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Anthelmintic Activity of Ivermectin Against *Ascaris, Trichuris* and *Metastrongylus* Infection in Swine

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Abstract

Two groups of six pigs, naturally infected with *Ascaris suum* and *Trichuris suis* and experimentally infected with *Metastrongylus apri,* were treated with ivermectin at a rate of 300 μg/kg body weight at 49 days postinfection with lungworm larvae. When injected subcutaneously, the anthelmintic efficacy was 98% for whipworms and 100% for ascarids and lungworms. These mean reductions from the control values were significant at the 5% level. When ivermectin was administrered in drinking water, the efficacy was 64% for whipworms, and 100% for ascarids and lungworms. These counts were compared with one group of six infected, untreated control pigs on the basis of postmortem worm counts.

Key words: Swine, internal parasites, *Ascaris, Trichuris, Metastrongylus,* anthelmintic, Ivermectin

Introduction

Burg *et al.* (1979) reported on the discovery of the avermectins, a new family of fermentation products, that possess potent activity against a broad spectrum of nematodes, insects and other arthropods. Ivermectin, 22,23 dihydroavermectin B_1, a synthetic derivative of the avermectins has demonstrated potent antiparasitic activity in a variety of laboratory and domestic animals (Egerton *et al.,* 1979, 1980).

The study reported herein was undertaken to investigate the anthelmintic activity of ivermectin administered in drinking water or by subcutaneous injection to pigs experimentally infected with *Metastrongylus apri* and naturally infected with *Ascaris suum* and *Trichuris suis.*

Materials and Methods

Experimental Pigs: Eighteen purebred Yorkshire pigs naturally infected with *Ascaris* and *Trichuris* were obtained at 10 weeks of age from a specific pathogen-free (SPF) herd. Pigs were housed in isolation rooms with concrete floors and fed a 16% crude proten corn-soybean meal diet fortified with minerals and vitamins. The diet was formulated at the University of Nebraska feed mill.

Lungworm Larvae: Adult *M. apri* were removed from lungs of infected pigs and placed in physiologic saline for 24 hrs at room temperature. This allowed the lungworms to release numerous eggs into the saline solution. Then the lungworms were minced thoroughly with scissors to release additional eggs. This mixture was poured onto a moistened filter paper in a culture can containing soil.

One hundred earthworms, *Eisenia foetida,* were placed on top of the filter paper in each culture can and covered with soil. Within 48 hrs, the earthworms had ingested the majority of lungworm eggs. Cultures were kept at room temperature and development of lungworm larvae was determined by dissecting an earthworm. Lungworm larvae reached the infective stage in 3 to 4 weeks following ingestion of *M. apri* eggs by the earthworms.

Preparation of Inoculum: Earthworms were taken from culture cans, washed two times with distilled water, cut into small pieces with

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scissors, and digested at 37°C for 4 hrs using half-strength artificial gastric juice. The latter was prepared by dissolving 1 g of pepsin in 122 ml of 0.2 *N* HCl. The suspension containing lungworm larvae and digestant was centrifuged, and the pellet was washed 4 times in sterile physiologic saline solution (Ferguson, 1971).

The number of infective lungworm larvae present was determined by counting the number of larvae in 9 aliquots of the total material. To establish *M. apri* infection, the inoculum containing 1,500 lungworm larvae was administered with a hypodermic syringe connected to a stomach tube. The syringe and stomach tube were rinsed with distilled water to ensure that each pig received the full dose of larvae.

Examination of Feces: Fecal samples from individual pigs were collected daily for 21 days starting at 39 days postlungworm infection and ending at the 59th day postinfection. Samples were examined microscopically, using a direct centrifugal flotation method. Saturated sodium nitrate was used as the flotation medium.

Administration of Ivermectin: Eighteen pigs infected with *Ascaris, Trichuris* and *Metastrongylus* were individually weighed 24 hrs before administration of ivermectin, and randomly assigned to the following treatments: (1) control (n=6); (2) 300 μg ivermectin injectable/kg body weight (n=6); and (3) 300 μg invermectin/kg body weight administered in drinking water (n=6).

Ivermectin was injected one time subcutaneously in the flank area of each pig in group 2. The six pigs in group 3 were placed in separate rooms and treated individually by placing the medicated water in a metal tub. During and following treatment, each pig in the two groups was closely observed for signs of drug toxicity. Pigs were maintained on the 16% crude protein diet.

Necropsy Findings: Pigs were euthanatized 10 to 14 days after treatment. Lungworm counts were made by opening the bronchial tree and removing the lungworms into a 0.85% saline solution to which 10% glycerol had been added. Lungworms could be kept in this solution for several hours without rupturing.

The small intestine, colon and cecum of each pig was examined grossly for ascarids and whipworms. The contents of each organ were washed in a fine screen (13 mesh per centimeter) and examined for helminths by using an illuminated, glass-bottomed dish. Worm counts were transformed to the logarithms of X+1 and subjected to an analysis of variance for a completely randomized design. Orthogonal comparisons were used to test the mean differences between the untreated control and dosage levels as well as linear effects of dosage levels (Snedecor and Cochran, 1967).

Results

Clinical signs resulting from lungworm infection were coughing, beginning at 10 to 12 days postinfection, and rapid shallow breathing. Pigs no. 12-18X (group 1) and no. 0-8 (group 2) seemed to be the most severely affected. Untreated controls developed a loose, husky cough which persisted until termination of the experiment 59 days postinfection.

The average number of *Ascaris* eggs per gram of feces of pigs in each experimental group is shown in Fig. 1. Nine days after treatment with ivermectin in drinking water, *Ascaris* eggs were not observed in the feces of pigs from group 3. Ten days after receiving ivermectin by injection, *Ascaris* eggs were not observed in the feces of pigs from group 2. Numerous *Ascaris* eggs were observed in the feces of the six untreated control pigs until termination of the experiment.

Trichuris eggs were observed in the feces of each of five pigs from groups 1 and 2, and four pigs from group 3 at the beginning of the experimental period. Nine days after receiving ivermectin by injection, whipworm eggs were not observed in feces of the five pigs from group 2. Whipworm eggs continued to be observed in feces of pig no. 14-10 (group 3) after receiving ivermectin in the water. Whipworm eggs were observed in feces of five untreated control pigs during the experimental period (Fig. 2).

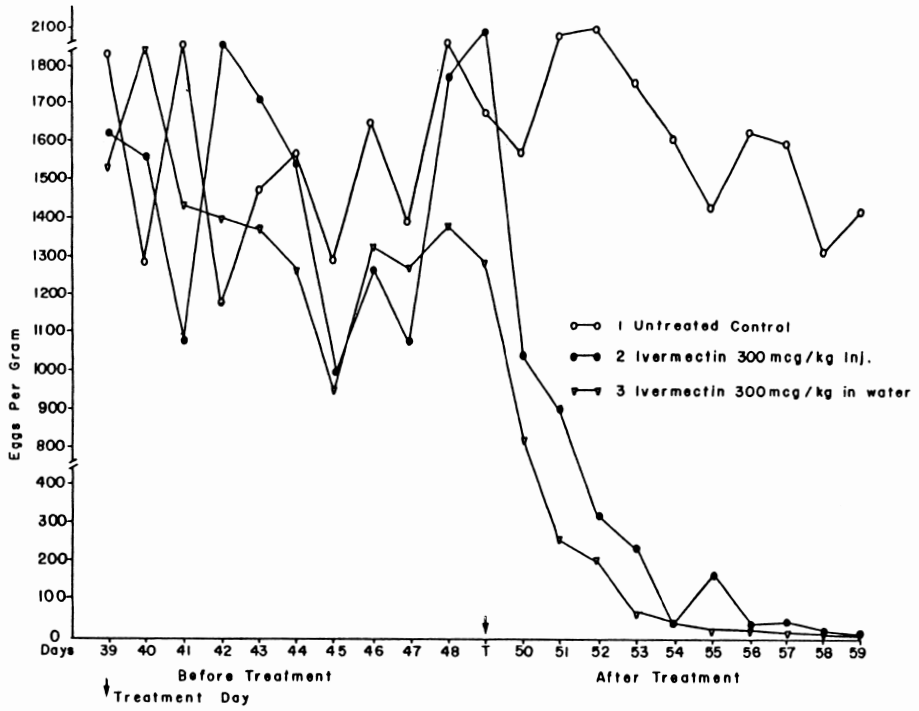

Fig. 1 *Ascaris* eggs in feces of naturally infected pigs before and after treatment with ivermectin.

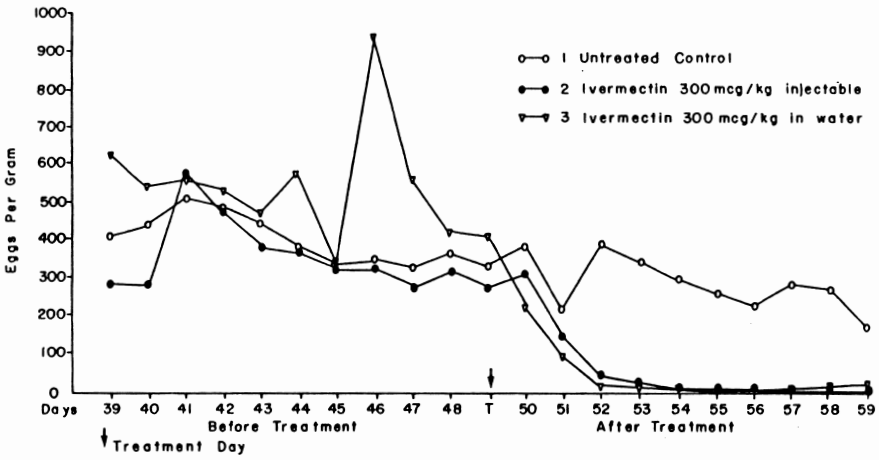

Fig. 2 *Trichuris* eggs in feces of naturally infected pigs before and after treatment with ivermectin.

The average number of *M. apri* eggs per gram of feces in each experimental group is shown in Fig. 3. Lungworm eggs were observed within 28 days after oral dosing with 1,500 third-stage infective larvae. Within six days after receiving ivermectin in drinking water or by injection, the number of lungworm eggs in the feces of each pig was markedly reduced. Lungworm eggs were observed in feces of the six untreated control pigs until termination of the experiment.

In the present study, ivermectin exhibited excellent anthelmintic activity against swine ascarids, whipworms, and lungworms when

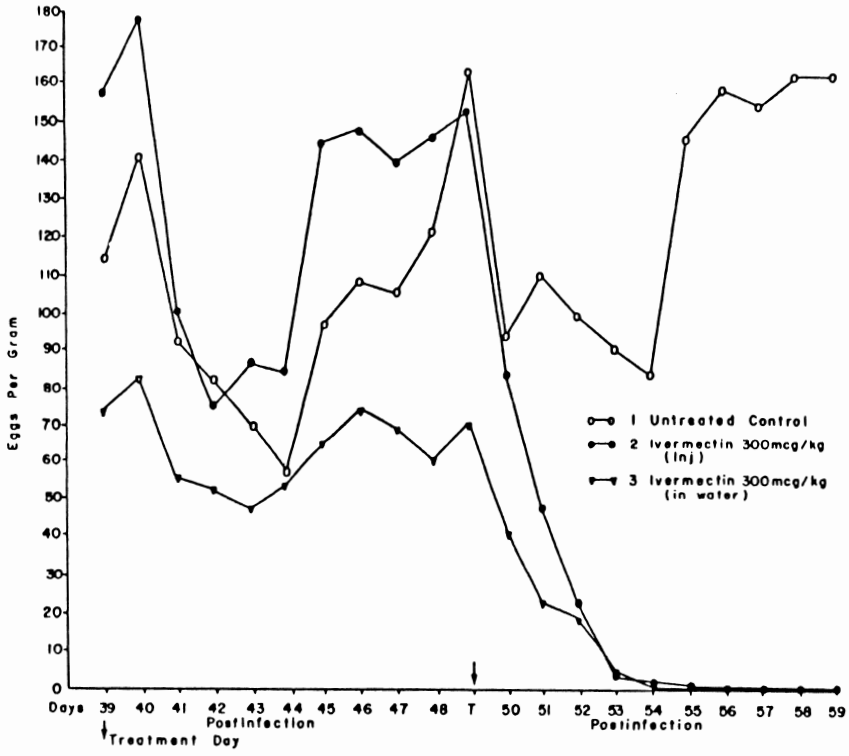

Fig. 3 *Metastrongylus* eggs in feces of experimentally infected pigs before and after treatment with ivermectin.

injected subcutaneously at a rate of 300 μg/kg of live body weight. Percentage of efficacy was determined by comparing the number of worms observed at necropsy in treated pigs with the number found in untreated controls. When injected at 49 days postlungworm infection,

Table 1 Anthelmintic activity of ivermectin against *Ascaris suum* infection in swine

Group no.	Pig no.	Dose (μg/kg)	Ascarids recovered	Total (mean)*	Anthelmintic efficacy (%)
1 Untreated control	11-12	—	23	18.5[a]*	
	11-18		27		
	12-18		15		
	12-18×		10		
	17-13		22		
	19-13		14		
2 Ivermectin injectable	0-8	300	0	0[b]	100
	10-1		0		
	10-18		0		
	13-2		0		
	13-16		0		
	18-1		0		
3 Ivermectin in water	1-17	300	0	0[b]	100
	12-11		0		
	13-18		0		
	14-10		0		
	16-8		0		
	17-15		0		

*Means with different superscripts are significantly different ($P \leq 0.05$)

Table 2 Anthelmintic activity of ivermectin against *Trichuris suis* infection in swine

Group no.	Pig no.	Dose (μg/kg)	Whipworms recovered	Total (mean)†	Anthelmintic efficacy (%)
1 Untreated control	11-12	—	25	245	
	11-18		0*		
	12-18		29		
	12-18×		246		
	17-13		4		
	19-13		921		
2 Ivermectin injectable	0-8	300	0	3.6	98.5
	10-1		0		
	10-18		0		
	13-2		18		
	13-16		0		
	18-1		0*		
3 Ivermectin in water	1-17	300	0	87.25	64.4
	12-11		0*		
	13-18		0*		
	14-10		349		
	16-8		0		
	17-15		0		

*Pig not infected with whipworms
†Means are not significantly different ($P \geq 0.05$)

Table 3 Anthelmintic activity of ivermectin against experiment *Metastrongylus apri* infection in swine

Group no.	Pig no.	Dose (μg/kg)	Lungworms recovered	Total (mean)*	Anthelmintic efficacy (%)
1 Untreated control	11-12	—	47	169.8[a]*	
	11-18		293		
	12-18		30		
	12-18×		634		
	17-13		4		
	19-13		11		
2 Ivermectin injectable	0-8	300	0	0[b]	100
	10-1		0		
	10-18		0		
	13-2		18		
	13-16		0		
	18-1		0		
3 Ivermectin in water	1-17	300	0	0[b]	100
	12-11		0		
	13-18		0		
	14-10		0		
	16-8		0		
	17-15		0		

*Means with different superscripts are significantly different ($P \leq 0.05$)

the anthelmintic efficacy was 100% for lungworms and ascarids, and 98% for whipworms. Eighteen whipworms were recovered from pig no. 13-2. These mean reductions from the control values were significant at the 5% level (Tables 1, 2 and 3).

When ivermectin was administered in drinking water, efficacy was 64% for whipworms and 100% for ascarids and lungworms. At necropsy, 349 whipworms were removed from the cecum and colon of pig no. 14-10. Whipworm were not recovered from the other three pigs.

Discussion

Ivermectin was reported by Stewart *et al.* (1981) to lack efficacy against *T. suis* of pigs when administered by subcutaneous injection at dosage levels of 20, 100 or 500 μg/kg body weight. Schillhorn van Veen and Gibson (1983)

investigated the efficacy of ivermectin at 300 μg/kg in feeder pigs naturally infected with low numbers of *A. suum* and *T. suis*. They reported a whipworm reduction in orally and subcutaneously treated pigs of 91% and 78%, respectively.

These differences in efficacy against whipworms could depend on the route of administration, as has recently been demonstrated by Bogan *et al.* (1982) working with levamisole in sheep. At a dose rate of 7.5 mg/kg, levamisole produced mean peak plasma concentrations of 3.1, 0.7 and 0.8 μg/ml in four sheeps after administrations by the subcutaneous, oral and intraruminal routes respectively. The bioavailability of levamisole to the systemic compartment was less after oral and intraruminal administration than after subcutaneous administration. In addition, Anderson and Roberson (1982) reported an efficacy of only 69% against adult *Toxascaris leonina* in dogs when ivermectin was given subcutaneously at 200 μg/kg, but Campell and Benz (1984) reported 95% of the worms were killed when the same dosage was given orally.

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