Persistence of Moxidectin Activity Against Nematodes in Red Deer

C.G. Mackintosh, T. Qureshi, K. Waldrup, R.E. Labes, M. Taylor, A. Murphy, P.Johnstone

Abstract

A field trial with red deer weaners showed that moxidectin 0.5% pour-on has persistent activity for 35 to 42 days against reinfection with lungworm, *Dictyocaulus viviparus,* under conditions of natural challenge augmented by inoculation with infective third stage larvae. Ivermectin 0.5% pour-on showed persistent activity for 21 to 28 days.

A controlled slaughter trial showed that moxidectin 0.5% pour-on had persistent activity against *D.viviparus, Ostertagia-type, Cooperia, Trichostrongylus, Oesophagostomum and Chabertia* for at least 42 days after treatment.

The prepatent periods of a number of parasites were determined by monitoring faecal egg or larvae output after experimental inoculation of parasite-free red deer weaners with infective larvae. Prepatent periods were : 24/25 days for *D. viviparus,* 17 days for *Cooperia,* 20 days *for Ostertagia-type* and 21 days for *Trichostrongylus species*

Introduction

Previous studies have demonstrated the high efficacy of moxidectin 0.5% pour-on against lungworm and gastrointestinal nematodes in red deer (Mackintosh *et aL,*1993; (Middleberg, 1994) and similar efficacy has been found in wapiti deer (Waldrup *et aL,* unpub.). Ivermectin 0.5% pour-on has also been shown to have persistent activity against nematodes for 28 days in cattle (McKenna, 1989; Hong *et aL* 1995) and moxidectin 0.5% pour-on has been shown to have persistent activity in cattle for five weeks against lungworm and for two to five weeks against various gastrointestinal nematodes. (Eysker & Eilers, 1995).

Two studies were undertaken in deer to study the persistent activity of moxidectin 0.5% pouron in deer. The first compared its activity with that of ivermectin against lungworm in a field trial and the second was a controlled slaughter trial.

Part A: Field Trial

Materials and methods

Thirty-five recently weaned 4 month old female red deer were randomly allocated to three groups:

- Group I (n= 1 5) untreated controls.
- Group 2 (n=10) calves treated with 500 gg/kg ivermectin 0.5% pour-on*
- Group 3 (n--10) calves treated with 500,4g/kg moxidectin 0.5% pour-on**

Groups 2 and 3 were treated on day 0 (April 7) and all calves (including 20 extra untreated calves which were subsequently used as Incubation Controls) were grazed together on pasture for the next 77 days (see Table 1). Because of unusually dry conditions the untreated animals failed to develop detectable faecal larvae counts and therefore the deer in Groups 2 and 3 were dosed with 177, 198, 204 and 234 infective third stage larvae of *Dictyocaulus viviparus on* days 35, 42, 49 and 56 respectively. On each of these four days an additional group of five animals (termed Incubation Controls 35, 42, 49 and 56) received the same inoculum as the Group 2 and 3 animals and were run with the mob. The Inoculation Control calves were treated with oral albendazole four days prior to being dosed with the *D. viviparus* L_3 larvae. Faecal larval counts (FLCS) were done on all calves on days 0, 7, 14, 21, 28, 35, 42, 49, 56, 63 and 70 and on Group 3 and Inoculation Control calves on day 77.

Results

Throughout the trial the untreated control deer showed very low FLCS. The proportion of untreated control (Group 1) animals which had positive FLCs rose gradually from 30% on day 21 to 87% on day 70. Of the Inoculation Control animals 60 to 100% became FLC positive 21 to 28 days after inoculation (see Table 1).

Of the treated animals, the first Group 2 (ivermectin) animal was FLC positive on day 49 with 30, 90 and 100% positive on days 56, 63 and 70 respectively. The first Group 3 (moxidectin) animal was FLC positive on day 63 with 20 and 50% positive on days 70 and 77.

All the FLC counts from treated animals were low (< I 1 larvae/g).

* Ivomec Pour-on, Merck Sharp and Dohme Ltd

** Vetdectin Pour-on, Cyanamid of New Zealand Ltd

Table 1. Percentage of animals in each group infected with lungworm, ie: had a positive FLC on at least one occasion

	No. in group	Treatment on Day 0	Inoc with L3 larvae	Percentage of deer in each group with positive faecal larval counts on days of field trial										
				7	14	21	28	35	42	49	56	63	70	77
Group 1	15	Control	Uninoc	0	0	27	33	40	40	40	53	67	93	
Group 2	10	Ivermectin pour-on	Inoc days 35,42, 49 & 56	0	0	0	0	0	0	10	30	90	100	
Group 3	10	Moxidectin Pour-on	Inoc days 35, 42, 49 * 56	0	0	0	0	0	0	0	0	10	20	50
Inoc control Day 35	5		Inoc day 35					0	0	0	100	100	100	
Inoc control Day 42	5		Inoc day 42					0	0	0	0	40	60	
Inoc control Day 49	5		Inoc day 49					0	0	0	0	0	0	60
Inoc control Day 56	5		Inoc day 56					0	0	0	0	0	20	80

Part B: Controlled slaughter trial

Materials and methods

In late March 1996, 30 newly weaned 3 to 4 (on day 0) month old female red deer were taken off pasture and kept indoors on *ad lib* lucerne hay and water. They were dosed with 3 ml low dose cattle oxfendazole on four occasions at weekly intervals (days -70, -63, -56 and -49). Day 0 (June 6, 1996) was the day when all deer were inoculated with infective larvae and days prior to this are denoted with a negative sign. On day -49 they were ranked by weight and blocked into six blocks of five animals. One animal from each block was randomly assigned to one of five treatment groups which were all kept in separate pens. Group 5 was treated with moxidectin 0.5 % pour-on at a rate of I ml/10kg liveweight on day -42, Group 4 on day -35, Group 3 on day -28 and Group 2 on day -21. Group I remained as untreated controls. On day 0 all 30 animals received an oral inoculum, by stomach tube, containing an estimated 11,600 Strongylate infective larvae and 1,400 *Dictyocaulus viviparus* infective larvae all of deer origin. The Strongylate larvae had a composition of approximately 29% *Ostertagia-type, 23% Trichostrongylus, 17% Cooperia* and 31% *Oesophagostomum/Chabertia.*

Faeces were collected from all deer on days -44, 0 and at slaughter. Faecal samples were collected daily from the control animals from day 10 after inoculation until slaughter on days 26 or 28, in order to determine prepatent periods. Three of the six animals in each group were slaughtered on day 26 and the rest on day 28.

Worm counts were made on lung, abomasum, abomasal digest, small intestine and large intestine.

Results

At slaughter only the control animals had detectable worm burdens which are presented in Table 2.

Table 2. Geometric mean numbers of worms from the control group deer at slaughter

Tag no.		B558	G541	G534	B546	G554	G523	Geometric mean
Abomasal	*Ostertagia*-type	4800	2500	2600	1400	1700	700	1932
	T. axei	200	100	0	100	0	0	0
Abomasal Digest	*Ostertagia*-type late L4	*0	0	0	0	400	100	12
	Ostertagia-type early L4	100	0	100	0	0	100	4
	T axei L5	0	0	0	0	0	0	1
SI	*Cooperia*	200	200	0	0	200	0	13
LI	*Oesophagostomum*	325	125	450	250	0	400	110
	Chabertia	50	300	675	625	475	325	316
Lungworms	Adult	122	178	51	225	345	79	138
	Immature	3	1	0	9	11	3	3

*0 = undetectable at the level of sensitivity for that sample (see text).

Bulked samples of *Ostertagia-type* nematodes from the abomasum were typed and the following species were present:

- *Spiculopteragia assymetrica* 35 %
- *Spiculopteragia spiculoptera* 27%
- *Ostertagia leptospicularis* 31%
- *Skrjobinagia kolchida* 7%

(note *S. kolchida* is considered an alternate polymorph of *0. leptospicularis)*

Prepatent periods (ie. time from inoculation of infective larvae to the first appearance of faecal larvae or **eggs)** were 24 to 25 days for *D. viviparus,* 17 days for *Cooperia,* 20 days for *Ostertagia-type* and 21 days for *Trichostrongylus.*

Discussion

Unseasonably dry weather conditions resulted in very little natural transmission of lungworm over the early stage of the Field Trial. This necessitated the weekly inoculation of the two treated groups with around 200 infective lungworm larvae for four weeks, from day 35 to 56, over the period when it was anticipated that the persistent anthelmintic activity would "run out". The prepatent period for lungworm was shown to be 24/25 days in the subsequent Controlled Slaughter Trial and therefore it appears that the combination

of natural and experimental challenge was infective because the majority of each Inoculation Control group animals started shedding 21 to 28 days after challenge. The first treated animal to develop positive FLC had received ivermectin 49 days previously. The first moxidectin treated animal became FLC positive 63 days after treatment. This suggests that the persistent activity against reinfection with *D. viviparus* first "ran out" after 24 or 25 days with ivermectin pour-on and 38 or 39 days with moxidectin pour-on. By 45 or 46 days after dosing 100% of ivermectin treated deer appear to have become infected while only 50% of moxidectin treated deer were infected by 52 or 53 days after treatment. The endpoint for moxidectin persistence was not measured

Based on these Field Trial results, the Controlled Slaughter Trial was designed to confirm the persistent activity of moxidectin against *D. viviparus* and to investigate its activity against gastrointestinal nematodes. Surprisingly it was shown that there was completely effective persistent activity which prevented infection by all the common deer nematodes for all treatments up to 42 days after pour-on treatment with moxidectin 0.5%.

Thus the Controlled Slaughter Trial confirmed the findings of the Field Trial, that moxidectin 0.5% pour-on at 500 gg/kg has persistent activity and prevents reinfection with *D. viviparus* in the majority of animals for at least 42 days after treatment and it also showed moxidectin at this dose rate to be effective at preventing reinfection by *Ostertagia-type, Cooperia, Trichostrong)ylus, Oesophagostomum and Chabertia* for up to 42 days after treatment.

References

Mackintosh, C G , Waldrup, K , Labes, R., Taylor, M (1993): Efficacy of ivermectin injection and moxidectin pour-on formulations in young red deer *(Cervus elaphus) Deer Branch (NZVA) Course No 10* . 143-150

Neddleburg, A. (1994): Efficacy of moxidectin pour-on in young red deer. *Deer Branch (NZVA) Course No. 11* · 203 -205

McKenna, P B (1989) Persistent anthelmintic activity of topically administered ivermectin in cattle. *N Z Vet. J 37* 146-147

Hong, C., Harris, T J., Gnmshaw, T.R , Newcomb, K.M. (1995) Persistent activity of ivermectin topical and moxidectin injection against *Ostertagia ostertagi and Dictyocaulus viviparus* in calves. *Vet. Rec 13* 7: 640-64 1.

Eysker, M., Eilers, C. (1995): Persistence of the effect of a moxidectin pour-on against naturally acquired cattle nematodes *Vet. Rec 137.* 457-460