated using all three formulae (based on FECR 1-3) in turn for *A. lumbricoides*, *Hookworm* and *T. trichiura* across the 3 senatorial district, age classes, sexes and pre-intervention infection intensities are summarized in Table 2.

However, the FEC reduction rate for FECR (1) was the highest for *A. lumbricoides* (98.5), followed by hookworm (89.4) and *T. trichiura* (89.1). The FECR (2), was resulted into lower value in all three STH when compared with FECR (1), Also, there was considerable variation in the FEC reduction rate among the Senatorial district, age classes and infection intensities at pre-intervention survey. For *A. lumbricoides*, the FEC reduction rate remained roughly unchanged over these variables, only ranging from 98.2 to 100. For *Hookworms* and *T. trichiura*, the differences between the trials were virtually negligible, all indicating a potent effect just short of the maximum 100 (FECR (2) >99.3).

When, FECR (3) result was considered, which mostly yielded lower values than those from FECR (1). The low values (sometimes negative) can be explained by subjects for whom the post-intervention FEC exceeded the pre-intervention FEC. These subjects contributed to a negative FEC reduction rate which had a significant impact on the final FEC reduction rate calculated with FECR (3).

This lowering of FECR (3) compared to FECR (1) for *A. lumbricoides* also occurred with age class (4-9) and (10-15) (FECR (1): 93; FECR (3): 98.6) and the low pre-intervention infection intensity level (FECR (1): 92.0; FECR (3): 98.9), but not for the remaining variables. The number of negative individual FEC reduction rates, and the magnitude of the difference between pre- and post-intervention FEC, both contributed to the discrepancies found for *T. trichiura* and hookworms.

FECR(1): group based and arithmetic mean; FECR(2): group based and geometric mean; FECR(3): individual based and arithmetic.

The albendazole used were therapeutically efficacious irrespective of the worm burden

harbored by the students in the case of Ascariasis, Hookworm and Trichiuriasis infections. But they were more efficacious for light infection than moderate infection as shown for *A. lumbricoides.*

The reduction and the maintenance of low worm burden have an important impact on the health of the community. The first sign of improvement is parasitological with a reduction of heavy infection, then nutritional, with an increase in iron stores, followed by an increase in hemoglobin level and finally by an increase in growth. At least two years of intervention are normally required before an increase in hemoglobin becomes evident and even longer period is required to exhibit improvement in growth. Improved indicators of school effects (school attendance, reenrollment, retention, and achievement) have been observed: iron load and increasing hemoglobin level, improving physical growth and cognitive capacity, educational achievement, and reduced school absence (30).

Without significant environmental and health behavioral improvement, reinfection will occur and may reach the same prevalence and intensity prior to the treatment. Jia *et al*. (31) found that reinfection will occur in 6-12 months after the treatment, while Appleton et al. (32) reported that within five months there had been a 75% reinfection of *A. lumbricoides*, 71% *T. trichiura* reinfection, and 28% reinfection of hookworm. Total re-infection will return within 12 months if no retreatment is applied.

Since it is difficult to change environmental and health behavioral patterns of rural people, mass drug treatment is required every six months for at least five consecutive years to control STH (33).

The study is the first to evaluate drug efficacy for STH in school children in Nigeria using a protocol which was standardized in terms of the treatment and accepted methods of reporting drug efficacy in the field by using Cure Rate(CR) was used previously (16).

However, this study back the previous reports that indicated that single dose ALB treatment is most effective for infection with A. lumbricoides, followed by hookworm and T. trichiura but contrary to similar studies (16, 17, 34-35) which reported that is relatively ineffective to T. trichiura. The reason for effectiveness may be due to low infection rate or due to a particular strain or genetic component of the people in the study area.

The cure rate of 100% against ascariasis (post-intervention) obtained with albendazole 400 in the present study is consistent with a study done in Bolivia in 1993 with a cure rate of 100. But, the CR of (84.5%)(Table 1) obtained, against hookworm is slightly higher than a report from Bolivia (that of Bolivia is 81.8). The Egg Reduction Rate (ERR) of the present study 98.1%; 99.1% and 99.0% for Ascaris, hookworm and Trichuris respectively varied slightly with a study done in Thailand (36) with 100, 96 and 87respectively.

Conclusion

Therefore, the efficacy of albendazole as the best drug of choice in the study area has been confirmed based on WHO standard that any drug of antihelminthic that had egg reduction rate (ERR) greater or equal 95%, for *Ascaris lumbricoides*, *Hookworm* greater or equal to 90% and finally *Trichuris trichiura* greater or equal 50% as shown in Table 1

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Declarations

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