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ASSESSMENT OF EFFICACY OF SINGLE-DOSE ALBENDAZOLE IN TREATMENT OF INTESTINAL HELMINTH PARASITES IN SCHOOL-CHILDREN OF BHAKTAPUR

RAIHAN SHRESTHA[1] AND MAHENDRA MAHARJAN[1] ✉
[1]Central Department of Zoology,Tribhuvan University
Kirtipur, Kathmandu, Nepal
mmaharjan@cdztu.edu.np

ABSTRACT

A total of 495 stool samples from the school children aged 9-12 years from Bhaktapur were examined for helminth parasites by direct smear method. Out of 495 children, 137 (27.68%) were found positive for one or more intestinal helminthic parasites. *Ascaris lumbricoides* (22.63%) showed highest prevalence rate followed by *Trichuris trichiura* (6.06%), *Strongyloides stercoralis* (1.82%), Hookworm (1.62%), *Taenia* sp. (1.01%), *Hymenolepis nana* (0.81%) and *Enterobius vermicularis* (0.40%). The helminthic infection was found to be almost equal in male and female children and statistically no significant difference was found ($\chi^2 = 8.31 \times 10^{-6}$, $p>0.05$). Higher percentages of students were infected with single parasites than double and multiple infections. All 137 positive cases were treated with single oral dose of 400 mg albendazole. Post-treatment stool samples were collected four weeks after treatment to determine the cure rate. Stool samples were again collected 24 weeks post-treatment to study the rate of re-infection. The Cure Rates (CR) for *A. lumbricoides* was 61.82%, *S. stercoralis* was 66.67%, *Taenia* sp., Hookworm and *E. vermicularis* were 100%, *T. trichiura* was 44.83% and *H. nana* was 0.00%. The post treatment examination after 24 weeks showed that re-infection was present in *A. lumbricoides* (20.29%) and *T. trichiura* (7.69%) only. New infection was recorded for *A. lumbricoides* (21.74%), *T. trichiura* (4.72%), *S. stercoralis* (1.60%) and *E. vermicularis* (0.76%). The study showed albendazole was comparatively less effective against *S. stercoralis, A. lumbricoides* and *T. trichiura* which may be due to development of drug resistance at certain level which needs to be explored.

Keywords: prevalence, reinfection, new infection, anthelminthic drugs, drug resistance

INTRODUCTION

Intestinal parasitic infections are major causes of morbidity and mortality among school aged children of developing countries (WHO, 1987). School-aged children and preschool children are the most vulnerable group as compared with any other age group. They harbour the greatest numbers of intestinal worms and as a result, they experience growth stunting and diminished physical fitness as well as impaired memory and cognition (Stephenson *et al*., 2000; Crompton & Nesheim, 2002; Bethony *et al*., 2006; Tchuem Tchuenté, 2011). Life in Nepal, like in most of the third world countries is characterized by poverty, ignorance and diseases. Intestinal infestations like giardiasis, amoebiasis, ascariasis, ancylostomiasis, fascioliasis and taeniasis are common in Nepal (Acharya, 1979). Children are found to be infected more frequently by

intestinal parasites than adults (Rai *et al*., 1994). Although parasitic diseases constitute the most wide-spread human health problem in the world today, they have for various reasons also been the most neglected (Katzung, 2001). Programmes targeted at school children have been shown to be extremely cost-effective, and hence this provides a realistic approach for combating these infections in the future (Chan, 1997). Nepal government has been administering albendazole linked with various programs like filariasis elimination programmes. Recently government of Nepal has declared days to give antihelminthic drug with Vit. E all over the country. Preventive chemotherapy is the mainstay of control, but only few drugs are reliable (Keiser & Utzinger, 2008). Albendazole has been enlisted among four anthelminthics for the treatment and control of Soil Transmitted Helminthes (STH) by WHO (WHO, 1997). Besides these four, more than a dozen of antihelminthics have been developed. There is increased trend of using antihelminthic drugs, directly without diagnosis, in schools and other public awareness programmes and general people are suggested to take anthelminthic drugs at regular intervals. While some anthelminthic drugs are only effective against specific parasites, efficacy of other drugs has not been verified under present circumstances. Also resistance to those drugs, previously considered very effective against helminth parasites, need to be considered. The major causes of drug resistance are inappropriate use of drugs, inadequate diagnosis of diseases, agricultural and veterinary use and mutation on part of microbes (Singh *et al*., 2006). Present study has been carried out among school-children to determine prevalence rate of different intestinal helminth parasites, the cure rates of oral single dose 400 mg albendazole against them and their rates of re-infection.

MATERIALS AND METHODS

Study area

The study was conducted among the school children aged 9-12 years of two schools of Bhaktapur municipality of Bhaktapur district. Bhaktapur district is situated at 27°36' to 27°44' latitude and 85°21' to 85°32' longitude. The two schools under study were Everest English School (EES) in ward no. 15, Mibachhen and Prabhat English Higher Secondary School (PEHSS) in ward no.10, Mahakalisthan, Byasi. These two schools were purposively selected for the study.

Sample size and study design

Stool samples from altogether 495 students (289 males and 206 females) were collected in the initial phase of study. 295 samples were made available from Everest English School while remaining 200 samples were contributed by students from Prabhat English Higher Secondary School. Collecting vials were distributed to the target students with sufficient detailed instructions required for stool collection. The following morning those stool samples were collected in the school. Immediately after collection, potassium dichromate ($K_2Cr_2O_7$) was added to stool sample in vials for preservation. During initial phase general prevalence of intestinal helminth parasites was determined. In second phase efficacy of albendazole against different intestinal helminth parasites and in third phase their re-infection rates were determined. Cure Rate (CR) alone was employed to determine efficacy of albendazole. To determine efficacy of single dose albendazole, 134 samples (82 from EES and 52 from PEHSS) were collected post

treatment, 4 weeks after medication. Similarly, 134 samples (83 from EES and 51 from PEHSS) were collected post treatment, 24 weeks after treatment. These samples were processed to determine rates of re-infection and new infection. Stool samples were examined through electric compound microscope by preparing direct smear, both unstained and stained for detection of intestinal helminth parasites. The trade name of albendazole used for medication was Zeroworm (Medindia4u.com Pvt. Ltd, Chennai). After examination of stool samples from first phase, all the positive school children were treated with oral single dose 400 mg albendazole.

RESULTS

Prevalence of Intestinal Helminth Parasites in School Children

In the present study, altogether seven helminthes were recovered, including two cestodes and five nematodes. *Ascaris lumbricoides* was the most common intestinal helminth parasite with a prevalence rate of 22.63%. *Enterobius vermicularis* was the least prevalent helminth parasite with prevalence rate of 0.40%. Other infections included 6.06% with *Trichuris trichiura,* 1.82% with *Strongyloides stercoralis*, 1.62% with Hookworm, 1.01% with *Taenia* sp. and 0.81% with *Hymenolepis nana* (table 1). Out of 495 students examined, 137 (27.68%) were found to be infected with one or more types of intestinal helminth parasites. Regarding different sexes, 27.68% (80/289) male children and 27.67% (57/206) female children were positive for intestinal helminth parasites. Statistically, no significant difference was found in prevalence of intestinal helminth parasites in male and female ($\chi^2 = 8.31 \times 10^{-6}$, $p > 0.05$). Infection with single helminth parasite (78.83%) in an individual was more common than double (18.98%) or multiple infections (2.19%). *A. lumbricoides* was the most prevalent helminth parasite in both male (21.11%) and female (24.76%) children. *E. vermicularis* was least prevalent among male children (0.69%) while *E. vermicularis* and *H. nana* were completely absent among female children (0.00%).

TABLE 1. Sex and species-wise prevalence of intestinal helminth parasites.

	Male (n=289)	Female (n=206)	Grand Total (N=495)	Prevalence %
A. lumbricoides	61 (21.11%)	51 (24.76%)	112	22.63
T. trichiura	21 (7.27%)	9 (4.37%)	30	6.06
E. vermicularis	2 (0.69%)	-	2	0.40
S. stercoralis	6 (2.08%)	3 (1.46%)	9	1.82
Hookworm	6 (2.08%)	2 (0.97%)	8	1.62
Taenia sp.	4 (1.38%)	1 (0.49%)	5	1.01
H. nana	4 (1.38%)	-	4	0.81
Total	**104**	**41**	**170**	

Efficacy of Albendazole Against Intestinal Helminth Parasites

The prevalence rates were found to be reduced in all helminth parasites except *H. nana*, in which it was constant, after four weeks of post treatment. The treatment with albendazole

showed good results against *Taenia* sp., Hookworm and *E. vermicularis* with 100% cure rate. Albendazole was not at all effective against *H. nana* and had 0.00% cure rate. Against *A. lumbricoides* and *S. stercoralis,* the drug showed comparatively less effectiveness with the cure rate of 61.82% and 66.67% respectively. The efficacy of albendazole against *T. trichiura* was very minimal with cure rate of 44.83% only (table 2). Against *S. stercoralis*, albendazole showed equal cure rate (66.67%) in both male and female children. Against *A. lumbricoides*, albendazole showed slightly higher efficacy in female children (62.75%) than in male children (61.02%) without significant difference ($\chi^2 = 3.461 \times 10^{-2}$, $p>0.05$). However against *T. trichiura* the drug was slightly more efficient in male children (45.00%) than in female (44.44%), again without any association ($\chi^2 = 0.141$, $p>0.05$).

TABLE 2. Species and sex-wise cure rate.

	Female				Male				Total			
	No. of Positive cases from first phase	No. of positive cases from second phase	No. of cured cases	Cure Rate (%)	No. of Positive cases from first phase	No. of positive cases from second phase	No. of cured cases	Cure Rate (%)	No. of Positive cases from first phase	No. of positive cases from second phase	No. of cured cases	Cure Rate (%)
A. lumbricoides	51	19	32	62.75	59	23	36	61.02	110	42	68	61.82
T. trichiura	9	5	4	44.44	20	11	9	45.00	29	16	13	44.83
Taenia sp.	1	0	1	100	4	0	4	100	5	0	5	100
E. *vermicularis*	-	-	-	-	2	0	2	100	2	0	2	100
S. stercoralis	3	1	2	66.67	6	2	4	66.67	9	3	6	66.67
Hookworm	2	0	2	100	6	0	6	100	8	0	8	100
H. nana	-	-	-	-	4	4	0	0.00	4	4	0	0

Re-infection and New Infection Rates of Intestinal Helminth Parasites

After 24 weeks of drug administration, stool samples from school children showed that the rate of re-infection was highest for *A. lumbricoides* (20.29%) followed by *T. trichiura* (7.69%). No infection for *Taenia* sp. and Hookworm were observed after 24 weeks. The infection with *H. nana* remained constant in this follow up as well. Also new infection was seen among some intestinal helminth parasites. *A. lumbricoides* showed highest rate of new infection (21.74%) followed by *T. trichiura* (4.72%), *S. stercoralis* (1.60%) and *E. vermicularis* (0.76%) (table 3).

The rates of re-infection by *A. lumbricoides* were 18.92% and 21.88% respectively for male and female children. However, statistical difference was insignificant (χ^2= 9.27×10^{-2}, p>0.05). Re-infection by *T. trichiura* was seen only among female children which accounted for 25.00%. New infection by *A. lumbricoides* was high among male children (23.53%) than among female children (16.67%). But rate of new infection by *A. lumbricoides* was independent of sex (χ^2= 5.07×10^{-2}, p>0.05). In *T. trichiura* also, male children (6.90%) showed higher new infection rate than female children (2.08%), although statistically no significant difference regarding new infection rate was observed (χ^2= 0.495, p>0.05). However, in *S. stercoralis*, female children (1.85%) showed higher rate of new infection than male children (1.41%). Here too, no association was observed between the sex and rate of new infection (χ^2= 0.274, p>0.05). Regarding *E. vermicularis*, new infection was seen only among male children (1.33%).

TABLE 3. Species-sex-wise rates of reinfection and new infection of intestinal helminth parasites.

	Female			Male			Total		
	No. of children susce-ptible for	No. of children Positive for	Positive %	No. of children susce-ptible for	No. of children Positive for	Positive %	No. of children susce-ptible for	No. of children Positive for	Positive %
A. lumbricoides reinfection	32	7	21.88%	37	7	18.92%	69	14	20.29%
A. lumbricoides new infection	6	1	16.67%	17	4	23.53%	23	5	21.74%
T. trichiura reinfection	4	1	25.00%	9	0	0.00%	13	1	7.69%
T. trichiura new infection	48	1	2.08%	58	4	6.90%	106	5	4.72%
S. stercoralis new infection	54	1	1.85%	71	1	1.41%	125	2	1.60%
E. vermicularis new infection	57	0	0.00%	75	1	1.33%	132	1	0.76%

DISCUSSION

Intestinal parasites are worldwide in distribution. Among them STHs and other helminth parasites pose serious threat in the physical well-being of human. Today, different types of antihelminthic drugs are available but only few are found to be reliable. Research regarding efficacy of anthelminthic are very rare in context of Nepal although much researches have been conducted worldwide. The present study indicated that the prevalence of intestinal helminthes (27.68%) in school children is remarkable. Comparable prevalences of helminthes were, however, reported in some other studies (Jha, 2004; Shakya *et al*., 2006; Mukhopadhyay

et al., 2007). Present findings showed that the rate of prevalence was independent of the sex of children (χ^2= 8.31×10^{-6}, p>0.05). Similar findings have also been reported previously (Manandhar, 2007). Several previous studies had shown that Hookworm was the most prevalent helminth parasite in Nepal (Estevez *et al*., 1983; Sherchand *et al*., 1997; Yong *et al*., 2000; Kunwar *et al*., 2006). Similarly, some other studies had shown *Trichuris trichiura* as the most common helminth (Shrestha, 1983; Uga *et al*., 2004; Pokhrel, 2005; Rai *et al*., 2005). However, the present study had shown that *A. lumbricoides* (22.63%) was the most prevalent intestinal helminth parasite followed by *T. trichiura* (6.06%). This result is in agreement with that reported previously (Gupta & Gupta, 1988; Chhetri, 1997; Manandhar, 2007; Sukupayo, 2007) which also showed *A. lumbricoides* as the most prevalent helminth in Nepal followed by *T. trichiura*. Regarding helminth infection in different sexes, *A. lumbricoides* was the most prevalent in both sexes (21.11% and 24.76% respectively).

Information about the efficacy of the treatment regimen and the rate of reinfection helps in effective control of helminth infections (Narain *et al*., 2004). After four weeks post treatment, the prevalence rates were found to be reduced. Albendazole was completely effective against *Taenia* sp. and *E. vermicularis* (CR= 100%). Albendazole also showed 100% cure rate against Hookworm. This result was comparable with some previous findings (Narain *et al*., 2004; Adugna *et al*., 2007; Vercruysse *et al*., 2011) against Hookworm. However, albendazole showed only partial effect against *A. lumbricoides* and *S. stercoralis* (CR= 61.82% and 66.67% respectively). The finding was comparable with other studies [Belizario *et al*., 2003 (CR= 69.7%); Narain *et al*., 2004 (CR= 70.8%)] against *A. lumbricoides*. The finding was not, however, coinciding with cute rates observed in case of *S. stercoralis* by Datry *et al*. (1994) (CR= 38%) or by Nkengazong *et al*. (2010) (CR= 100%). Albendazole showed no effect on *H. nana* (CR= 0.00%) while it showed very less effect on curing *T. trichiura* (CR= 44.83%). Against *T. trichiura,* similar findings were reported previously [Belizario *et al*., 2003 (CR= 31.5%), Vercruysse *et al*. 2011 (CR= 46.6%)]. Cure rate against all helminth parasites was independent to sex of children.

In the present study, stool examination after 24 weeks of drug treatment, showed reduction in prevalence rates of intestinal helminthes. Re-infection was seen only in *A. lumbricoides* and *T. trichiura* (re-infection rates being 20.29% and 7.69% respectively). Female children showed higher rate of re-infection by *A. lumbricoides* than male (21.88% and 18.92% respectively) without significant difference (χ^2= 9.27×10^{-2}, p>0.05). Re-infection by *T. trichiura* was seen only in female children (25.00%). This finding also supported the fact that *Ascaris* show higher influence in children and soil transmitted helminthes are important public health problem in developing countries. New infections were seen in *A. lumbricoides* (21.74%), *T. trichiura* (4.72%), *S. stercoralis* (1.60%) and *E. vermicularis* (0.76%). The present study showed that albendazole was moderately effective against *A. lumbricoides* and *S. stercoralis*. Albendazole showed low efficacy against *T. trichiura* while it was completely ineffective against *H. nana*. Although the drug was extremely highly effective against *Taenia* sp., Hookworm and *E. vermicularis,* the number of samples for study was very less. So, nothing significant could be concluded from them. Also rates of re-infection and new infection were moderately high for *A. lumbricoides* and *T. trichiura*. These results have prompted a necessity to develop another broad spectrum highly effective anthelminthic drug. Mass Drug Administration (MDA) needs to be continued nationwide

to keep the prevalence rate to much low figure. Also further studies at various levels should be conducted to determine the efficacy of commonly used drugs. Researches, for producing new anthelminthic drugs, which have higher efficacy and low toxicity, have become a necessity.

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