EFFICACY OF DORAMECTIN AGAINST NATURALLY ACQUIRED NEMATODE INFECTIONS IN SHEEP

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SUMMARY: A study was conducted from December 1996 to January 1997, in Bagé, State of Rio Grande do Sul, Brazil, to evaluate the therapeutic efficacy of doramectin injectable administered intramuscularly at dose rates of 200 and 300 mg/kg of body weight to sheep harbouring naturally acquired nematode infections. Thirty crossbred Corriedale castrated males, 12 to 16 months of age, were selected for the study. The sheep were randomly allocated to 3 groups (T1, T2, and T3) of 10 animals each, based on the mean number of nematode eggs per gram (e.p.g.) of faeces counted on days -3 and 0 before treatment. On day 7, the sheep in group T1 were treated with an intramuscular injection of saline solution (1 mL/50 kg) and those in groups T2 and T3 were treated with doramectin at dose rates of 200 mg/kg and 300 mg/kg, respectively. On day 21, all animals from each group were necropsied and their parasite burdens were determined. On days -3, 0, 7, and 21, individual faecal samples were collected for e.p.g. counts. Doramectin, administered as a single intramuscular injection at dose rates of 200 or 300 mg/kg, was highly efficacious in eliminating nematode infections in sheep. Both dosages significantly ($p < 0.05$) reduced the total worm burden compared with that for the saline control. There was no significant difference between the 200 and 300 mg/kg dose rates. Efficacy of doramectin at either 200 or 300 mg/kg of body weight was 100% against adult stages of *Ostertagia circumcincta, O. ostertagi, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. punctata,* and *Oesophagostomum venulosum*. The efficacy of doramectin at dose rates of 200 and 300 mg/kg against adult *Haemonchus contortus* was 97.3% and 98.5%, respectively and against adult *Nematodirus spathiger*, it was 99.4% and 98.8%, respectively. Both dosages were 98.2% efficacious against adult *Trichuris ovis*. Against the L4 stage of *Ostertagia circumcincta* and *O. ostertagi*, efficacy was 100% for both dosages. There was no significant difference between the 200 and 300 mg/kg dose rates and there were no adverse reactions detected in any of the doramectin-treated animals.

KEY WORDS: Doramectin, nematode, efficacy, sheep.

INTRODUCTION

Gastrointestinal nematode parasites are an important cause of economic losses in many parts of the world as it depresses weight gains and may even cause mortality in the most susceptible animals. The climate conditions prevailing in Brazil suit many of the gastrointestinal nematodes of sheep. *Haemonchus contortus* is the most important, causing outbreaks of disease, usually during the autumn. Lambs can become infected while they are with their dams in the spring, but is usually after weaning (Dec/Jan) that they are exposed to a greater challenge, with losses then occurring during their first autumn. Adult sheep do not develop a good immunity to *Haemonchus spp* and can also show signs of acute clinical disease in the autumn. Other important nematodes occurring in the Southern regions of Latin America are *Ostertagia* spp. and *Trichostrongylus axei* in the abomasum, and *T. colubriformis* and *Nematodirus spathiger* in the small intestine. Gastrointestinal nematodes such as *Strongyloides papilosus, Cooperia* spp., *Moniezia expansa, Oesophagostomum columbianum, O. venulosum,* and *Trichuris ovis* occur in low numbers, as do the lungworms, *Muellerius capillaris* and *Dictyocaulus filaria* (ECHEVARRIA, 1996).

Doramectin, a new broad spectrum compound of the avermectin class (GOUDIE *et alii.*, 1993), has been reported to be highly effective against internal parasites of cattle (EDDI *et alii.*, 1993; JONES *et alii.*, 1993), warbles (HENDRICKX *et alii.*, 1993), tropical warbles (MOYA-BORJA *et alii.*, 1993b) lice and

mites (LOGAN *et alii*., 1993), and screwworms (MOYA-BORJA *et alii*, 1993a) when administered to cattle at the dose rate of 200 mg/kg of body weight.

A chemical with such a broad anthelmintic spectrum would be a valuable addition to those compounds currently available for controlling gastrointestinal parasites of sheep. The few reports on the use of doramectin in sheep primarily involve its efficacy against external parasites. Doramectin has been shown to have high efficacy against the blowfly *Lucilia cuprina* (DE BRUIN, 1997), *Psoroptes ovis* (McKENZIE, 1997), and screwworm myiasis caused by *Cochliomyia hominivorax* larvae (UMEHARA, 1997). Doramectin has also been shown to significantly reduce gastrointestinal nematode e.p.g. counts in sheep in India (SISODIA *et alii*, 1996).

The purpose of the present study was to evaluate the therapeutic efficacy of doramectin injectable, administered intramuscularly at dose rates of 200 and 300 mg/kg of body weight, against naturally acquired nematode infections of sheep under field conditions in Brazil.

MATERIALS AND METHODS

The study was conducted from December 1996 to January 1997. A total of 33 Corriedale weathers, aged 12 to16 months and weighing 18 to 26 kg, that were harbouring naturally acquired mixed field infections of gastrointestinal nematodes were obtained for the study. These sheep were selected from a large herd on a farm known to have animals carrying gastrointestinal nematode infections. Necropsy of 3 representative sheep confirmed the infections. On days -3 and 0, individual faecal samples were collected for worm egg counts (e.p.g.). On day 0, the sheep were housed and on day 1 they were individually weighed and allocated to 3 treatment groups of 10 sheep each, on the basis of mean e.p.g. at days -3 and 0. The animals were ranked in descending order of e.p.g. counts, and the first 3 animals were randomly allocated to T1, T2, and T3 groups. The procedure was repeated until 30 animals were allocated to the 3 different groups. The remaining 3 animals served as sentinels. Throughout the study, animals were fed dry grass hay. On day 7, individual faecal samples were collected for e.p.g. counts and treatments were administered to the three groups according to the following study design:

Doramectin injectable was administered by intramuscular injection in the semimembranous /semitendinous muscles of the right limb of sheep in groups T2 and T3. Animals of group T1 received an injection of saline solution (0.9%) at the same location. All animals were observed for 5 hours after treatment for signs of adverse reactions. Also on day 7, the 3 sentinel animals, that received no treatment, were necropsied and the parasite burdens of the lungs, abomasum, and small and large intestines were determined.

Table 1 - Study design

Group	Treatment	Route	Treatment Day	Number of Animals	Day of Slaughter
T1	Saline Solution (1 µL/50kg)	IM	7	10	21
T2	Doramectin (200 µg /kg)	IM	7	10	21
T3	Doramectin (300 µg/kg)	IM	7	10	21

On day 21 (14 days after treatment), individual faecal samples were collected from all animals for e.p.g. determination. On the same day, sheep from the 3 treatment groups were slaughtered for worm counting and samples were processed according to standard procedures (ANONYMOUS, 1979; POWERS *et. alii*. 1982)

Statistical Analysis

Worm egg counts and nematode counts at necropsy were analysed by using an ANOVA of the natural log of the count +1. Worm egg counts were analysed separately for each day of the study. The nematode counts were analysed by species and stage (L_4 or adult) and the percent efficacy for each species (L_4 or adult) and treatment group was calculated by using the geometric means and the following formula:

$$\text{Percent efficacy} = \frac{\text{Mean worm count in control group} - \text{Mean worm count in treated group}}{\text{Mean worm count in control group}} \times 100$$

RESULTS AND DISCUSSION

Results from worm counts and e.p.g. determinations are summarised in Tables 2 and 3, respectively. These results indicated that the sheep used in this study were harbouring reasonable worm burdens of the most important gastrointestinal nematodes of sheep grazing on pastures in southern regions of Brazil (i.e., *Haemonchus contortus, Ostertagia circumcincta, O. ostertagi, Trichostrongylus axei, T. colubriformis, Cooperia* spp., and *Oesophagostomum venulosum. Trichuris ovis* was present in low numbers).

Treatment with doramectin with dosages of 200 mg/kg or 300 mg/kg was highly effective in removing naturally acquired field infections of gastrointestinal nematodes of sheep. Doramectin was 100% effective at both dose levels used against adult stages of *Ostertagia circumcincta, O. ostertagi, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. punctata,* and *Oesophagostomum venulosum.* The efficacy of doramectin at a dosage of 200 and 300 mg/kg against adult *Haemonchus contortus* was 97.3% and 98.5%, respectively, and against adult *Nematodirus spathiger,* it was 99.4% and 98.8%, respectively. Both dosages were 98.2% efficacious against adult *Trichuris ovis.* Against the L_4 stage of *Ostertagia circumcincta* and *O. ostertagi,* both dosages were 100% efficacious (Table 2).

Doramectin (200 and 300 mg/kg) significantly ($p<0.05$) reduced the total worm burden (Table 1) and e.p.g. counts (Table

Table 2 - Arithmetic mean number and range ( ) of nematodes[1] by species, stage, and percent efficacy of doramectin in sheep.

Nematodes		Saline	Doramectin (200 µg/kg)		Doramectin (300 µg/kg)	
		Mean number (range)	Mean number (range)	Efficacy (%)	Mean number (range)	Efficacy (%)
Haemonchus contortus						
	Adults	617.5[a] (180-1220)	17.0[b] (0-80)	97.3	9.0b (0-70)	98.5
Ostertagia circumcincta						
	L4	35.5[a] (0-140)	0[b]	100	0[b]	100
	Adults	486.5[a] (170-860)	0[b]	100	0[b]	100
Ostertagia ostertagi						
	L4	6.5[a] (0-65)	0[a]	100	0[a]	100
	Adults	196.0[a] (70-360)	0[b]	100	0[b]	100
Trichostrongylus axei						
	Adults	1,061.5[a] (10-4920)	0[b]	100	0[b]	100
Trichostrongylus colubriformis						
	Adults	121.0[a] (0-390)	0[b]	100	0[b]	100
Cooperia oncophora						
	Adults	433.0[a] (70-1640)	0[b]	100	0[b]	100
Cooperia punctata						
	Adults	202.0[a] (0-810)	0[b]	100	0[b]	100
Nematodirus spathiger						
	Adults	330.0[a] (100-630)	2.0[b] (0-10)	99.4	4.0[b] (0-20)	98.8
Oesophagostomum venulosum						
	Adults	37.8[a] (2-134)	0[b]	100	0[b]	100
Trichuris ovis						
	Adults	5.5[a] (1-14)	0.1[b] (0-1)	98.2	0.1[b] (0-1)	98.2

[1] Statistical analyses were conducted on log transformed data but results are presented here as arithmetic means (% efficacy calculated from geometric means).
[a,b] Results on the same row with different superscripts are significantly different at $P \leq 0.05$.

Table 3 - Arithmetic mean e.p.g. counts from groups of sheep treated with 200 and 300 mg/kg of doramectin, compared with that for the saline-treated sheep.

Day of study	Mean number[1] of eggs per gram of faeces (e.p.g.)		
	Saline	Doramectin 200 µg/kg	Doramectin 300 mg/kg
-3	5950[a]	6510[a]	6880[a]
0	7610[a]	6760[a]	6540[a]
7*	16270[a]	14833[a]	9260[a]
21	17920[a]	180[b]	90[b]

* Treatment administered on day 7.
[1] Statistical analyses were conducted on log transformed data but results are presented here as arithmetic means.
[a,b] Results on the same row with different superscripts are significantly different at P £ 0.05.

2) compared with that for the saline control and there was no significant difference between the 200 and 300 mg/kg dosages.

As in cattle, where its efficacy at a dosage of 200 mg/kg has been well documented (EDDI *et alii*, 1993), doramectin administered in a single intramuscular injection at dosages of 200 or 300 mg/kg was highly efficacious in the reduction of naturally acquired nematode infections in sheep.

None of the doramectin-treated sheep in either treatment group presented any clinical signs of adverse reactions.

Doramectin was 100% effective at both dosages used against adult stages of *Ostertagia circumcincta, O. ostertagi, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. punctata,* and *Oesophagostomum venulosum*. The efficacy of doramectin at dosages of 200 and 300 mg/kg against adult *Haemonchus contortus* was 97.3% and 98.5%, respectively, and against adult *Nematodirus spathiger,* it was 99.4% and 98.8%, respectively. Both dosages were 98.2% efficacious against adult *Trichuris ovis*. Against L_4 stage of *Ostertagia circumcincta*

and *O. ostertagi,* both dosages were 100% efficacious. There was no significant difference between the 200 and 300 mg/kg dosages and there were no clinical signs of adverse reactions in any of the doramectin-treated animals.

SUMÁRIO

Um estudo foi conduzido em Bagé, RS, Brasil, para avaliar a eficácia terapêutica da doramectin injetável e administrada via intramuscular nas dose de 200 e 300 mg/kg de peso em ovinos naturalmente infectados por nematódeos gastrintestinais. Trinta borregos Corriedale, machos castrados e com idade variando de 12 a 16 meses de idade foram selecionados para este trabalho. Os mesmos foram distribuidos, a três grupos (T1, T2 e T3) de 10 animais cada com base nos exames de fezes (o.pg.) realizados nos dias –3 e 0 antes do tratamento. No dia 7, todos animais do grupo T1 foram tratados com uma injeção intramuscular de uma solução salina (1ml/50kg) enquanto os animais dos grupos T2 e T3 receberam 200 mg/kg and 300 mg/kg of doramectin, respectivamente. No dia 21, isto é 14 dias após o tratamento, todos os animais foram necropsiados para determinação da contagem de helmintos. Nos dias –3, 0, 7 e 21, todos os animais tiveream fezes coletadas para contagens de o.p.g. Dorametin em única aplicação intramuscular de 200 ou 300 mg/kg foi altamente eficacaz em eliminar infecções por nematódeos em ovinos. Ambas dosagens reduziram significativamente ($p<0.05$) as contagens de helmintos em relação ao grupo não medicado. Não houve diferença significativa ($p>0.05$) entre as dosagens de 200 e 300 mg/kg. A eficácia da doramectin nas dosagens de 200 or 300 mg/kg foi 100% contra estádios adultos *Ostertagia circumcincta, O. ostertagi, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. punctata,* e *Oesophagostomum venulosum.* A eficácia das dosagens de doramectin a 200 mg/kg e a 300 mg/kg, contra formas adultas de *Haemonchus contortus* foi 97.3% e 98.5%, respectivamente e contra adultos de *Nematodirus spathiger* foi de 99.4% and 98.8%, respectivamente. Ambas dosagens tiveram eficácias de 98.2% contra forma adultas de *Trichuris ovis.* Contra estádios L_4 de *Ostertagia circumcincta* e *O. ostertagi* a eficácia foi de 100% para ambas dosagens de 200 e 300 mg/kg. Não houve diferença significativa ($p>0.05$) entre 200 and 300 mg/kg e não foram detectados sinais clínicos ou reações adversas em nenhum dos animais tratados com doramectin.

PALAVRAS-CHAVES: Doramectin, nematóides, eficácia, ovinos.

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