

Albendazole in the treatment of *Hymenolepiasis* in school children

Wali Khan^{1*}, Jahangir Khan², Aziz Ur Rahman², Hamid Ullah³, Mohammad Salim⁴,
Mudassar Iqbal¹, Israr Khan¹, Muhammad Salman¹ and Bakht Munir¹

¹Department of Zoology, University of Malakand, Chakdara, Lower Dir, Khyber Pakhtunkhwa, Pakistan

²Department of Pharmacy, University of Malakand, Lower Dir, Khyber Pakhtunkhwa, Pakistan

³Department of Zoology, University of Peshawar, Khyber Pakhtunkhwa, Pakistan

⁴Department of Forestry and Wildlife Management, The University of Haripur, Khyber Pakhtunkhwa, Pakistan

Abstract: Hymenolepiasis is a helminthic and occasionally fatal disease of human imposing heavy economic losses to human society. Present study was aimed to diagnose the school children for the prevalence and control of Hymenolepiasis. A school based cross-sectional analysis of stool samples collected from 188 children aged 06-15 years was carried out (February to June 2016). Two stool samples were collected from each student before diagnosing and after treatment. The samples were fixed in 10% formalin and observed under the light microscope using the methods of direct smear in Lugol's solution, normal saline and flotation techniques. On the basis of drugs accessibility all the *H. nana* infected children were divided in to 2- groups. Children in group A were treated with albendazole (bendazol) 400mg once orally, group B was treated with albendazole (zental) 200mg orally. Eggs per gram of faeces were counted in each group before and after treatment. Of the 188 children, current study reveals only 6.08% (n=18/296) infection with *H.nana* and 10.5% (n=16/151) were diagnosed with co infections. The % efficacy of albendazole (Zental) and albendazole (bendazol) against *Hymenolepis nana* infection was reported as 83% and 75% respectively. Present study was concluded that albendazole (zental) is the drug of choice for the treatment of hymenolepiasis in children

Keywords: Hymenolepiasis, School children, Zental, EPG, Albendazole.

INTRODUCTION

Hymenolepis nana (the dwarf tapeworm) has cosmopolitan in distribution commonly infects the people in Africa, Eastern, Southern Europe and Asia (Huda-Thaheer, 2012). It has been estimated that *H. Nana* infect 75 million people in the world (Crompton, 1999). It is one of the small intestinal cestodes infecting man. It is small and thread-like, measuring 1 to 4cm in length and 1mm in width. This tapeworm may be present in large numbers (from 1,000 to a maximum of 8,000). Life span of the adult worm is about 2 weeks. It complete its life cycle in one host can easily transmitted from one individual to another (autoinfection) and easily renewed by new generation (Mirdha and Samantary, 2002).

Hymenolepiasis is normally an asymptomatic infection when the intensity of infection is low but in case of load of parasites it can cause dizziness, Headache, abdominal pain and diarrhea (Huda-Thaheer, 2012). According to Muhammad and Hegazi, 2007 *H. nana* infection is a source to cause deficiency of vitamin B12 in the intestine. *H. nana* has a worldwide distribution studied by different workers in different parts of the world including Pakistan.

There has been a growing awareness in the chemotherapy of cestode parasites in man over the last several decades. A number of synthetic drugs have been manufactured in succession and used for the treatment of cestode infection.

It is well known that Niclosamide is effective against *Hymenolepis nana* infection in man (Salem and El-Allaf, 1969). Albendazole and praziquantel have been shown to eliminate completely *H. diminuta* infection in rats at 800 and 250mg/kg/day for 3 consecutive days and against adult *H.nana* in mice (Schenone, 1980). However, studies on efficacy of albendazole (zental) and albendazole (bendazol) against *H. nana* in children have not yet been fully investigated in Pakistan. Present study was aimed to recognize that (1) albendazole (zental) was showing significant rate of efficacy over albendazole (bendazol) used and (2) Risk factors which play a role in disease transmission need to be taken during formulating sustainable control strategies for Hymenolepiasis and other intestinal parasites in Pakistan and other parts of the world.

MATERIALS AND METHODS

Study area and climatic conditions

District Lower Dir is located in Northwest of Pakistan (34° 22' and 35° 50' North and 71° 02' and 72° 30' East) characterized by hot summer and cold winter. The annual average maximum and minimum temperatures are about 29°C and 12°C respectively. The annual rainfall varies between 600 mm to 1100 mm. Snowfall is rarely occurs on the tops of some mountains, which is once followed by fast melting. Frost starts by the mid of the November. The overall weather is extreme. Agriculture is the main stay of life followed by livestock rearing. Current trial was made in school children of University of Malakand, Lower Dir,

*Corresponding author: e-mail: walikhan.pk@gmail.com

KPK, Pakistan (February to June 2016). Participants in the study were non-symptomatic, usually attending their classes on routine basis.

Data collection and processing

Single fecal sample was collected from each of the student prior the diagnosing and 3 days after treatment with prescribed drug. The samples collected were fixed in 10% formalin, and transported to the Laboratory of Parasitology, Department of Zoology, University of Malakand, KPK, Pakistan, where they were studied under the light microscope using the methods of direct smear in Lugol's solution, normal saline solution, and flotation techniques. Each of the samples collected from every student was tested by means of all three methods. Thus, 552 parasitological tests were performed in total.

Experimental design and ethical approval

Range of EPG before and after treatment with albendazole (zental) and albendazole (bendazol) was noted. A standard EPG diagnostic approach determining the extent of infection by the eggs was employed to determine the efficacies of the therapeutic agents used. On the basis of the drug used the subjects infected with *H.nana* were divided in to 02 groups (A, and B). A consent letter was issued to the parents /guardians of the students. The approval was obtained from the ethical review committee of the University of Malakand. The students in Group A were treated with albendazole (bendazol) systematic: IUPAC) Glaxo Smith Kline Pakistan, 200- 400 mg orally as a single dose once a time. Students in group B were treated with albendazole (zental), 20mg. reg. no. Q/12/75, Gloxosmithklin South Africa (Pty) limited. Fecal samples collected were analyzed in Laboratory of Parasitology, Department of Zoology, University of Malakand. EPG count was performed by using McMaster Techniques described by (Jarvie *et al.*, 2005). The % efficacies of the drugs used were measured by stool eggs per gram counts reduction (SECR) test calculated from the arithmetic mean of the group EPGs as per the formula given below (Trustfield, 2005).

Efficacy of drug treatment (%) = $\frac{\text{Mean pre-treatment EPG} - \text{Mean-Post treatment EPG}}{\text{Mean pre-treatment EPG}} \times 100$

Study chart and Techniques

At the start of the study, the section heads of the schools were requested for consent to carry out the experiment at their school. The guardians of the children were issued an informed letter, so that they could be aware by the risks and benefits of the study. The respondents were given a mini-plastic bottle together with a consent form; both labeled with tag numbers (ID) for identification. Each of the bottle and consent form were labeled with name, age, sex, and class of the chilled on the school. Each of the

participants were called to return the container containing 10 grams of fresh stool sample approximately at the next morning together with the signed consent form. Each of the student who returned a signed informed consent and had stool sample were assigned to one of the four treatment groups. Before drug administration, all children were informed to consult with a physician via their parents/guardians. Evidence of any abnormal medical condition, observed by the physician; history of acute or severe chronic disease (tumor, diabetes, chronic heart, liver, or renal disease); and recent use of anthelmintic drugs (within past one month) were omitted. Height and weight of all children were measured. Three days after treatment with prescribed drugs another unfilled container was given out to each of the studied student for the next collection of a single stool sample. The stool samples were collected and diagnosed for the EPG and thus the difference prior to treatment and after treatment was noted.

STATISTICAL ANALYSIS

The data were analyzed for the difference within treatment group by chi square test, using the Graph Pad Prism 5. P value of less than 0.005 were taken as statistically significant.

RESULTS

The EPG values in stool samples in both the treatment groups are given in table 1. For groups A and B the two tailed P value is non-significant (P value 0.16669 with 95% CI). The number of eggs per gram after treatment was decreased progressively in both the groups treated. A vs B was not significant. Moreover clinically no adverse effect except for albendazole used were observed. The percent efficacies of different drugs against Hymelanopiasis are shown in table 1. The efficacies 82.95% and 76.94% for albendazole (zental) and albendazole (bendazol) were reported respectively.

Adherence

Of the total 288 children invited to participate in the trial, 100 refused to participate or did not return a signed consent form, 02 children lost their IDs on the stool samples, two children received anthelmintic treatment before the launching of the trial, all these children were therefore excluded from the trial. The remaining 184 children were assigned to one of the two drugs, of these 166 were *H. nana* negative and therefore excluded from the final round of examination. (fig. 1). Four children lost the first treatment, and 5 children were absent on the second day of treatment. At follow-up, 145 children did not provide stool sample after treatment and were excluded. In total 166 *H. nana* infected children were lost during treatment and follow-up. Hence, 18 children were included in the per-protocol analysis. The group that

Table 1: Eggs per gram (EPG) counts of 184 school children in University of Malakand, Lower Dir Pakistan. (UPS=University Public School).

Groups	EPG Before treatment	EPG After treatment	Drugs	P-value (95%CI)
Group A	162.49±124.95	40.27±25.08	Albendazole (bendazol)	0.16669
Group B	358.32±444.07	61.07±61.18	Albendazole (zental)	

Table 2: Egg negative rates (%) among subjects positive for *H. Nana*, in the infected (n = 184) from UPS with drugs used.

Drugs	<i>Hymenolepis nana</i> (EPG)		
	Number tested positive	Number becoming negative	Egg negative rate (%)
Albendazole (zental)	358	297	83
Albendazole (bendazol)	163	122	75

could be treated with albendazole was missed the 90 participants.

Baseline characteristics

Hymenolepis nana was reported only 6.08% (n=18/296) in single or combined association with other helminths. *H. nana* was diagnosed in single as 1.3% (n=2/151). *H. nana* + *T. saginata* in 1.98% (n=3/151), *H. nana* + *A. duodenale* 0.66% (n=1/151) as double; *H. nana* + *T. saginata* + *A. duodenale* 2.64% (n=4/151), *H. nana* + *T. saginata* + *E. histolytica* 0.66% (n=1/151), *H. nana* + *T. saginata* + *A. duodenale* 1.32% (n=2/151), *H. nana* + *A. duodenale* + *A. lumbricoides* 1.32% (n=2/151) as triple and *H. nana* + *A. duodenale*, *F. hepatica* + *A. lumbricoides* 1.98% (n=3/151), as quadruple infection. The mean age of the children was 14 years (range 10–16 years). Female students were not participating in the study due to religious and cultural restriction.

Efficacy of drugs prescribed

Efficacy of the drugs prescribed was noted via the counting of eggs in per gram of the stool after treatment. Percent high egg negative rate (%ENR) was observed for the sequentially administered albendazole (zental) followed by abendazole (bendazole). Albendazole (bendazol) achieved an ENR 75%, whereas single doses of albendazole (zental) resulted 83% of ENR (table 2). Comparing the treatment outcomes using the chi square test revealed that albendazole (zental) had a high but not significant effect on infections with *H.nana*, No adverse effect was observed during the medication.

DISCUSSION

Intestinal parasitic infection is one the major health problem, closely related to poverty, living condition, insufficient health care, overcrowding, individual and community hygiene, poor sanitation, insufficient supply of clean water (Chaudhry et al., 2004). The hygienic conditions in Pakistan are interesting and no importance is yet given to the disposal of animal and human excreta, so because of which there is a cumulative increase in parasitic infections. The villagers are usually having lack sense of sanitation and hygiene because of poverty.

Hymenolepiasis is principally an infection of young children which is normally treated with anticestode drugs such as praziquantel and albendazole derivatives, therefore a continued follow up is necessary. *Hymenolepis* sp. eggs rather than its proglottids are usually detected in stools and disappear more rapidly after treatment. The results of the current experiments indicate that children are susceptible to infection with *H.nana* and that the cestode may produce intestinal obstruction. It appears that at level of infection 162 to 358 eggs/g before treatment and 40 to 61 eggs/g of faecal sample after treatment of groups (table 1 group A and B). This low level of infection are not usually associated with any important signs of morbidity or death. The present experiments have shown that the faecal egg counts are considerable and special attention should be focused on the evaluation of anticestodal drugs.

Current trial was pinpoint to understand the resistance of *H. nana* against the drugs prescribed in school children of Public School, University of Malakand, KPK, Pakistan. We carried out a randomized, single-dose trial administered orally as albendazole (bendazol), 400mg and albendazole (zental) 20mg once. Shared chemotherapy is being encouraged as it enhances efficacy and lowers the risk of resistance development. In a study conducted by Horton in which albendazole was administered orally and showed 68% cure rate against Hymelanopiasis, while in present trial this rate was 75% against this infection. Present trial demonstrate the highest evidence of *H.nana* with *A. lumbricoides* and *Taenia saginata* in 2.64% prevalence. Recent studies have been carried out on intestinal parasitosis in Pakistan as Wahidullah et al., 2014; Khan et al., 2014., Shah et al., 2006; Khan et al., 2015; Noor-un-Nisa et al., 2011; Mumtaz et al., 2009; Mehraj et al., 2008; Khan et al., 2016 while very few have studied the effectiveness of drugs used in treating intestinal parasitosis. The present study was conducted in order to evaluate the resistance of *H. nana* against albendazole (zental) and albendazole (bendazol) in school children of Public School, University of Malakand. Present trial likes that of (Theodorides et al., 1976) and (Georgi et al., 1980) has shown that albendazole (zental)

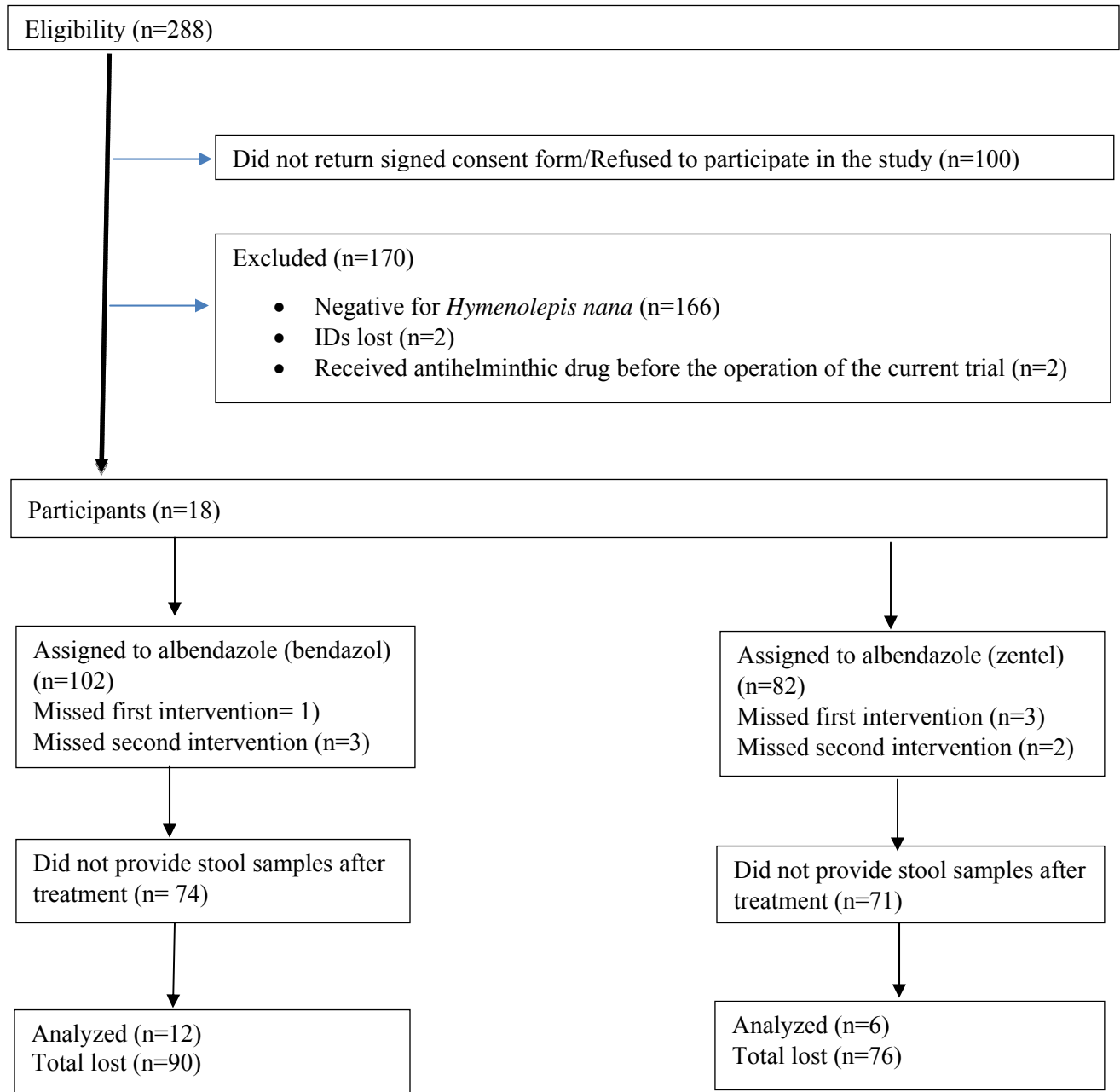


Fig. 1: Flow chart illustrating the randomized control trial assessing the efficacy of albendazole (zental) and albendazole (bendazol) administered separately on two consecutive days, in the treatment of *Hymenolepis nana* infection.

is a broad spectrum anthelmintic drug than albendazole (bendazol). The conditions in which multiple doses cause problems of patient compliance, the introduction of a single dose effective broad spectrum anthelmintic should be welcomed. The side effects were also very minor and for short time. Prevalence of *H. nana* varied geographically, it is lowest at high altitude than the lowers.

CONCLUSIONS

Based on the investigation of present experiment trial to control Hymenolepiasis should continue time by time, changes in the intensity of infection attributable to a decrease in prevalence, taken into account by comparing the drugs: Albendazole (zental) show higher efficacy than albendazole (bendazole). Present study provide effective

control of Hymenolepiasis even in the absence of other preventive measures.

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