Reprinted from

veterinary parasitology

An International Scientific Journal

Veterinary Parasitology 87 (2000) 243–247

Short communication

Persistent activity of doramectin and ivermectin in the prevention of cutaneous myiasis in cattle experimentally infested with *Cochliomyia hominivorax*

O.S. Anziani [a,*], S.G. Flores [b], H. Moltedo [c], C. Derozier [d], A.A. Guglielmone [a], G.A. Zimmermann [a], O. Wanker [a]

[a] *EEA INTA Rafaela, cc 22, 2300 Rafaela, Santa Fe, Argentina*

[b] *Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba, Córdoba, Argentina*

[c] *Pfizer Inc., Buenos Aires, Argentina*

[d] *Pfizer, Animal Health Group, New York, USA*

Received 23 February 1999; accepted 6 July 1999

ELSEVIER

ELSEVIER

Veterinary Parasitology 87 (2000) 243–247

veterinary parasitology

www.elsevier.com/locate/vetpar

Short communication

Persistent activity of doramectin and ivermectin in the prevention of cutaneous myiasis in cattle experimentally infested with *Cochliomyia hominivorax*

O.S. Anziani [a,*], S.G. Flores [b], H. Moltedo [c], C. Derozier [d], A.A. Guglielmone [a], G.A. Zimmermann [a], O. Wanker [a]

[a] *EEA INTA Rafaela, cc 22, 2300 Rafaela, Santa Fe, Argentina*

[b] *Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba, Córdoba, Argentina*

[c] *Pfizer Inc., Buenos Aires, Argentina*

[d] *Pfizer, Animal Health Group, New York, USA*

Received 23 February 1999; accepted 6 July 1999

Abstract

A study was conducted to evaluate the activity of a single administration of doramectin or ivermectin against severe, induced infestations of *Cochliomyia hominivorax*. Twenty-four Holstein bull calves were allocated to four groups of six animals each and treated either with saline, doramectin 1%, or either one of two formulations of ivermectin 1% at a dose rate of 200 μg/kg. On Day 12 after treatment, each calf was anesthetized and two wounds were created on the left side of the shoulder and rump of each calf and 2 h later, each wound was implanted with 100 newly hatched larvae of *C. hominivorax*. On Day 15 after treatment, the procedure was repeated on the right side of each calf. Wounds were examined daily for 5 days and evidence of live larvae was recorded. Doramectin provided reduction in myiasis of 90.9 and 83.3% at 12 and 15 days after treatment, respectively, compared to the saline control treatment ($P < 0.0001$). In contrast, there were no significant differences in the number of calves with myiasis between those treated with either of the ivermectin formulations and the saline control.

Keywords: *Cochliomyia hominivorax*; Doramectin; Ivermectin; Myiasis; Screwworm

* Corresponding author. Tel.: +54-492-40121; fax: +54-492-40114.
E-mail address: oanziani@inta.gov.ar (O.S. Anziani)

0304-4017/00/$ – see front matter
PII: S0304-4017(99)00167-3

1. Introduction

The New World screwworm fly, *Cochliomyia hominivorax* is a severe pest of livestock, wildlife, pets and occasionally humans. *C. hominivorax* has been eradicated from North America (Knipling, 1985) and some areas of Central America (Galvin and Wyss, 1996) by using the sterile insect technique. However, in the rest of Central and South America, *C. hominivorax* is still the cause of severe monetary losses to animal producers as a result of mortality, diminished productivity and additional costs incurred as a result of control methods and treatments (Vargas Terán, 1991).

In these geographic areas and for the near future, insecticides will continue to play a major role in the control of screwworm larvae infestation. Repeated treatment of *C. hominivorax* myiasis exerts a mayor economic impact in extensive livestock production (Grindle, 1991) but the residual action of insecticides provides a degree of prophilaxis of susceptible wounds. The objective of the present study was to evaluate the persistent activity of doramectin 1% and two new long acting formulations of ivermectin 1% against severe, induced infestation of cattle with *C. hominivorax* larvae.

2. Material and methods

2.1. Experimental design, procedures and treatments

The study was conducted at the experimental station of the Instituto Nacional de Tecnología Agropecuaria located at Rafaela, Santa Fe province (31°11′S, 61°29′W), Argentina. Twenty-four, 4–5-month-old purebreed Holstein bull calves were individually weighed and allocated to four treatment groups according to a complete block design. Animals of group 1 (T1) were treated with saline solution (1 ml/50 kg), group 2 (T2) with a commercial formulation of doramectin 1% (Dectomax ™, Pfizer Inc.; lot # 705-54006-3), and groups 3 (T3) and 4 (T4) with commercial formulations of ivermectin 1% (Ivermectin A = Baymec Prolong ™, Bayer; lot # 007/97 and Ivermectin B = Fenomax™, Hoescht; lot # 001/97, respectively). All treatments were administered by subcutaneous injection and the dosage rate for the doramectin and ivermectin formulations was 200 μg/kg.

On Day 12 after treatment, all calves were challenged with induced infestations of *C. hominivorax* first-instar larvae. Under local anesthesia, two circular incisions of 4 cm in diameter were made over the areas of the shoulder and hip on the left side of each calf. The skin was removed to expose the muscle, and each wound was infested with 100 newly hatched, 3–6 h-old first-instar larvae from the *C. hominivorax* colony (Raf 8 strain) maintained at the Parasitology Laboratory of the INTA Rafaela Experimental Station. On Day 15 after treatment, the procedure was repeated on the right side of each calf. Calves were inspected on a daily basis and any wound with live larvae after 48 h of infestation was considered as active myiasis. In these wounds, mature larvae were removed 5 days after implantation and samples were placed in dry sand to allow pupation. Fly puparia were then transported to insect cages and held at 25°C and 70–80% relative humidity to assess adult emergence.

Table 1
Induced infestation of *C. hominivorax* in calves treated 12 and 15 days before with doramectin and two commercial formulations of ivermectin

Treatment/ Number of calves	Number of wounds with myiasis to total wounds challenged		*P* value		% of efficacy		Mean number and standard deviation of mature larvae by group[a,b]	
	Days		Days		Days		Days	
	12	15	12	15	12	15	12	15
Control/6	11/12	12/12	–	–	–	–	116 (30.7) a	96.6 (40.8) a
Doramectin/6	1/12	2/12	0.00004	0.00003	90.9	83.3	1.3 (3.2) b	10 (15.5) b
Ivermectin A/6	7/12	10/12	0.059	0.139	n.a.[c]	n.a.	78.3 (48.3) a	86.6 (36.4) a
Ivermectin B/6	8/12	11/12	0.131	0.307	n.a.	n.a.	90 (67.9) a	95 (38.3) a

[a] The values of standard deviation are given in parentheses.
[b] Between treatments, number with dissimilar letters are different ($P < 0.05$).
[c] n.a.: Not applicable (no significant differences with control).

2.2. Data analysis

The difference in proportion of animals with infested and noninfested wounds and the percentage of adult emergence from the collected larvae were analyzed by using chi-square distribution. When significant ($P < 0.05$) differences between a treated group and the saline-control group were observed in the number of calves with myiasis, the percent efficacy for each observation day was calculated according to the following formula:

$$\text{Percent of efficacy} = \frac{\text{Number of calves with myiasis in control group} - \text{Number of calves with myiasis in treated group}}{\text{Number of calves with myiasis in control group}} \times 100$$

The mean number of larvae collected between groups was tested by analysis of variance.

3. Results

The effects of the treatments on the larvae implants performed on Days 12 and 15 after treatment are presented in Table 1. In control animals (T1), the larvae implants resulted in an overall development of active myiasis of 95.8%.

Doramectin treatment (T2) resulted in a significantly lower ($P < 0.0001$) number of calves having wounds with active myiasis compared to that for the saline-treatment (T1). Doramectin was most effective when the period between treatment and challenge was shorter, with an efficacy of 90.9 and 83.3% for Days 12 and 15, respectively. The number of larvae collected in group-T2 calves was also significantly different ($P < 0.0001$) compared to that for group-T1 calves. The adult emergence observed in the few larvae obtained from calves in group T2 was similar to that for those collected from calves in group T1.

No significant differences were observed in the number of calves with myiasis or in larvae numbers between the animals treated with either of the ivermectin formulations and

those treated with saline at either 12 or 15 days after treatment. The percentage of adult emergence was also similar between larvae obtained from calves in groups T1, T3 and T4 on Days 12 and 15 after treatment.

4. Discussion

Currently the alternatives for screwworm control include the sterile insect release programs and the use of larvicidal insecticides on livestock. There is no conflict between these technologies and, in fact, they are complementary. In this context, the FAO has recommended that the efficacy and duration of protection against *C. hominivorax* be evaluated under simulated and field conditions for some members of the avermectin family (FAO, 1995).

In cattle, it has been reported that a single injection of doramectin was 100% effective in preventing development of myiasis in induced and natural infestations (Moya Borja et al., 1993; Muñiz et al., 1995a, b). The prophylactic period of doramectin has also been evaluated by use of experimentally induced and naturally acquired challenges. In induced infestations, doramectin was 100% effective in preventing development of *C. hominivorax* for 14 and 21 days after treatment (Moya Borja et al., 1993, 1997). Under natural conditions and when calves from several farms were castrated 10 days after treatment, doramectin had an overall mean efficacy of 94.6% (Caproni et al., 1998).

These percentages were similar to those reported under natural challenge conditions when the drug was administered 10 days before castration. The reason for the differences in the protection period observed in other induced infestation studies (Moya Borja et al., 1993, 1997) compared to this study are unknown. It can be speculated that they might be the result of differences in the number of larvae used in the challenges. In the present study, approximately 100 newborn larvae were implanted in each wound, whereas in the former studies, the challenges were performed with only 30 newborn larvae. In addition, some differences might relate to the breed of cattle used in the studies, with purebred Holstein calves used in our study and mostly Zebu crossbred cattle used in the other studies.

Studies involving ivermectin and abamectin activity were reported in Argentina and Brazil under field conditions when the drugs were administered to newborn calves or at castration to prevent navel or scrotal wounds against *C. hominivorax* myiasis, respectively (Anziani and Lorefice, 1993; Anziani et al., 1996; Benitez Usher et al., 1997). However, the residual action of ivermectin appears to be short and the duration of protection has been reported to be significantly less than for doramectin (Moya Borja et al., 1997; Caproni et al., 1998).

The results of the present study using doramectin and long acting formulation confirm these previous observations. Although, these endectocide molecules are similar, slight differences in physiochemical properties may account for differences in formulation flexibility and disposition kinetics affecting the persistance of antiparasitic activity (Shoop et al., 1995). In this context, Lanusse et al. (1997) suggested that differences in the doramectin formulation and probably a slowed metabolic rate may contribute to the higher plasma availability of this drug compared to ivermectin.

Acknowledgements

This project was partially supported by Pfizer, Animal Health Group, New York, USA.

References

Anziani, O.S., Lorefice, C., 1993. Prevention of cutaneous myiasis caused by screw worm larvae (*Cochliomyia hominivorax*) using ivermectin. J. Vet. Med. B 40, 287–290.

Anziani, O.S., Guglielmone, A.A., Aguirre, D.H., 1996. Larvicidal activity of abamectin against natural *Cochliomyia hominivorax* larvae infestation. Ann. NY Acad. Sci. 791, 443–444.

Benitez Usher, C., Cruz, J., Carvalho, L., Bridi, A., Farrington, D., Barrick, R.A., Eagleson, J., 1997. Prophylactic use of ivermectin against cattle myiasis caused by *Cochliomyia hominivorax* (Coquerel, 1858). Vet. Parasitol. 72, 215–220.

Caproni, L., Umehara, O., Goncalves, L.C.B., Moro, E., 1998. Persistent efficacy of doramectin and ivermectin in the prevention of natural *Cochliomyia hominivorax* infestations in cattle castrated 10 days after treatment. Brazil J. Vet. Parasitol. 7, 57–61.

FAO, 1995. Insecticidal Control of the New World screwworm. SCNA/INT/001/MUL, 34 p.

Galvin, J.T., Wyss, J.H., 1996. Screwworm eradication program in Central America. Ann. NY Acad. Sci. 791, 237–240.

Grindle, J., 1991. Economic impact of NWS eradication from North Africa. FAO, SECNA/INT/001/MUL, 33 p.

Knipling, E.F., 1985. Sterile insect technique as a screwworm control measure: the concept and its development. Misc. Publ. Entomol. Soc. Am. 62, 4–7.

Lanusse, C., Lifschitz, A., Virkel, G., Alvarez, L., Sánchez, S., Sutra, J.F., Galtier, P., Alvinerie, M., 1997. Comparative plasma disposition kinetics of ivermectin, moxidectin and doramectin in cattle. J. Vet. Pharmacol. Therap. 20, 01–09.

Moya Borja, G.E., Oliveira, C.M.B., Muñiz, R.A., Goncalves, L.C.B., 1993. The prophylactic and persistent efficacy of doramectin against *Cochliomyia hominivorax* in cattle. Vet. Parasitol. 49, 95–105.

Moya Borja, G.E., Muñiz, R.A., Umehara, O., Goncalves, L.C.B., Silva, D.S.F., McKenzie, M.E., 1997. Protective efficacy of doramectin and ivermectin against *Cochliomyia hominivorax*. Vet. Parasitol. 72, 101–109.

Muñiz, R.A., Anziani, O.S., Ordoñez, J., Errecalde, J., Moreno, J., Rew, R.S., 1995a. Efficacy of doramectin in the protection of neonatal calves and post-parturient cows against field strikes of *Cochliomyia hominivorax*. Vet. Parasitol. 58, 155–161.

Muñiz, R.A., Coronado, A., Anziani, O.S., Sanavria, A., Moreno, J., Errecalde, J., Goncalves, L.C.B., 1995b. Efficacy of injectable doramectin in the protection of castrated cattle against field infestations of *Cochliomyia hominivorax*. Vet. Parasitol. 58, 327–333.

Shoop, W., Mrozik, H., Fisher, M., 1995. Structure and activity of avermectins and milbemycins in animal health. Vet. Parasitol. 59, 139–156.

Vargas Terán, M., 1991. The New World screwworm in Mexico and Central America. World Anim. Rev., Special Issue, October 1991, 28–35.