

## Efficacy of Metronidazole, Mebendazole and Albendazole Against Giardiasis and its Effects on Body Weight & Feed Intake in Cattle

<sup>1</sup>Sultan Ayaz, <sup>1</sup>Muhib Ullah, <sup>2</sup>Farman Ullah Khan, <sup>2</sup>Iqbal Hussain,  
<sup>2</sup>Riaz Ullah Ihsan Ullah Khan and <sup>2</sup>Zia Muhammad

<sup>1</sup>Department of Zoology, Kohat University of Science and Technology Kohat-26000,  
Khyber Pukhtun Khwa Pakistan

<sup>2</sup>Department of Chemistry, Kohat University of Science and Technology Kohat-26000,  
Khyber Pukhtun Khwa Pakistan

**Abstract:** Efficacy of metronidazole, mebendazole and albendazole in reduction of the Giardia cyst from infected cattle were evaluated in field farm trials. Metronidazole with three different dose level of 150mg, 100mg and 50mg /kg body weight was orally administered and the efficacy were 94.02%, 87.8% and 85.4% in reduction of cysts shedding on 27 day of post medication respectively. Mebendazole with three different dose levels of 15mg, 10mg and 7.5mg /kg body weight was given and its efficacy was 90.4%, 87.3% and 81.15% on 27 day of post medication. Similarly albendazole at a three different dose level of 20mg, 15mg and 10mg/kg was orally given and its efficacy were 98.5%, 100% and 86.3% on 27day of post treatment was observed. During statistical analysis  $P < 0.05$  was noted. Statistically insignificant difference in increase in body weight was noted and significant increase in feed intake was evaluated.

**Key words:** Metronidazole • Mebendazole • Albendazole • Feed intake • Bodyweight • Giardiasis and cattle

### INTRODUCTION

*Giardia lamblia*, is a protozoan parasite that inhabits the small intestine that causes extensive morbidity worldwide. *Giardia* was seen under the microscope and described by Antony Van Leeuwenhock during 1681 [1]. It was rediscovered by Vilim Lambli in 1859.

*G. duodenalis* is capable of infecting a wide variety of mammalian hosts as well as birds, reptiles and amphibians [2, 3]. Aquatic animals have been described in contamination of water sources with *Giardia* cysts [4-6]. The infection rate of calves varied from 1% to 100% and were associated with diarrhoea and ill health [7-9].

Chemotherapy is most effective in eliminating the *Giardia* infection in livestock, pre-infections usually occurs because the sources of environmental contamination are not eliminated and the frequency of transmission is high in that particular area. This could be applied to both human and animal infection in any given area [10, 2, 11]. Nitroimidazole has been widely used in human being as well as in livestock particularly in

calves against giardiasis [7, 12, 8, 13, 9]. It was suggested by the researcher that the albendazole and mebendazole have the clinical efficacy against human giardiasis [14, 15] and mebendazole was considered as carcinogenic and its application was disputed [15, 16, 17]. Albendazole, Mebendazole and Fenbendazole were more effective against *Giardia* trophozoites than Nitroimidazole in vitro investigation [18]. There have been several studies available in mice and dogs in eliminating the *Giardia* infection through albendazole and Fenbendazole, to evaluate its efficacy in vivo [19]. The present study was design to evaluate the efficacy of albendazole, mebendazole and Nitroimidazole in eliminating the *Giardia* cysts by infected young cattle.

### MATERIALS AND METHODS

One hundred & fifty cattle age ranged from of 2-3 years were used in the experiments. The management and hygiene measures were maintained at the farms. The animals were randomly divided into five groups

i.e. A, B, C, D and E, having 30 animals in each group. Animals in group A were further sub-divided into three sub-groups i.e. A1, A2 and A3, with ten animals in each sub-group. Animals in group A1, A2 and A3 were given Albendazole at 20, 15 and 10mg/kg body weight respectively by oral route. All animals were treated daily for five days. Animals in group B were sub-divided into three groups i.e. B1, B2 and B3, each having 10 animals and were respectively given metronidazole (flagyl) at 150, 100 and 50mg/kg, body weight orally. Similarly, all animals were treated daily for five days.

Animals (30) in group C were sub-divided into three groups i.e. C1, C2 and C3. Animals in group C1, C2 and C3 were respectively given mebendazole at 20, 10 and 7mg/kg, body weight orally for five days. The *Giardia* infection was given orally to four groups of animals i.e. A, B, C and D at 200 cyst/gm of faeces, which was isolated during epidemiological study. After 10 days, the cyst/gm of feces of each group of animals was recorded. The three drugs at different dose level were administered orally for five consecutive days and the counting of cyst / gram of faeces was recorded for evaluating the efficacy of the drugs.

Animals (30) in group D were kept as positive control having the same animals as the other groups and *Giardia* infection was given at same rate i.e. 200 cyst/gram of faeces and after 10 days cyst counting was started up to the end of the experiments. The counting was made on zero, 6th, 13th, 20th and 27th day post treatment. Animals (30) in-group E were served as negative control.

**Counting of Cyst:** The faecal samples were collected directly from the rectum of animal and were kept in labeled plastic bags, which were placed in ice cold container and transported to postgraduate laboratory of Parasitology department, university of veterinary and animal sciences, Lahore. The cysts were isolated & stained with iron Haematoxylin and examined under the microscope at 10x, 40x and 100x. The cysts were counted by using the formula as adopted by Handley, et al. [20].

**Efficacy of the Drugs:** The efficacy of the different dose levels of the drugs i.e. albendazole, metronidazole and mebendazole was assessed on the basis of shedding of cyst in faeces after treatment. The cysts were counted on days zero, 06, 13, 20 and 27 day post treatment.

The cysts were isolated by floatation & sedimentation techniques from faeces and smears were prepared from each animal and stained with iron Haematoxylin. The cysts were counted under the microscope at 10x, 40x and 100x as the method was described by Handley, et al. [20]. Thus achieved the cysts/ gram of faeces. Efficacy of the drugs was calculated as per formula, described by [21].

$$\text{Efficacy (\%)} = \frac{(\text{Total no. cysts before treatment} - \text{Total cysts after treatment})}{\text{Total no. Cysts before treatment.}} \times 100$$

**Effect on Weight and Feed Intake:** Effect of treatment on body weight and feed intake was also noted in animals from each group/sub group.

**Physiological & Clinical Examination:** The clinical examination was carried out in animals, which were selected for the chemotherapeutic trials before and after the *Giardia* infection. The weight of each animal was recorded on alternate days and Pulse rate, rectal temperature, heart rate, respiration rate palpation of lymph node and abdomen, were also recorded. The consistency of the faeces was also recorded throughout the experiment.

## RESULTS

The efficacy (%) of the different drugs was calculated on the basis of reduction in the cyst per gram of faeces after treatment. The mean % of the *Giardia* cyst number of each treated group was compared with each other and with control group.

**Efficacy of Albendazole (Group A):** Cyst per gram of faeces (CPG) of *Giardiasis* in cattle treated with Albendazole is shown in Table 1. CPG count showed an increasing trend in control (untreated) animals. A dose of 20mg/kg body weight of Albendazole caused a significant decrease in CPG count from 6 day post treatment onward ( $P < 0.05$ ). The efficacy of Albendazole was 77.2% at 13 day post treatment, 92% on 20 day post treatment and 98.5% at 27 day post treatment were noted during the experiment. Statistical analysis by using the Duncan test showed the significant difference ( $P < 0.05$ ) decrease in the CPG count after treatment, when the data was analyzed (Table 1 & 2).

Table 1: Cyst per gram of faeces in Cattle treated with different drugs on different days

				Cyst per gram of faces on different days				
Group	Drug	Subgroups (n=10)	Dose Mg/kg.body.wt	0	6	13	20	27
A	Albendazole	A1	20mg/kg.b.wt	878	600	200	62	12
		A2	15mg/kg.b.wt	875	362	100	25	0
		A3	10mg/kg.b.wt	825	560	362	200	112
B	Metronidazole	B1	150mg/kg.b.wt	837	487	262	125	50
		B2	100mg/kg.b.wt	825	525	375	225	100
		B3	50mg/kg.b.wt	857	612	362	225	125
C	Mebendazole	C1	15mg/kg.b.wt	912	712	410	187	87
		C2	10mg/kg.b.wt	887	700	412	202	112
		C3	7.5mg/kg.b.wt	862	715	515	312	162
D. Group (infected positive control)		878	1045	1170	1304	1429		
E. Group (negative non infected control).		0	0	0	0	0		

Statistical analysis: Univariate ANOVA, Duncan test. Significant ( $P < 0.05$ )

Table 2: Comparative efficacy (%) of different drugs against *Giardiasis* in cattle

Group	Drug	Subgroups (n=10)	Dose Mg/kg.b.wt	Efficacy %			
				06day	13day	20day	27day
A	Albendazole	A1	20mg/kg. b.wt	31.6	77.2	92	98.5
		A2	15mg/kg. b.wt	58.7	88.5	97.1	100
		A3	10mg/kg. b.wt	32.1	56	75	86.3
B	Metronidazole	B1	150mg/kg.b.wt	41.7	68.6	85.0	94.02
		B2	100mg/kg.b.wt	36.3	54.5	72.7	87.8
		B3	50mg/kg. b.wt	28.5	57.7	73.7	85.4
C	Mebendazole	C1	15mg/kg. b.wt	21.19	55	79.4	90.4
		C2	10mg/kg. b.wt	21.12	53	77.1	87.3
		C3	7.5mg/kg.b.wt	17.1	40.2	63.7	81.15

Mean %, Univariate ANOVA comparison within group by Tukey's test  $A=P<0.05$ ,  $B=P<0.05$  and  $C=P<0.05$

At 15mg/kg body weight of Albendazole caused a significant decrease in CPG count from 06 day post treatment onward ( $P<0.05$ ). The efficacy of Albendazole was 88.5% at 13 day post treatment, 97.1% on 20 day post treatment and 100% at 27 day post treatment were noted during the experiment. Duncan test showed the significant difference ( $P<0.05$ ) decrease in the CPG count after treatment, when the data was analyzed (Table 1 & 2).

At 10 mg/kg body weight of Albendazole caused a significant decrease in CPG count from 6 day post treatment onward ( $P<0.05$ ). The efficacy of Albendazole was 56% at 13 day post treatment, 75% on 20 day post treatment and 86.3% at 27 day post treatment. Duncan test showed the significant difference ( $P<0.05$ ) decrease in the CPG count after treatment, when the data was analyzed (Table 1 & 2).

**Efficacy of Metronidazole (Group B):** A dose of 50 mg/kg body weight of Metronidazole caused a significant decrease in CPG count from 6 day post treatment onward ( $P<0.05$ ). The drugs caused 57.7% reduction in CPG count on 13 day post treatment ( $P<0.05$ ). The efficacy

of Metronidazole was 73.7% at 20 day post treatment and 85.4% on 27 day post treatment respectively. Univariate ANOVA and Duncan test showed the significant ( $P<0.05$ ) decrease in the CPG count after treatment in all days (Table 1 & 2).

At 100mg/kg body weight of Metronidazole caused a significant decrease in CPG count from 06 day post treatment onward ( $P<0.05$ ). The drugs caused 54.5% reduction in CPG count on 13 day post treatment ( $P<0.05$ ). The efficacy of Metronidazole was 72.7% at 20 day post treatment and 87.8% on 27 day post treatment were noted respectively (Table 2).

At 150mg/kg.body weight of Metronidazole caused a significant decrease in CPG count from 6 day post treatment onward ( $P<0.05$ ). The drugs caused 68.6% reduction in CPG count on 13 day post treatment ( $P<0.05$ ). The efficacy of Metronidazole 85.0% at 20 day post treatment and 94.02% on 27 day post treatment were noted respectively. When the data was analyzed using the Duncan test, the significant difference ( $P<0.05$ ) in decrease in the CPG count after treatment in all days was observed (Table 2).

Table 3: Comparison of Body Weight (Kg) and Feed Intake (Kg/day) Before and After Treatment of Cattle

Groups	Sub Groups	Body weight (Kg) n=5			Feed (Kg/day) n=5		
		Before Treatment	After Treatment	Increase/ Decrease (%)	Before Treatment	After Treatment	Increase/ Decrease (%)
A	A1	188.32±15	224.98±19	19.14 ↑	3.75±0.31	4.75±0.14	26.66 ↑
	A2	191.93±19	205.24±21	6.93 ↑	3.83±0.38	4.92±0.50	28.45 ↑
	A3	189.11±14	196.73±15	4.02 ↑	3.78±0.29	4.32±0.33	14.28 ↑
B	B1	186.03±10	207.78±15	11.60 ↑	3.71±0.21	4.35±0.31	17.25 ↑
	B2	186.74±15	205.61±7	10.10 ↑	3.73±0.31	4.51±0.16	20.91 ↑
	B3	203.22±10	211.16±11	3.90 ↑	3.65±0.19	4.21±0.22	15.34 ↑
C	C1	184.19±12	190.52±13	3.43 ↑	2.94±0.19	3.42±0.24	38.09 ↑
	C2	188.81±22	195.41±23	3.49 ↑	3.01±0.35	3.7±0.45	22.92 ↑
	C3	204.18±8	212.17±8	3.91 ↑	3.24±0.14	3.81±0.15	17.59 ↑
D		186.89±12	155.18±12	16.96 ↓	3.73±0.25	2.84±0.21	23.86 ↓
E		183.07±25	213.46±13	1.82	3.65±0.50	4.44±0.29	0.024

Mean ± Standard Error. (X ± S.E); Student's *t* test  $p < 0.05$  Sig \*,  $p > 0.05$  NS†

**Efficacy of Mebendazole (Group C):** CPG count showed an increasing trend in untreated control animals. A dose of 15mg/kg body weight of Mebendazole caused a significant decrease in CPG count from 6 day post treatment onward ( $P < 0.05$ ). The drugs caused 55% reduction in CPG count on 13 day post treatment ( $P < 0.05$ ). The efficacy of Mebendazole was 79.4% at 20 day post treatment and 90.4% on 27 day post treatment were noted respectively. When the data was analyzed, the significant difference ( $P < 0.05$ ) in decrease in the CPG count after treatment in all days was observed (Table 2).

At 10mg/kg body weight of Mebendazole caused a significant decrease in CPG count from 6 day post treatment onward ( $P < 0.05$ ). The drugs caused 53% reduction in CPG count on 13 day post treatment ( $P < 0.05$ ). The efficacy of Mebendazole 77.1% at 20 day post treatment and 87.3% on 27 day post treatment were noted respectively.

At 7.5mg/kg body weight of Mebendazole caused a significant decrease in CPG count from 6 day post treatment onward ( $P < 0.05$ ). The drugs caused 40.2% reduction in CPG count on 13 day post treatment ( $P < 0.05$ ). The efficacy of Mebendazole was 63.7% at 20 day post treatment and 81.15% on 27 day post treatment were noted respectively. When the data was analyzed by using the Duncan test, the significant difference ( $P < 0.05$ ) in decrease in the CPG count after treatment in all days was observed (Table 2).

From the Table 11, 12 and Fig. 8.1 showed that all three drugs *i.e.* Albendazole, Metronidazole and mebendazole were effective against *Giardiasis* in regarding the reducing the CPG count at different dose level. Of these, the efficacy of Albendazole at dose of 15mg/kg body weight was better in reducing the CPG count.

**Effect on Body Weight and Feed Intake:** In all the groups, increase in body weight was noted except group D (infected control). Statistically insignificant difference was noted by using student *t* test and significant increase in the feed intake was noted (Table 3).

## DISCUSSION

In the present study, three different anti-giardial drugs, an albendazole (Valbazen –Pfizer), metronidazole (Flagyl) and mebendazole (Zentel) at three different dose levels, were evaluated. Albendazole at 10mg/kg.b.wt in cattle gave 86.36% reduction in cpg on 27th day respectively. At 15mg/kg.b.wt. and 20mg/kg.b.wt. efficacy was 98.5% and 100% respectively. This was significant ( $P < 0.05$ ) by a Duncan test when compared with the untreated control group. Similar findings of albendazole at 20mg/kg.b.wt in calves with efficacy 98.5, 97.6 and 90 percent were noted on 1, 2 and 6 weeks by [22]. Albendazole can attached the cytoskeletal structure of ventral disk of *Giardia* and disrupt the glucose intake and causes parasite death [23, 22]. Metronidazole (Flagyl) group B at dose rate of 50mg/kg.b.wt reduced the cyst per gram of faeces 85.88% on 27th day post treatment. At the dosage level of 100mg/kg and 150mg/kg, body weight the efficacy was 87.88% and 94.02% on 27th day respectively. A significant difference ( $P < 0.05$ ) was noted with Duncan test when compared with the controls. Similar findings were reported by [24, 23]. The efficacy of mebendazole at the dose of 7mg/kg.b.wt was 81.15% on the 27<sup>th</sup> day post treatment. Similarly at the dose rates of 10mg and 20mg/kg body weight were 87.3% and 90.4% on 27th day respectively. Duncan test showed that statistically significant different was noted when compared with infected untreated control group.

Similar results were also reported by [25]. All the three drugs used in the present study i.e. albendazole, metronidazole and mebendazole were appeared to be effective in suppressing and eliminating the cyst of *Giardia* from infected cattle.

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