Persistent efficacy of topical doramectin and eprinomectin against *Ostertagia ostertagi* and *Cooperia oncophora* infections in cattle

P. DORNY, D. DEMEULENAERE, K. SMETS, E. CLAEREBOUT, J. VERCRUYSSE

Veterinary Record (2000) **147**, 139-140

P. Dorny, DVM, DTVM, PhD,
D. Demeulenaere,
K. Smets, DVM,
E. Claerebout, DVM, PhD,
J. Vercruysse, DVM, DTVM, Department of Parasitology, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium

Dr Dorny is also at the Department of Veterinary Medicine, Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium

DORAMECTIN and eprinomectin are macrocyclic lactones with a high efficacy against cattle strongyle nematodes (Shoop and others 1996, Conder and others 1998). They also show a persistence of activity of several weeks, which makes them particularly attractive for the strategic control of gastrointestinal nematodes in calves (Eagleson and Langholff 1997, Molento and others 1999). Both compounds are available as pour-on formulations for easier administration. Doramectin pour-on is licensed in some countries for use in a chemoprophylactic system for nematode control in first grazing season calves given at turnout and again eight weeks later (Vercruysse and others 1998); the same chemoprophylactic design was used with eprinomectin pour-on in some field experiments (Epe and others 1999, Dorny and others 2000). The duration of persistent activity of doramectin pour-on has been reported to be 28 days and 35 days against *Cooperia oncophora* and *Ostertagia ostertagi*, respectively (Molento and others 1999); for eprinomectin it has been reported to be 21 days and 28 days, respectively, against the same nematode species (Eagleson and Langholff 1997). However, it has been demonstrated that trial design, parasite and/or host factors may affect the length of activity of macrocyclic lactones (Deroover and others 1997, Vercruysse and others 2000) and this may be the reason for the wide range of persistent efficacy described in literature for injectable formulations of these drugs. The aim of this study was to compare, under the same experimental conditions, the persistent efficacy of doramectin and eprinomectin pour-on formulations against *C oncophora* and *O ostertagi* infections in cattle.

The study was performed under pen conditions at the experimental farm of Ghent University. On day –5 of the study, 35 helminth-naive, Holstein cross bull calves, eight to nine months of age, were randomly allocated to one of five groups (T1 to T5), each containing seven animals. Animals in the T1 group served as negative controls and received no treatment. On day 0, the calves in groups T2 and T4 were given either doramectin pour-on (group T2) or eprinomectin pour-on (group T4), both at a dose rate of 500 µg/kg bodyweight. On day 7, the calves in groups T3 and T5 were topically treated with either doramectin (group T3) or eprinomectin (group T5) at the same dosage. All animals received an oral daily infection of 1000 L3 of *C oncophora* from day 14 to day 35, and 1000 L3 of *O ostertagi* from day 21 to day 42. All calves were penned in treatment groups, such that no physical contact was possible between animals in different groups. However, before infections started, they were randomly reassigned to separate stalls. The animals were fed grass and corn silage, and soy concentrate. Faecal egg counts were determined by a modified McMaster method (Thienpont and others 1979) on days 0, 34, 38, 41, 45, 48, 52 and 55. On day 55, the calves were slaughtered and necropsied for nematode burden determination using standard techniques (MAFF 1986).

Faecal egg counts and worm counts are expressed as geometric means (GMs). A log transformation (ln[worm count + 1]) was applied to worm count data before statistical analysis, to obtain the normal distribution. Analysis of variance was used to determine if the worm counts differed significantly between the control group and treated groups. Significant group effects were followed by pairwise comparisons, using the multiple comparison test of Bonferroni. Efficacy of the treatments was calculated using the following formula:

$$\text{Percentage efficacy} = \frac{\text{GM worm burden in group T1} - \text{GM worm burden in treated group}}{\text{GM worm burden in group T1}} \times 100$$

Percentage efficacy was calculated only when the counts were significantly different ($P<0.05$) between the control and treated groups (Vercruysse and others 1999).

No adverse reaction to treatment was observed in any of the calves. One calf in the T5 group died from bacterial pneumonia on day 19. The results of the faecal egg counts for the five groups are shown in Table 1. In group T1, the first strongyle eggs appeared in the faeces of one calf on day 38. From day 45 onwards all the animals in this group were passing eggs. Faecal egg counts were very low in the T2 group which had been treated with doramectin on day 0, and one or two calves passed low numbers of eggs from day 48 onwards. No eggs were passed with the faeces in the calves treated with doramectin on day 7 (group T3) until the end of the study (day 55). In contrast, the faecal egg counts of the two groups treated with eprinomectin were higher, and most animals in groups T4 and T5 were passing eggs at the end of the study. The results of the worm counts for the five groups are shown in Table 2.

A high establishment rate was observed for *O ostertagi* (range 45 to 80 per cent) in group T1; for *C oncophora* this was more variable (range 5 to 60 per cent). Both *C oncophora* and *O ostertagi* counts were significantly reduced in the groups treated with doramectin on day 0 (group T2) ($P<0.001$) and day 7 (group T3) ($P<0.001$). The percentage efficacy of doramectin was 99·6 per cent and 100 per cent against *C oncophora* in groups T2 and T3, respectively. The efficacy against *O ostertagi* was 99·9 per cent in both group T2 and group T3. From these results it can be calculated that doramectin pour-on had a persistent efficacy against *C oncophora* and *O ostertagi* of at least 35 days and 42 days, respectively. In contrast, *C oncophora* and *O ostertagi* counts were not significantly affected by the eprinomectin treatments given either on day 0 or on day 7. Therefore, it can be concluded that eprinomectin pour-on had a persistent efficacy against *C oncophora* of less than 28 days and against *O ostertagi* of less than 35 days.

The duration of persistent efficacy of doramectin pour-on against *C oncophora* and *O ostertagi* was longer than that described by Molento and others (1999), who observed a persistence of 28 and 35 days for *C oncophora* and *O ostertagi*, respectively. The duration of persistent efficacy for eprinomectin could not be determined in the present study, but it was less than 28 days against *C oncophora* and less than 35

TABLE 1: Geometric mean faecal egg counts (number of calves excreting/number of calves in the group)

Group	Treatment (day)	Day 38	41	45	48	52	55
T1	None	1 (1/7)	3 (2/7)	111 (7/7)	233 (7/7)	119 (7/7)	495 (7/7)
T2	Doramectin (0)	0 (0/7)	0 (0/7)	0 (0/7)	2 (2/7)	2 (2/7)	1 (1/7)
T3	Doramectin (7)	0 (0/7)	0 (0/7)	0 (0/7)	0 (0/7)	0 (0/7)	0 (0/7)
T4	Eprinomectin (0)	0 (0/7)	0 (0/7)	2 (2/7)	4 (3/7)	17 (5/7)	38 (6/7)
T5	Eprinomectin (7)	0 (0/6)	0 (0/6)	1 (1/6)	0 (0/6)	3 (2/6)	33 (5/6)

TABLE 2: Geometric mean worm counts

Group	Treatment (day)	*Cooperia oncophora* Number of calves infected	*Cooperia oncophora* Worm counts (range)	*Cooperia oncophora* Efficacy (%)	*Osteragia ostertagi* Number of calves infected	*Osteragia ostertagi* Worm counts (range)	*Osteragia ostertagi* Efficacy (%)
T1	None	7/7	6600 (1050-12,650)	–	7/7	12,655 (9450-16,800)	–
T2	Doramectin pour/on (0)	4/7	27* (0-1450)	99·6	4/7	18* (0-1000)	99·9
T3	Doramectin (7)	1/7	1* (0-50)	100	3/7	11* (0-1750)	99·9
T4	Eprinomectin pour/on (0)	6/7	169 (0-6000)	NC	7/7	3785 (150-15,500)	NC
T5	Eprinomectin (7)	5/6	183 (0-1200)	NC	6/6	3014 (450-6600)	NC

* Significantly different from the mean of the control group ($P<0.001$)
NC Not calculated since not significantly different from the mean of the control group ($P>0.05$)

days against *O ostertagi*. Large individual variations in worm counts were observed in both eprinomectin-treated groups, suggesting important individual variations in persistent efficacy.

The present results demonstrate that the duration of activity for the macrocyclic lactone class of anthelmintics is variable, depending on the drug and the worm species tested. Other factors such as trial design, intensity and frequency of challenge, which have been suggested to affect the results of persistent efficacy studies, are ruled out when the experimental conditions are identical. The difference in persistence between both drugs tested means that product strategy will have to be adapted when designing chemoprophylaxis. To obtain a strategic effect, it is critical that the interval between when the first dose loses it efficacy and the second treatment is reasonably short, so that the resulting worm burden and pasture contamination will be low (Epe and others 1999). This interval may be longer for eprinomectin than for doramectin.

ACKNOWLEDGEMENTS

This study was supported by Pfizer, New York. The authors would like to thank Dr J. Agneessens, F. De Smet and N. Dierickx for their technical assistance.

References

CONDER, G. A., ROONEY, K. A., ILLYES, E. F., KELLER, D. S., MEINERT, T. R. & LOGAN, N. B. (1998) Field efficacy of doramectin pour-on against naturally-acquired, gastrointestinal nematodes of cattle in North America. *Veterinary Parasitology* **77**, 259-265

DEROOVER, E., COBB, R., ROCK, D. W. & GUERINO, F. (1997) Persistent efficacy: importance and impact of trial design. *Veterinary Parasitology* **73**, 365-371

DORNY, P., DEMEULENAERE, D., SMETS, K. & VERCRUYSSE, J. (2000) Control of gastrointestinal nematodes in first season grazing calves by two strategic treatments with eprinomectin. *Veterinary Parasitology* **89**, 277-286

EAGLESON, J. S. & LANGHOLFF, W. K. (1997) Persistent efficacy of eprinomectin pour-on against gastrointestinal and pulmonary nematodes in cattle. Proceedings of the 16th International Conference of the World Association for the Advancement of Veterinary Parasitology. Sun City, South Africa, August 1997

EPE, C., WOIDTKE, S., PAPE, M., HEISE, M., KRAEMER, F., KOHLMETZ, C. & SCHNIEDER, T. (1999) Strategic control of gastrointestinal nematode and lungworm infections with eprinomectin at turnout and eight weeks later. *Veterinary Record* **144**, 380-382

MAFF (1986) Manual of Veterinary Parasitological Techniques, Ministry of Agriculture, Fisheries and Food. 3rd edn. HMSO, London

MOLENTO, M. B., TRUDEAU, C., PRICHARD, R. K., ZIMMERMAN, G. L., JOHNSON, E. G., MARLEY, S. & CONDER, G. A. (1999) Persistent efficacy of doramectin pour-on against artificially induced infections of nematodes in cattle. *Veterinary Parasitology* **82**, 297-303

SHOOP, W. L., EGERTON, J. R., EARY, C. H., HAINES, H. W., MICHAEL, B. F., MROZIK, H., ESKOLA, P., FISHER, M. H., SLAYTON, L., OSTLIND, D. A., SKELLY, B. J., FULTON, R. K., BARTH, D., COSTA, S., GREGORY, L. M., CAMPBELL, W. C., SEWARD, R. L. & TURNER, M. J. (1996) Eprinomectin: a novel avermectin for use as a topical endectocide for cattle. *International Journal for Parasitology* **26**, 1237-1242

THIENPONT, D., ROCHETTE, F. & VAN PARIJS, O. F. J. (1979) Diagnosing helminthiasis by coprological examination. Beerse, Janssen Research Foundation. p 187

VERCRUYSSE, J., BARTH, D., CONDER, G., HOLDSWORTH, G., LETONJA, P., OKANO, T., SASAKI, K. & SASAKI, N. (1999) VICH harmonization of veterinary anthelmintic guidelines. Proceedings of the 17th International Conference of the World Association for the Advancement of Veterinary Parasitology. Copenhagen, Denmark, August 1999. F5·08

VERCRUYSSE, J., DORNY, P., CLAEREBOUT, E., DEMEULENAERE, D., SMETS, K. & AGNEESSENS, J. (2000) Evaluation of the persistent efficacy of doramectin and ivermectin injectable against *Ostertagia ostertagi* and *Cooperia oncophora* in cattle. *Veterinary Parasitology* **89**, 63-69

VERCRUYSSE, J., DORNY, P., CLAEREBOUT, E. & WEATHERLEY, A. (1998) Field evaluation of a topical doramectin formulation for the chemoprophylaxis of parasitic bronchitis in calves. *Veterinary Parasitology* **75**, 169-179

ABSTRACT

Treatment of dogs with leptospirosis

TWENTY-TWO of 36 dogs with leptospirosis had moderately raised blood urea concentrations, and the other 14 had very high urea concentrations. The first group were treated conservatively, but the second group were treated by haemodialysis. In 16 of the dogs the serum antibody titres were highest to *Leptospira pomona*, in nine to *Leptospira bratislava*, and in one to *Leptospira hardjo*. Eight of the dogs had high titres to *L pomona* and *L bratislava*, one had high titres to *Leptospira grippotyphosa* and *Leptospira canicola*, and one had high titres to *L grippotyphosa*, *L pomona*, *L canicola* and *L bratislava*. Twelve of the 14 dogs treated by haemodialysis survived, and 18 of the 22 treated conservatively survived. Infections with atypical leptospira serovars resulted in acute renal failure. The prognosis for the dogs with moderate uraemia was good, and haemodialysis improved the prognosis for the more severely affected dogs.

ADIN, C. A. & COWGILL, L. D. (2000) Treatment and outcome of dogs with leptospirosis: 36 cases (1990-1998). *Journal of the American Veterinary Medical Association* **216**, 371-375