

## Efficacy of a Fenbendazole–Triclabendazole Combination against *Fasciola hepatica* and Gastrointestinal Nematodes in Sheep

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### ABSTRACT

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A fenbendazole and triclabendazole combination was tested against experimentally induced 6- and 14-week-old infections of *Fasciola hepatica* and naturally acquired infections of gastrointestinal nematodes in sheep. Forty-eight sheep were divided randomly into six treatment groups of eight animals each. At 7.5 and 10.0 mg kg<sup>-1</sup> body weight (BW) (3.75 and 5.0 mg kg<sup>-1</sup> BW of each drug), the drug combination was 98.3 and 99.7% effective against 6-week-old *F. hepatica* infections, and 100 and 99.9% effective against 14-week-old infections. At the same drug dosages, the drug combination was effective against naturally acquired adult *Ostertagia* spp. (97.3–100%) and adult *Nematodirus* spp. (90.3–99.9%). No adverse effects associated with treatment were noted.

### INTRODUCTION

Efficacy of triclabendazole has been reported to be > 95% against immature and mature *Fasciola hepatica* in sheep. Field trials using triclabendazole in naturally infected sheep resulted in a 99.3% efficacy at a single dose of 5 mg kg<sup>-1</sup> body weight (BW) (Boray et al., 1985) and 99.8% efficacy at a single dose of 10 mg kg<sup>-1</sup> BW (Güralp and Tinai, 1984). Clinical trials using triclabendazole at 5 mg kg<sup>-1</sup> BW in sheep experimentally infected with *F. hepatica* resulted in efficacies of 92% at 4 weeks post infection (p.i.), 99.7% at 6 weeks p.i., and 99.7–100% at 12 weeks p.i. (Boray et al., 1983; Turner et al., 1984). Similar trials of triclabendazole at 10 mg kg<sup>-1</sup> BW resulted in 100% efficacy at 4, 6 and 13 weeks p.i. (Boray et al., 1983; Wolff et al., 1983).

Fenbendazole at 7.5 or 10.0 mg kg<sup>-1</sup> BW is highly effective against gastrointestinal nematodes in sheep, including both mature and immature forms of

*Haemonchus*, *Trichostrongylus*, *Cooperia*, *Ostertagia*, *Nematodirus*, *Bunostomum*, *Dictyocaulus* and *Trichuris* (Kennedy and Todd, 1975; Todd et al., 1976; Yazwinski et al., 1983). However, fenbendazole is not effective against *F. hepatica* at these dosages.

A fenbendazole and triclabendazole combination at 7.5 and 10 mg kg<sup>-1</sup> BW (3.75 and 5.0 mg kg<sup>-1</sup> BW of each drug) was evaluated against experimentally induced 6- and 14-week-old infections of *F. hepatica*, and against naturally acquired nematode infections in domestic sheep.

## MATERIALS AND METHODS

A total of 48 lambs that each weighed 58–89 pounds were obtained from the Washington State University Sheep Center, Pullman, Washington. The sheep were Columbia and Suffolk breeds, and were ewes and wethers. Metacercariae of *Fasciola hepatica* were obtained from Baldwin Enterprises, Monmouth, Oregon. Viability of metacercariae was determined by their microscopic appearance, i.e. movement within the metacercariae. Each sheep was inoculated orally with 250 viable metacercariae in a gelatin capsule.

Six weeks after inoculation, sheep were divided randomly into six treatment groups of eight animals each. Each treatment group was maintained in a separate outdoor pen (20 × 45 m). Each pen had a dirt floor and contained a feeder, water trough and trace mineral salt in a separate feeder. All sheep were fed a standard pelleted ration which consisted of 69% alfalfa and 31% barley. Free-choice salt and water were available at all times.

The treatment groups were as follows: Group I — eight sheep were treated with 7.5 mg kg<sup>-1</sup> BW (3.75 mg kg<sup>-1</sup> BW of each drug) of fenbendazole–triclabendazole combination 6 weeks after inoculation and euthanatized 9 weeks after inoculation (3 weeks after treatment); Group II — same as Group I, except the drug level was 10 mg kg<sup>-1</sup> BW (5.0 mg kg<sup>-1</sup> BW of each drug); Group III — eight sheep in this group were not treated (controls) and were killed 9 weeks after inoculation at the same time as Groups I and II; Group IV — eight sheep were treated with 7.5 mg kg<sup>-1</sup> BW of the fenbendazole–triclabendazole combination 14 weeks after inoculation with 250 metacercariae and killed 17 weeks after inoculation (3 weeks after treatment); Group V — same as Group IV, except level of drug was 10 mg kg<sup>-1</sup> BW; Group VI — eight sheep in this group were killed 17 weeks after inoculation at the same time as Groups IV and V.

On the scheduled day, all sheep were killed with a captive bolt. Livers and 10 cm of duodenum were removed from each sheep, and the bile ducts and gall bladder were opened and washed into a bucket of water. Large *F. hepatica* were removed and counted. Smaller *F. hepatica* were detected under a stereoscopic microscope (4 ×). The liver was then sliced at 0.5–1.0-cm intervals and, after

soaking in water for 30 min, the liver slices and sediment were examined microscopically ( $4\times$ ) for *F. hepatica*.

The abomasum and small intestines were removed and standard parasitologic techniques were followed for parasite recovery. A 10% aliquot was used for parasite evaluation. Percentage efficacy was determined by the following formula:

$$\frac{\text{Number of parasites in nontreated group} - \text{Number of parasites in treated group}}{\text{Number of parasites in the nontreated group}} \times 100$$

Data were analyzed statistically using analysis of variance with Dunnett's *t*-test.

## RESULTS

The combination of fenbendazole–triclabendazole at  $7.5 \text{ mg kg}^{-1}$  BW was 98.3% effective against 6-week-old *F. hepatica* when compared to the controls (Table I). At  $10.0 \text{ mg kg}^{-1}$  BW, the efficacy was 99.7% (Table I). In the first set of sheep examined (Groups I–III), efficacy against *Ostertagia* spp. (*O. circumcincta* and *O. marshalli*) was 100% at  $7.5 \text{ mg kg}^{-1}$  BW and 97.3% at  $10.0 \text{ mg kg}^{-1}$  BW (Table I). Efficacy against *Nematodirus* spp. (*N. filicollis* and *N. spathiger*) was 99.5% at  $7.5 \text{ mg kg}^{-1}$  BW and 98.4% at  $10.0 \text{ mg kg}^{-1}$  BW (Table I).

The fenbendazole–triclabendazole combination at  $7.5 \text{ mg kg}^{-1}$  BW was 100% effective against 14-week-old *F. hepatica* and 99.9% effective at  $10.0 \text{ mg kg}^{-1}$  BW (Table II). In Groups IV and V, the efficacy against *Ostertagia* spp. (*O. circumcincta* and *O. marshalli*) at  $7.5 \text{ mg kg}^{-1}$  BW was 96.8% and at  $10.0 \text{ mg kg}^{-1}$  BW was 94.7% (Table II). The efficacy against *Nematodirus* spp. (*N. filicollis* and *N. spathiger*) at  $7.5 \text{ mg kg}^{-1}$  BW was 91.2% and at  $10.0 \text{ mg kg}^{-1}$  BW was 93.5% (Table II).

No adverse effects associated with drug treatment were noted.

## DISCUSSION

The results of this study indicate that triclabendazole and fenbendazole, given in combination, retain a high efficacy against both *F. hepatica* and common nematode infections in sheep. The efficacy of triclabendazole–fenbendazole combination was found to be 98.3–99.7% against *F. hepatica* at 6 weeks p.i., and 99.9–100% effective at 14 weeks p.i. In addition, the overall efficacy of the combination against common nematode parasites of sheep in

TABLE I

Efficacy of fenbendazole-triclabendazole combination against experimentally induced 6-week-old infections of *Fasciola hepatica* and naturally acquired nematode infections in sheep

Group	No. of animals	Treatment	<i>Fasciola hepatica</i>	<i>Ostertagia circumcincta</i>	<i>Ostertagia marshalli</i>	<i>Nematodirus filicollis</i>	<i>Nematodirus spathiger</i>
I	8	Triclabendazole/Fenbendazole, 3.75 mg kg <sup>-1</sup> BW of each drug	Average	0*	0*	1*	0*
			Range	(0-3)	(0)	(0-10)	(0)
II	8	Triclabendazole/Fenbendazole, 5.0 mg kg <sup>-1</sup> BW of each drug	Efficacy (%)	100	100	99.8	100
			Average	<1*	8.8*	5*	0*
III	8	Controls (no drugs)	Range	(0-1)	(0)	(0-30)	(0)
			Efficacy (%)	99.7	90	99.0	100
			Average	302.5	26.3	287.5	21.3
			Range	(50-840)	(0-60)	(20-820)	(0-70)

\*Significantly different from controls ( $P < 0.01$ ).

TABLE II

Efficacy of fenbendazole-triclabendazole combination against experimentally induced 14-week-old infections of *Fasciola hepatica* and naturally acquired nematode infections in sheep

Group	No. of animals	Treatment	<i>Fasciola hepatica</i>	<i>Ostertagia circumcincta</i>	<i>Ostertagia marshalli</i>	<i>Nematodirus filicollis</i>	<i>Nematodirus spathiger</i>
IV	8	Triclabendazole/Fenbendazole, 3.75 mg kg <sup>-1</sup> BW of each drug	Average 0* Range (0) Efficacy (%) 100	4 (0-20) 85.5	0* (0) 100	25* (0-70) 91.9	5 (0-40) 86.7
V	8	Triclabendazole/Fenbendazole, 5.0 mg kg <sup>-1</sup> BW of each drug	Average <1* Range (0-1) Efficacy (%) 99.9	6 (0-20) 90.4	0* (0) 100	18.8* (0-40) 95.5	4 (0-10) 92.4
VI	8	Control (no drugs)	Average 89.9 Range (20-239)	90 (0-430)	27.5 (0-120)	308.7 (10-880)	37.5 (0-130)

\*Significantly different from controls ( $P < 0.01$ ).

the Pacific Northwest of U.S.A. (*Ostertagia* and *Nematodirus* spp.) was greater than 91.2% at 7.5 mg kg<sup>-1</sup> BW and 93.5% at 10 mg kg<sup>-1</sup> BW.

These results agree with recent studies indicating the effectiveness of triclabendazole against *F. hepatica* in sheep (Boray et al., 1983, 1985; Smeal and Hall, 1983; Wolff et al., 1983; Güralp and Tinai, 1984; Turner et al., 1984) and in cattle (Craig and Huey, 1984). Although previous work indicated that higher dosages of triclabendazole are more effective against *F. hepatica* (Turner et al., 1984), there was little difference in efficacy at the dosages used in this study. The maximum tolerated dose of triclabendazole in sheep has been established at 200 mg kg<sup>-1</sup> BW (Boray et al., 1983).

Fenbendazole has been reported to be highly effective against nematode parasites in both sheep and cattle (Kennedy and Todd, 1975; Todd et al., 1976; Crowley et al., 1977; Craig and Bell, 1978; Drudge et al., 1978). Fenbendazole has been shown to be safe in cattle and sheep when given at normal anthelmintic dosages (Kennedy and Todd, 1975; Todd et al., 1976; Crowley et al., 1977; Drudge et al., 1978; Benz and Ernst, 1978), and when given at dosages as much as 2000 mg kg<sup>-1</sup> BW in cattle, signs of toxicity were not observed (Muser and Paul, 1984). Pregnant ewes were not adversely affected when fenbendazole at elevated levels of 15 mg kg<sup>-1</sup> BW was given six times during gestation (Muser and Paul, 1984).

This study supports the results of other studies (Buescher and Duewel, 1985; Echevarria, 1985) that have reported the effectiveness of triclabendazole and fenbendazole combinations for the treatment of *F. hepatica* and gastrointestinal nematodes in sheep.

## REFERENCES

- Benz, G.W. and Ernst, J.V., 1978. Anthelmintic activity of fenbendazole against gastrointestinal nematodes in calves. *Am. J. Vet. Res.*, 39: 1103-1105.
- Boray, J.C., Crowfoot, P.D., Strong, M.B., Allison, J.R., Schellenbaum, M., Von Orelli, M. and Sarasin, G., 1983. Treatment of immature and mature *Fasciola hepatica* infections in sheep with triclabendazole. *Vet. Rec.*, 113: 315-317.
- Boray, J.C., Jackson, R. and Strong, M.B., 1985. Chemoprophylaxis of fascioliasis with triclabendazole. *N. Z. Vet. J.*, 33: 182-185.
- Buescher, G. and Duewel, D., 1985. The efficacy of a triclabendazole/fenbendazole combination on helminths in sheep under laboratory conditions. *World Assoc. Adv. Vet. Parasitol.*, Rio de Janeiro, Brazil, abstract No. 70.
- Craig, T.M. and Bell, R.R., 1978. Evaluation of fenbendazole as an anthelmintic for gastrointestinal nematodes of cattle. *Am. J. Vet. Res.*, 39: 1037-1038.
- Craig, T.M. and Huey, R.L., 1984. Efficacy of triclabendazole against *Fasciola hepatica* and *Fascioloides magna* in naturally infected calves. *Am. J. Vet. Res.*, 45: 1644-1645.
- Crowley, J.W., Foreyt, W.J., Bliss, D.H. and Todd, A.C., 1977. Further controlled evaluations of fenbendazole as a bovine anthelmintic. *Am. J. Vet. Res.*, 38: 689-692.
- Drudge, J.H., Lyons, E.T. and Tolliver, S.C., 1978. Controlled-test evaluation of fenbendazole against natural infections of lungworms in calves. *Vet. Med./Sm. Anim. Clin.*, 73: 623-625.

- Echevarria, F.A.M., 1985. The anthelmintic efficacy of the triclabendazole/fenbendazole-combination against naturally acquired infections of *Fasciola hepatica* and gastrointestinal nematodes in sheep. World Assoc. Adv. Vet. Parasitol., Rio de Janeiro, Brazil, abstract No. 73.
- Güralp, N. and Tinai, R., 1984. Trematodiasis in Turkey: Comparative efficacy of triclabendazole, and niclofolan against infections of *Fasciola hepatica* and *F. gigantica* in sheep. J. Helminthol., 58: 113-116.
- Kennedy, T.J. and Todd, A.C., 1975. Efficacy of fenbendazole against gastrointestinal parasites of sheep. Am. J. Vet. Res., 36: 1465-1467.
- Muser, R.K. and Paul, J.W., 1984. Safety of fenbendazole use in cattle. Mod. Vet. Pract., 5: 371-374.
- Smeal, M.G. and Hall, C.A., 1983. The activity of triclabendazole against immature and adult *Fasciola hepatica* infections in sheep. Aust. Vet. J., 60: 329-331.
- Todd, A.C., Bliss, D., Scholl, P. and Crowley, J.W., 1976. Controlled evaluation of fenbendazole as a bovine anthelmintic. Am. J. Vet. Res., 37: 439-441.
- Turner, K., Armour, J. and Richards, R.J., 1984. Anthelmintic efficacy of triclabendazole against *Fasciola hepatica* in sheep. Vet. Rec., 114: 41-42.
- Wolff, K., Eckert, J., Schneiter, G. and Lutz, H., 1983. Efficacy of triclabendazole against *Fasciola hepatica* in sheep and goats. Vet. Parasitol., 13: 145-150.
- Yazwinski, T.A., Greenway, T., Pote, L., Presson, B. and Featherstone, H., 1983. Anthelmintic efficacy of fenbendazole in sheep. Vet. Med./Sm. Anim. Clin., 78: 243-244.