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Comparative efficacy of Levamisole, Mebendalzole and Pyrantel Pamoate against common intestinal nematodes among children in Calabar, South-South Nigeria

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Abstract *Introduction*: Continued endemicity of intestinal nematodes infestation in children in our environment despite availability of potent and safe anthelmintic drugs is of public health interest.
Objective: This study assessed the comparative efficacy of selected anthelmintic drugs namely Mebendazole, pyrantel pamoate and levamisole-against common intestinal nematodes namely *Ascaris lumbricoides*, Hookworm (*Ancylostoma duodenale* and *Necator americanus*) and *Trichuris trichuria* in children in Calabar Municipality, South-South Nigeria
Method: One hundred and thirty eight pupils from four primary schools in Ikot Ishie/Ikot Ansa communities of Calabar with worm infestation (*Ascaris*, hookworm and *Trichuris* including mixed infestation) were randomized by simple balloting to one of the following anthelmintic drugs (Mebendazole 500mg, Pyrantel 10mg/kg or Levamisole 2.5mg/kg). The efficacy of the drugs was determined by the level of clearance of worm egg/ova from fresh stool samples of the pupils on post-treatment examination.
Result: The study showed the three anthelmintic drugs displaying one hundred percent (100%) efficacy in respect of Ascaris and trichuris worms, but less so for hookworm. Mebendazole displayed 90.48%, Pyrantel 45.16%) and Levamisole (17.86%) efficacy level against hookworm.
Conclusion: The overall result indicates that Mebendazole was the most efficacious agent against the three common intestinal worms.

Keywords: Anthelminthic, nematodes, children, Nigeria

Introduction

Intestinal helminthiasis is a recognized public health problem, worse in the tropical and subtropical developing areas[1]; certain areas of Asia, Africa, and Latin America[2]. This may be related to the standard of living and environmental hygiene. *Ascaris lumbricoides*, *Trichuris trichiura* and hook worm (*Ancylostoma duodenale* and *Necator americanus*) are the most common infections in human with an estimated global burden of 39 million disability-adjusted life years lost (DALYs)[3,4]. The disease of intestinal helminthiasis has been associated with some effects which manifest by many symptoms and complications in growing children. These effects include malnutrition, stunting of growth and reduced cognitive ability, which in general hamper optimal child growth and development[5].

World Health Organization (WHO) in its concern for the disease aims at eradication with chemotherapy and improved and high-quality socio-cultural habits (personal hygiene, environmental sanitation, good waste/sewage disposal and portable water supply). Chemotherapy forms the mainstay of control of infestation[6].

Mebendazole, Pyrantel pamoate and Levamisole are recommended drugs against intestinal nematodes. The current anthelmintic drugs have been in use for decades[6] starting with Pyrantel pamoate in the 1960s[7]. It is therefore important to assess the efficacy of the available antihelmintic agents in current use from time to time. The relevance of such assessment lies in the possibility of development of resistance by these worms to these agents, as already reported in animals[8].

Considering the rate of drug abuse and misuse in our

environment, it is worthwhile to assess the efficacy of these drugs against these common intestinal worms. The pattern of activity of each drug against the different worms tested may be useful in future trials, choice of treatment or anthelmintic drug policy, as is the case with malaria treatment. This is also in keeping with, and provides data for, the current practice of "Evidence-based-medicine". The object of this study was to assess the efficacy of three most commonly used anthelmintic drugs in Nigeria namely, Mebendazole, Pyrantel pamoate and Levamisole in school children identified with intestinal nematodes (*Ascaris lumbricoides*, *Ancylostoma duodenale* and *Necator americanus* and *Trichuris trichuria*) in Calabar-Nigeria.

Subjects and Method

This open-label randomized comparative study was carried out between November and December 2005 in Calabar Municipality, Nigeria. Four hundred and forty pupils were selected from four primary schools in Ikot Ishie and Ikot Ansa community within the Local Government Area. Ethical clearance for the study was obtained from the University of Calabar Teaching Hospital Ethical Committee. The Cross River State Ministry of Education gave formal approval and permission for the study. Written informed consent was acquired from the children's parents or legal guardians to participate in the study with emphasis made on voluntary participation and possible withdrawal at any time during the study.

Children of parent who consented were given an empty stool container, labeled with their names and class grade and asked to return it with a fresh sample of stool the next day.

The sample was tested for intestinal nematode infestation by microscopic examination of fresh stool samples using brine flotation method[9]. The method is simple, straight forward and suitable for field study. Samples were analyzed with a time frame of 45 to 60 minutes beyond which the adherent eggs/ova would sink down the solution[9]. One hundred and thirty eight (138, 48.59%) of the screened population were identified with various worms (*Ascaris lumbricoides*, *Ancylostoma duodenale*, *Necator americanus* and *Trichuris trichuria*) by virtue of eggs/ova in stool.

The infested pupils were randomly assigned to one of the three treatment schedules, of single dose of either mebendazole (wormin^{R} brand) 500mg or pyprantel pamoate (combantrin^{R} brand) 10mg/kg or Levamisole (levax^{R} brand) 2.5 mg/kg using simple balloting irrespective of polyparasitism or mono-infection. All the treatments was ingested with water and given in the school classrooms under direct observation of the study personnel. Pupils were given the next dose above the calculated dosage (mg/kg). Pupils were observed for about 30 minutes after administration of drug and treatment was repeated once if patient vomited within 30 minutes of drug administration. To ensure that other types of anti-helminthics were not administered at home, pupils were sent home with a letter to their parents emphasizing the importance of not administering any other drug to the child during the period of the study and if need be, should contact the trial physician whose number was written in the letter.

Post-treatment stool examination was again conducted after one week using the same method used for the pre-treatment stool examination and the end point was cure rate (proportion of egg-positive at baseline, which became egg-negative after treatment). Single stool analysis was employed in this study and this has been shown to be effective[10-13]. The results were recorded and analyzed using Chi-squared statistics to observed if there will be a significant different in the efficacy of the three drugs against the different parasite.

Results

Four hundred and forty pupils' who met the inclusion criteria: age between 4 and 12years (both males & females), residence within the community for 6 months and above, written consent from parents/guardian and ability to ingest tablet with water were enrolled for the study. Two hundred and eighty four pupils returned with their stool samples the next day and were screened for intestinal nematode infestation. One hundred and thirty eight (138) pupils were found to be infested with worms giving an overall average of 48.59% worm infestation. The distribution of the different type of worms is shown in Table 1. Most children were diagnosed with hookworm infection (35.6%). The overall infection rates of *A. lumbricoides*, *T. trichuris* and mixed infection are 26.1%, 6.7% and 16.5% respectively.

Table 1: Distribution of helminthes

Type of helminth	Number found	% number found (N = 284)
Ascaris	74	26.1
Hookworm	101	35.6
Trichuris	19	6.7
Mixed	47	16.5

Overall, 138 were infested; 49 pupils receiving Mebendazole (19 *Ascaris*, 38 Hookworm and 7 *Trichuris*); 47 recieving Pyrantel pamoate (31, 14 and 6 for *Ascaris*, Hookworm and *Trichuris* respectively) and 42 received Levamisole (24 *Ascaris*, 5 hookworm and 6 *Trichuris*). The efficacy of the drugs is shown in table 2. The three drugs showed 100% efficacy against *Ascaris* and *Trichuris*, but less so against hookworm. Mebendazole, however, displayed better efficacy (90.48%) than pyrantel pamoate (45.16%) and Levamisole (17.86%) against hook worm. There was a significant difference between the efficacies of the three anthelmintic drugs against Hookworm (Xcal > Xtable). No adverse events were observed on either of the drugs during the study period.

Table 2: Comparative efficacy of drugs on different worms

Drug type	No. of pupils treated	Efficacy of drugs against different worms*		
		Ascaris	Hookworm	*Trichuris*
Mebendazole	49	19/19(100%)	38/42(90.48%)	7/7(100%)
Pyrantel pamoate	47	31/31(100%)	14/31(45.16%)	6/6(100%)
Levamisole	42	24/24(100%)	5/28(17.86%)	6/6(100%)

*Fractions represent the total number of worms cleared in each group and not number of individuals freed of worms infestation.

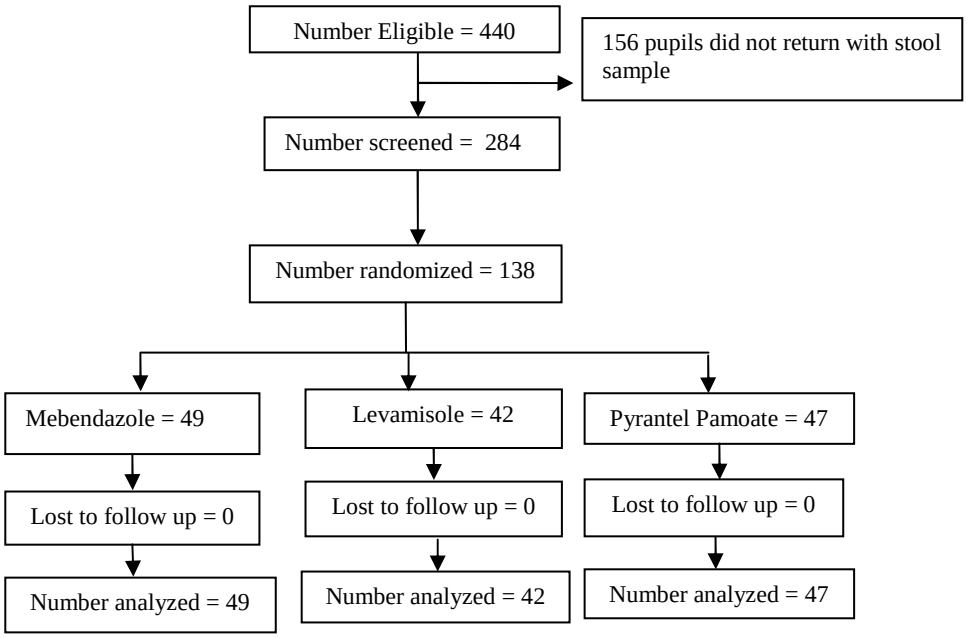

Fig 1: Flow chart showing study participation and compliance

Discussion

This study showed a prevalence rate of intestinal nematodes of 48.59% which is comparable to 46.5% reported by by Ikpeme in school age children in 2005 but lower a prevalence rate of 67.2% obtained by Meremikwu et al, 1995 in preschool children in the same community[1,13]. The downward trend evident from these reports may be due to difference in age and changes in living conditions. Improvement in socio-economic status tends to lower the risk of worm infestation[14] even though this study was carried out in the rural area of Calabar Municipality.

The prevalence of the each infection was 35.6%, 26.1%, 6.7% and 16.5% for Hookworm, *Ascaris*, *Trichuris* and polyparasitism respectively. It would have been expected that *Ascaris* have the greater prevalence due of its mode of transmission but high rate of hookworm have also been restricted to areas with rural poverty[15].

The result of the comparative efficacy of three drugs against the different worms showed a high efficacy rate for Mebendazole across the three worms. This finding is in agreement with observation of de Silva (1997) that Mebendazole is highly effective against these common nematodes with better higher activity against *Ascaris* than hookworm[16]. This is surprising as Mebendazole is poorly absorbed unlike Levamisole which has an oral absorption rate of 96.5 percent and Pyrantel Pamoate has a low absorption rate.

The three Levamisole, Mebendazole and Pyrantel pamoate drugs were 100% effective against *Ascaris* and *Trichuris*. The efficacy for *Ascaris* was comparable with other studies; a study from China reported cure rate of over 95%[17] and a review on antihelminths studies reported cure rate of between 97.5 – 100%[18]. This suggests that despite widespread use of these drugs over the past few decades, the worms have not developed resistance against these drugs. However, the case differs with *Trichuris* as studies in the past had reported variable cure rate ranging from 22.2% to 86.8 for the three drugs[19]. Keiser and Utzinger in their review concluded that the treatment of *Trichuris* with single oral doses of current anthelminths is unsatisfactory[18]. Another study concluded that Pyrantel pamoate for *Trichuris* was inefficacious[17]. The low prevalence of *Trichuris* in this study makes it difficult to draw any relevant conclusion.

In the case of hookworm, the efficacy of three drugs varied remarkably. The efficacy of Levamisole, Pyrantel pamoate and Mebendazole against hookworm was 17.86%, 45.16% and 90.48% respectively. The drug efficacies in T. trichiura infection were similar to those reported in previous studies, with Mebendazole greatly reducing the prevalence followed by Pyrantel pamoate and Levamisole having a much smaller effect[18,19].

Mebendazole is the only one of the three drugs that is

known to inhibit the development and growth of larval stage of hookworm and *Trichuris*[2] which may explain the high efficacy of this compound against these nematodes.

The number of pupils screened was far less than the number registered. This was due to failure of the pupils to return stool samples. Many of them returned consent form signed by their parent but could not pass stool before coming to school. Others forgot even the stool already collected in the sample bottle at home. This resulted in loss of many sample bottles even after several visits to each school, hence limitation of sample size. Another limitation is that monoparasitism and polyparasitism was not separated during the randomization process.

Conclusion

The study assessed the efficacy of mebendazole, pyrantel and Levamisole against intestinal nematodes in primary school pupils in a rural Nigeria community with Mebendazole being the most effective anthelminthic drug against the three commonest intestimal worms in this community with efficacy exceeding 90% in all cases. The result of this study supports the World Health Organization (WHO) recommendation for the use of mebendazole in the integrated management of childhood infection, mass treatment programs and school health program[15]. Evidence from this study can influence anthelmintic drug policy in this country as is the case with malaria, in line with "evidence-based-medicine", and suggest clinical selectivity and choice of anthelmintic drug in contemporary helminthic control programs.

Authors Contributions

Ekenjoku AJ: participated effectively in the planning, data collection and analysis, and writing of the manuscript/paper, supervision of study.

Oringanje C: took part in sample analysis and preparation of the manuscript.

Meremikwu MM: Contributed in the planning of the study, preparation of protocol and of the manuscript.

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