EFFICACY OF IVERMECTIN PLUS PYRANTEL IN A CHEWABLE FORMULATION FOR HEARTWORM PREVENTION AND TREATMENT OF HOOKWORM AND ASCARID INFECTIONS.

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SUMMARY: The efficacy, acceptability and safety of a chewable formulation of ivermectin/pyrantel was evaluated for the prevention of *Dirofilaria immitis* and intestinal nematode infections in 102 dogs under field conditions. All dogs were tested for *D. immitis* and intestinal nematodes prior to the start of the trial, at 5 months after the first treatment and at 0-28 days after the final dose. Only dogs that were negative for microfilariae and for occult heartworm infection were included in the trial. Each dog was treated monthly by the owner for nine months. Prior to treatment on Day 0, fecal examinations identified hookworm infections in 41 of the 102 dogs (40%), ascarids in 14 (14%) and whipworms in 8 (8%). Of the 43 dogs with nematode-egg positive feces, 17 had mixed parasite infections. By days 135-150 all dogs were either negative, or in four cases, had reduced counts of hookworm eggs. Whipworm ova were cleared from the feces of all dogs at the Day 135-150 tests, and all except two dogs at the final sampling. Ascarid ova were cleared from the feces of all dogs at the Day 135-150 tests, and from all but one dog at the final sampling. Fecal examinations were negative for all other dogs at each testing occasion. All dogs were negative for circulating microfilariae and heartworm antigen at each testing occasion. The combination chewable was given in association with several other medications commonly administered in routine veterinary practice and no adverse reactions were attributed to concurrent use of these products. The data support the use of an ivermectin plus pyrantel combination in a chewable formulation as a broad spectrum product, for the prevention of heartworm infection and the treatment and control of gastrointestinal parasite infection in dogs.

KEY WORDS: Ivermectin, Pyrantel, Heartworm, Hookworm, Roundworm, *D. immitis, Toxocara* spp, *Ancylostoma* spp, Dog.

INTRODUCTION

Parasitism is an important cause of disease in dogs living in Rio de Janeiro, Brazil. Among nematodes, the most common are *Dirofilaria immitis* (ALMEIDA, 1981; GUERRERO *et alii*, 1989; LABARTHE *et alii*, 1990, SOUZA, 1992), *Ancylostoma* spp and *Toxocara* spp (NOBRE E CASTRO, 1994). Infection with *D. immitis*, may be either asymptomatic or associated with clinical signs which may range from mild to chronic congestive heart failure, or sudden death due to vena cava syndrome (PLUE *et alii*, 1989). Intestinal parasites such as *Ancylostoma* spp and *Toxocara* spp are responsible for clinical disease in dogs that manifests as mild general clinical signs or, as severe anemia, weight loss, diarrhea and death (GEORGI & GEORGI, 1992). Besides being a problem for companion animals, these parasites are of zoonotic interest because of their capacity in causing pulmonary granulomas in man (SCHNEIDER *et alii*, 1986; KNIGHT, 1987), visceral larval migrans (WOODRUFF, 1975) and cutaneous larval migrans (REY, 1991).

To control these parasites, veterinarians have several anthelmintics available (ACHA & SYFRES, 1986). These include ivermectin and pyrantel pamoate. At the 5 mg/kg dosage, pyrantel pamoate is proved to be safe and of good efficacy against *Toxocara canis*, *Toxascaris leonina* and *Ancylostoma caninum* (LINDQUIST, 1975; CLARK *et alii*, 1992). At the 6 mcg/kg dosage, ivermectin is highly effective and possess a wide safety margin when used to prevent

infections with *D. immitis* (OHISHI *et alii*, 1987 and 1988; PLUE *et alii*, 1989; PAUL *et alii*, 1991; SOLL *et alii*, 1991).

A formulation containing both ivermectin and pyrantel pamoate has been shown to be a safe and effective broad spectrum anthelmintic capable of preventing *D. immitis* infection and controlling and treating *Toxocara* and *Toxascaris* spp, *Uncinaria* spp and *Ancylostoma* spp infections (CLARK *et alii*, 1992). In order to confirm this, a chewable formulation of ivermectin plus pyrantel pamoate was tested in 102 dogs living in endemic areas of the State of Rio de Janeiro, Brazil.

MATERIALS AND METHODS

Forty-three intact males, 1 castrated male, 46 intact females and 12 spayed females of various breed, 3-70 Kg body weight, 8 months to 13 years of age and living in Rio de Janeiro State in Brazil were used (Table 1). All animals were tested for the presence of *D. immitis* by the modified Knott test and ELISA antigen test and for the presence of intestinal nematodes by fecal flotation (GEORGI & GEORGI, 1982) prior to the start of the trial, and again at 5 months after the first treatment and at 0-28 days after the final dose. Only dogs that were negative for heartworm infection prior to the start were included in the trial. All dogs were kept with their owners and were managed according to their usual habits.

All dogs were weighed and received a chewable formulation of ivermectin and pyrantel pamoate (ivermectin 6 mcg/kg and pyrantel 5 mg free base/kg) monthly for 9 months. Animals were treated according to weight as follows:
Up to 11 Kg received 68 mcg ivermectin/ 58 mg pyrantel pamoate;
12-22 Kg received 136 mcg ivermectin/ 117 mg pyrantel pamoate;
22-45 Kg received 272 mcg ivermectin/ 234 mg pyrantel pamoate.
Dogs heavier than 45 Kg received appropriate combination of chewable sizes.

The owner recorded the acceptability of each treatment as follows:

1 = Accepted readily (within 10 minutes)
2 = Consumed with encouragement and/or time (maximum: 20 minutes)
3 = Consumed at later offer (maximum: 3 days)
4 = Refused — Not consumed

The first dose was administered by the owner in front of the investigator. The owner's comments and administration of medication with food were recorded.

Dogs were closely observed by the owners for at least 8 hours after each treatment. Any altered behavior or adverse clinical reactions observed were reported to the investigator and recorded. All concurrent medications, therapies or treatments were recorded.

RESULTS AND DISCUSSION

Details of animal identification, age, weight, sex, breed and dose administration are included in Table 1. Eighty-six dogs completed the trial and received 10 treatments. Among the dogs not completing the trial, six received eight treatments, one received seven, one received five, three received four, two received three and three received only one treatment. Prior to treatment on Day 0, fecal examinations identified hookworm infections in 41 of the 102 dogs (40%), ascarids in 14 (14%) and whipworms in 8 (8%). Of the 43 dogs with nematode-egg positive feces, 17 had mixed parasite infections. By days 135-150, all dogs were either negative or, in four cases had reduced counts of hookworm eggs. Whipworm ova were cleared from the feces of all dogs at the Day 135-150 tests, and all except two dogs at the final sampling. Ascarid ova were cleared from the feces of all dogs at the Day 135-150 tests, and from all but one dog at the final sampling (Table 2). Fecal examinations were negative for all other dogs at each testing occasion. These results are very close to the results reported before for the control of *Ancylostoma* spp and *Toxocara* spp (TODD *et alii*, 1975) and for *Toxocara* spp and *Ancylostoma* spp. (DZIMIANSKI *et alii*, 1992).

All dogs were negative for circulating microfilariae and adult *D. immitis* antigen at each testing occasion. Considering that 20 to 25% of the dogs in Rio de Janeiro State harbor heartworms (LABARTHE *et alii*, 1990; SOUZA, 1992), it was concluded that the medication was effective as a preventive, as has been previously reported (PAUL *et alii*, 1992; PLUE *et alii*, 1992 and DZIMIANSKI *et alii*, 1992).

A variety of clinical observations including diarrhea and vomiting were noted. Other than one dog that had fever, vomiting and diarrhea, there was no illness reported in dogs that received treatment. The frequency of these clinical signs were considered close to the frequency observed in any dog population, as has been reported (PLUE *et alii*, 1992).

The combination chewable was given in association with several other medications commonly administered in routine veterinary practice such as antibiotics, shampoos, vaccines, anesthesia, etc., and no adverse reactions were attributed to concurrent use of these products.

Table 1. Identification, age[1], weight, sex and breed of dogs.

DOG ID	AGE (yr)	WEIGHT (kg)	SEX	BREED	DOG ID	AGE (yr)	WEIGHT (kg)	SEX	BREED
AM1	1	6	F[3]	Mongrel	AM5	1	4	M	Poodle
AM2	3	10	F	Mongrel	CN19	2	7	M	Poodle
AM7	1	25	M[4]	Mongrel	R19	2	8	F	Poodle
AM8	1	15	M	Mongrel	R24	4	10	M	Poodle
AM12	6	6	F	Mongrel	R14	7	5	F[3]	Miniature Pinscher
AM19	4	15	M	Mongrel	R15	2	4.5	F	Miniature Pinscher
AM20	4	14	M	Mongrel	R16	2	6.5	F	Miniature Pinscher
AM21	2	20	SF[5]	Mongrel	R25	2	6.5	M[4]	Miniature Pinscher
AM22	5	31	SF	Mongrel	R26	4	6	F	Miniature Pinscher
AM27	4	20	F	Mongrel	R30	2	8	M	Miniature Pinscher
CN09	6	11	F	Mongrel	AM24	4	18	F	Boxer
CN17	5	9	F	Mongrel	AM25	4	19	M	Boxer
CN21	6	8	M	Mongrel	CN23	1	35	M	Boxer
CN24	2	8	SF	Mongrel	CN25	4	28	M	Boxer
CN26	7	15	M	Mongrel	CN44	1	31	M	Boxer
CN27	5	10	M	Mongrel	AM9	6	21	F	Doberman Pinscher
CN32	4	25	SF	Mongrel	AM11	9	25	F	Doberman Pinscher
CN33	1	22	M	Mongrel	CN22	1	25	F	Doberman Pinscher
CN34	2½	13	F	Mongrel	R06	10m[5]	20	F	Doberman Pinscher
CN42	3	11	F	Mongrel	R22	2	32.5	F	Doberman Pinscher
CN43	5	16	M	Mongrel	AM10	8	28	F	Rottweiler
R01	2	24	M	Mongrel	CN35	7	35	SF[6]	Rottweiler
R02	5	23	M	Mongrel	CN36	6	36	SF	Rottweiler
R09	1	10	F	Mongrel	CN37	4	50	F	Rottweiler
R11	11	15	M	Mongrel	CN38	7	55	MC[7]	Rottweiler
R12	4	9	F	Mongrel	R03	8	18	F	Cocker Spaniel
R17	4	11	F	Mongrel	R04	3	16	F	Cocker Spaniel
R18	3	5.5	F	Mongrel	R05	3	16	F	Cocker Spaniel
R20	2	5	F	Mongrel	R10	8	19	M	Cocker Spaniel
R23	3	9	M	Mongrel	CN12	6	19	M	Collie
R27	4	32	F	Mongrel	CN13	7	19	SF	Collie
R28	13	8	F	Mongrel	CN14	11	20	SF	Collie
R29	3	16	M	Mongrel	CN15	2	43	M	Canadian Shepherd
CN02	8	60	M	German Shepherd	CN16	4	35	F	Canadian Shepherd
CN10	3	28	F	German Shepherd	CN18	2	43	M	Canadian Shepherd
CN28	1½	32	M	German Shepherd	AM13	1½	16	F	Siberian husky
CN29	1½	30	F	German Shepherd	AM14	6	15	F	Siberian husky
CN41	4	30	F	German Shepherd	AM16	8	20	F	Siberian husky
R07	4	27	F	German Shepherd	AM17	8	34	M	Pointer
R13	4	28	M	German Shepherd	AM18	8	35	M	Pointer
R21	10m	29	M	German Shepherd	AM23	7	33	SF	Pointer
CN01	7	70	M	Fila Brasileiro	AM15	11	11	F	Beagle
CN04	2	40	F	Fila Brasileiro	AM28	3	13	M	Beagle
CN05	2	30	F	Fila Brasileiro	AM6	8	7.5	SF	Dachshund
CN06	5	30	F	Fila Brasileiro	AM26	2	3	SF	Dachshund
CN07	2	45	F	Fila Brasileiro	CN40	3	12.5	M	Dachshund
CN08	5	34	F	Fila Brasileiro	CN03	5	25	M	Irish Setter
CN39	8m[5]	37	M	Fila Brasileiro	CN20	2	40	F	Great Dane
R08	3	41	M	Fila Brasileiro	CN30	2	25	M	German Shepherd cross
AM3	3	3.5	SF	Poodle	CN45	2	42	M	German Shepherd/Doberman cross
AM4	4	7	M	Poodle	CN31	2½	35	M	Pointer cross

[1] Age at the beginning of the trial [2]F= Female [3] M= Male [4]SF= Spayed female [5] m= months [6]MC=Male castrate

During the trial period, there were 10 deliveries and 60 puppies were born. All puppies were followed up to whelping and most of them were in good health. The only observation was the death of one litter two days after birth. The cause of the death of this litter was thought to have been a result of a restricted weight losing diet to which the dam was submitted. There were no adverse effects seen attributable to treatment.

The results of this trial demonstrates that a combination of ivermectin and pyrantel pamoate in a chewable formulation is effective for heartworm prevention and in controlling intestinal nematodes and that such a formulation is safe and well accepted by dogs.

Table 2 - Fecal flotation results for ascarids, hookworms and whipworms.

DOG ID	PARASITE[2]	EGGS PER GRAM[1]		
		PRIOR TO FIRST DOSE	135-150 DAYS	0-28 DAYS AFTER FINAL DOSE
AM4	H	200	N[3]	N
AM8	H	40	N	N
AM13	H	200	N	N
AM15	A	200	N	N
AM26	H	160	N	N
CN01	H	40	N	N
CNO4[4]	A	40	-[6]	-
CN05[4]	H&A	40/40	N	-
CN07[4]	H&A	160/40	-	-
CN08[4]	H	80	-	-
CN13	A&W	N	N	40/80
CN21	H	80	N	N
CN25	H	40	N	N
CN27	H	40	N	N
CN39[5]	H	40	-	-
CN41	H	80	N	N
CN42	H	120	N	N
R01	H,A&W	360H/40A	N	40H/40W
R02	H&A	1040/160	N	80H
R03	H&A480/80	N	N	
R04	H	320	N	N
R05	H&A	240/40	N	N
R06	H	160	N	N
R07[4]	H,A&W	200/40/80	-	-
R08	H	240	80	80
R09	H&A	440/200	N	N
R10	H&W	240/80	N	N
R11	H&W	160/40	40H	N
R12	H&A	280/1120	N	N
R13	H	240	N	N
R14	H	120	N	N
R15	H	200	N	N
R16	H	160	N	N
R17[5]	H	160	N	-
R18[5]	H	120	N	-
R19[5]	H	40	N	-
R20[5]	H	40	N	-
R22	H&W	720/120	80H	40H
R23	H&A	480/80	N	N
R24	H&A	320/40	N	N
R25	H&W	920/40	N	40H
R26	H&W	1080/200	160H	40H
R27	H	480	N	N
R30	H	720	N	N

[1] All other dogs were negative at all sampling times
[2] A= Ascarids
H= Hookworms
W= Whipworms
[3] N= Negative
[4] Euthanized or died during the trial period
[5] Dropped from trial: owner noncompliance
[6] -= Not done

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