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Research Article

COMPARATIVE THERAPEUTIC AND PERSISTENT EFFICACIES OF DORAMECTIN AND RAFOXANIDE AGAINST FENBENDAZOLE/MORANTEL RESISTANT HAEMONCHUS CONTORTUS IN SHEEP AND GOATS

MEENA DAS[1] and SATYAVIR SINGH[2]
Department of Veterinary Parasitology, College of Veterinary Sciences
CCS Haryana Agricultural University, Hisar-125 004

ABSTRACT

Therapeutic and persistent efficacies of rafoxanide and doramectin against fenbendazole/morantel resistant *Haemonchus contortus* in naturally infected sheep and goats were studied on three sheep and three goat farms by faecal egg count reduction (FECR) test. Doramectin (0.2 mg/kg s/c) was > 95% effective on all farms whereas rafoxanide (10 mg/kg b.wt., orally) was > 95% effective on four farms but only 78.13% and 36.64% effective on two farms, respectively indicating moderate to severe resistance. The effect (>95%) of rafoxanide and doramectin persisted up to 56 days and 70 days, respectively on four farms and while on two farms the effect (>95%) of doramectin persisted up to 28 days and 14 days, respectively while rafoxanide was not effective. Thus present study showed that prolonged persistent effect of doramectin and rafoxanide can be used successfully for the control of fenbendazole/morantel resistant *H. contortus* in sheep and goats.

Key words: Doramectin, fenbendazole, goat, *Haemonchus contortus*, morantel, rafoxanide, sheep

Parasitic gastroenteritis caused by nematodes is an important manifestation in sheep and goats and *Haemonchus contortus* is the species responsible for high mortality and morbidity in India (Yadav, 1997). Traditionally, conventional anthelmintics have been used for their control. The wide spread use, suppressive dosing and misuse have led to the development of anthelmintic resistance (Waller, 1986) against gastrointestinal nematodes (Singh and Yadav, 1997, Coles, 1997) posing serious limitation on the use of anthelmintics. Therefore, there is a need for introduction of alternative anthelmintics with different mode of action and prolonged effects (Kerboeuf *et al.*, 1995, Vereruysse *et al.*, 1996). However, it is essential to test efficacies of anthelmintics for their use in field. The present communication describes the comparative therapeutic and persistent efficacies of doramectin and rafoxanide against fenbendazole/morantel resistant *Haemonchus contortus* in sheep and goats.

MATERIALS AND METHODS

Survey of fenbendazole/morantel resistance: A survey was conducted on three sheep and three goat farms including two organized and one unorganized in each situated in and around Hisar to assess the prevalence of fenbendazole/morantel resistant gastrointestinal nematodes by faecal egg count reduction (FECR) test (Table 1). The animals of organized farms were set stocked and had been receiving regular anthelmintic treatment. On university sheep and goat breeding farms, animals were being grazed on permanent pastures and received four anthelmintic treatments per year with closantel/rafoxanide/doramectin while on government sheep and goat breeding farms animals were being grazed on free range and received 3-4 anthelmintic treatments per year mainly with benzimidazoles (fenbendazole/albendazole), during the previous 10 years. No regular deworming schedule was followed for animals of unorganized farms. Thirty animals with faecal egg counts of at least 150 eggs per gram (EPG) were identified from each farm, individually numbered, weighed and allotted to three groups of ten animals each. Two of the three groups were administered orally with fenbendazole and morantel, respectively and third group served as untreated control. Rectal faecal samples were collected from each animal to estimate the faecal egg counts by the modified

[1]Division of Parasitology, ICAR Research Complex for NEH Region, Umiam, Meghalaya
[2]Corresponding author

Table 1

Percentage reduction in faecal egg counts in sheep and goats treated with fenbendazole and morantel

Name of the farm	Fenbendazole (5 mg/kg orally)			Morantel (10 mg/kg orally)		
	Faecal egg count reduction %	95% confidence interval		Faecal egg count reduction %	95% confidence interval	
		Lower	Upper		Lower	Upper
Government Sheep Breeding Farm	69.03	28	87	96.46	90	99
University Sheep Breeding Farm	92.14	81	97	51.89	67	86
Unorganized sheep farm	65.98	44	79	98.36	96	99
Government Goat Breeding Farm	71.66	39	87	96.36	87	98
University Goat Breeding Farm	86.93	57	96	98.48	94	99
Unorganized goat farm	59.81	37	75	96.39	93	98

McMaster technique before the start of treatment and 10 days post treatment. Pooled faecal cultures were made from each group before and 10 days post treatment to ascertain the larval composition by Bearmann technique (Anonymous, 1977), cleaned by repeated centrifugation and decantation and identified as per technique of Keith (1953). The percentage reduction in faecal egg counts were calculated by the method of Coles *et al.* (1992).

Therapeutic and persistent efficacy of doramectin and rafoxanide: Thirty animals each, with faecal egg counts of at least 150 eggs per gram, were identified from all six farms where fenbendazole/morantel resistance had been detected during the survey. They were individually numbered and allotted to three groups having ten animals in each. Animals of group 1 were treated with doramectin @ 0.2 mg/kg subcutaneously and group 2 with rafoxanide orally @10 mg/kg b.wt. (Table 2, 3) keeping group 3 as untreated control. Rectal faecal samples were collected from each animal to estimate the faecal egg counts and faecal culture on day 0, 14. 28, 42. 56,70 and 84 post-treatment. The per cent reduction in faecal egg counts were determined (Coles *et al.*, 1992). The data obtained was analyzed by using Student's 't' test (Snedecor and Cochran, 1968)

RESULTS AND DISCUSSION

The percent reduction in faecal egg count (FECR%) of naturally infected sheep and goats with gastrointestinal nematodes at three sheep and three goat farms indicated moderate to severe fenbendazole resistance (Table 1). On government sheep and goat

Table 2

Persistent effect of anthelmintics on faecal egg counts of sheep naturally infected with resistant *Haemonchus contortus*

Name of the farm	Treatment group	Average faecal egg count on days post-treatment						
		0	14	28	42	56	70	84
Government Sheep Breeding Farm	Doramectin	725±391	0±0 (100)*	0±0 (100)	10±6 (98.66)	0±0 (100)	5±5 (99.51)	65±7 (94.35)
	Rafoxanide	610±191	0±0 (100)	5±5 (99.2)	20±8 (97.32)	25±11 (96.93)	75±11 (92.65)	135±18 (85.26)
	Control	700±271	685±129	625±179	745±114	815±101	1020±88	1150±111
University Sheep Breeding Farm	Doramectin	1640±508	70±26 (95.63)	60±16 (95.71)	85±21 (94.14)	125±23 (91.78)	165±31 (89.97)	250±28 (84.85)
	Rafoxanide	1665±550	350±45 (78.13)	345±46 (75.36)	550±46 (62.07)	605±62 (60.20)	675±55 (58.97)	700±71 (57.58)
	Control	1585±597	1600±585	1400±310	1450±357	1520±235	1645±207	1650±181
Unorganized sheep farm	Doramectin	1100±284	0±0 (100)	0±0 (100)	5±5 (99.59)	0±0 (100)	25±8 (98.04)	115±13 (92.18)
	Rafoxanide	1060±298	0±0 (100)	20±8 (98.47)	50±10 (95.88)	30±8 (98.09)	75±7 (94.11)	145±24 (90.14)
	Control	1110±284	1210±135	1310±177	1215±120	1570±175	1275±125	1470±230

*Figures in parenthesis show per cent efficacy

Table 3

Persistent effect of anthelmintics on faecal egg counts of goats naturally infected with resistant *Haemonchus contortus*

Name of the farm	Treatment group	Average faecal egg count on days post-treatment						
		0	14	28	42	56	70	84
Government Goat Breeding Farm	Doramectin	1315±505	0±0 (100)*	0±0 (100)	0±0 (100)	5±5 (99.64)	25±11 (98.28)	110±10 (91.85)
	Rafoxanide	1215±394	0±0 (100)	15±7 (98.81)	25±11 (98.11)	45±11 (96.76)	75±8 (94.85)	185±18 (86.30)
	Control	1240±390	1250±398	1260±415	1375±181	1390±172	1455±144	1350±120
University Goat Breeding Farm	Doramectin	1665±439	75±27 (95.50)	150±19 (90.91)	155±29 (90.12)	175±40 (89.03)	265±35 (85.75)	350±40 (81.77)
	Rafoxanide	1650±557	1055±491 (36.64)	1085±496 (34.24)	1225±487 (29.80)	1230±481 (22.88)	1460±471 (21.51)	1565±245 (18.49)
	Control	1670±438	1665±633	1650±442	1745±403	1595±298	1860±184	1920±190
Unorganized goat farm	Doramectin	1145±290	0±0 (100)	0±0 (100)	0±0 (100)	5±5 (99.61)	10±6 (99.28)	115±13 (92.18)
	Rafoxanide	1175±294	0±0 (100)	5±5 (99.58)	40±10 (97.09)	25±8 (98.06)	80±13 (94.24)	145±24 (90.14)
	Control	1185±295	1260±193	1195±150	1375±220	1290±156	1390±215	1470±230

*Figures in parenthesis show per cent efficacy

breeding farms, where benzimidazoles (fenbendazole and albendazole) had been used once in three to four months and the animals had been grazed for years on free range area had only fenbendazole resistance. However, lower confidence limit < 90% in goats of government goat breeding farm also indicated resistance against morantel. On university goat and sheep breeding farms, where closantel and rafoxanide had been used on an average once in three months for 6 years and later on discontinued and replaced by doramectin and the animals on these farms had been grazed on the same pasture after treatment for several years showed cross-resistance to fenbendazole and rafoxanide and multiple resistance to fenbendazole, morantel and rafoxanide, respectively. On unorganized sheep and goat farms, only fenbendazole resistance was detected. The level and type of anthelmintic resistance in the parasites on different farms in the present study appeared to be associated with the type and frequency of anthelmintic used and with the management practices on the farms (Singh and Yadav, 1997, Das and Singh, 2005). The predominant larva recovered from faecal culture before start of treatment was *H. contortus* and few larvae of *Trichostrongylus* sp., *Oesophagostomum* sp., *Strongyloides papillosus* and *Bunostomum* sp. were also recovered. The larvae which survived after treatment comprised *H. contortus* only.

The persistent efficacy of doramectin and rafoxanide in sheep and goats infected with fenbendazole/ morantel resistant gastrointestinal nematodes are shown in Table 2 and 3, respectively. The comparison among the groups revealed that FEC in doramectin treated group was lower than those treated with rafoxanide throughout the observation period on all farms. The FECR test showed that the effect (>95%) of rafoxanide and doramectin persisted up to 56 days and 70 days, respectively on organized (Government) and unorganized sheep and goat farms. On university sheep breeding farm and university goat breeding farm the effect of doramectin persisted up to 28 days and 14 days, respectively but rafoxanide was not found to be effective indicating moderate to severe resistance. It appeared to be associated with frequent use of rafoxanide on these farms as evidenced by the history of anthelmintic use on these farms (Das and Singh, 2005). The treated sheep and goats of all six farms showed neither signs of haemonchosis nor mortality. In the untreated controls a few animals showed emaciation, anaemia with intermittent diarrhoea but without any mortality. The larvae obtained from faecal cultures of all the groups were identified to be of *H. contortus*. Earlier the persistent effect of salicylanilides was reported for 4-8 weeks (Dorchies *et al.*, 1988, Mage, 1990) and 8-10 weeks (Vassilev, 1995, Rana, *et al.*,

2001). The high efficacy of rafoxanide was attributed to the long half life of the drugs in plasma proteins (Maes *et al.*, 1988) and consequently prolonged activity against blood feeding parasites. Since *H. contortus* is a voracious blood feeding parasite (Georgi and Georgi, 1990) and is thereby exposed to high concentrations of plasma bound drug. Further, the prolonged activity of rafoxanide can be explained in terms of its plasma binding properties (Mohammed Ali and Bogan, 1987) and feeding requirement of *H. contortus*. Hertzberg *et al.* (2001) observed persistent effect of doramectin up to 8 weeks while Umur and Arslan (2000) evidenced up to 4-6 weeks. The persistent effect of doramectin observed for 70 days can be explained by its presence in the plasma as soon as one hour after administration and thereafter for atleast 60 days (Alvinerie *et al., 1998)*. The differences in observed persistent effect may be due to varying endemicity or susceptibility of various breeds (Singh *et al.*, 1997) or differences in grazing system (Singh and Yadav, 1997).

In addition to their high effectiveness against fenbendazole or morantel resistant strain of *H. contortus*, the persistent effect of drug could prevent the establishment of incoming larvae, thereby reducing the rate of reinfection and pasture contamination and increase interval between treatments (Dash, 1986). Prolonged effect of these drugs could also reduce the number of treatments during the year because of increase in intervals between treatments. Further, lesser the frequency of anthelmintic treatments, lesser will be chances in the parasites to get selected for resistance.

It can be concluded from the present studies that *H. contortus*, the most prevalent and pathogenic nematode resistant to fenbendazole/morantel can be effectively controlled by either doramectin or rafoxanide where resistance against these anthelmintics have not been detected. The longer persistent efficacy of these drugs could be useful in reducing the treatments to susceptible flocks and pasture contamination.

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