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Studies on the anti-parasitic efficacy and safety of ivermectin and pyrantel pamoate compound against *Dirofilaria immitis* in dogs

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Abstract : *Dirofilaria* (*D.*) *immitis* is an important canine parasitic nematode in dogs. *D. immitis* parasitizes the right ventricle and pulmonary artery of dogs. An ivermectin and pyrantel pamoate compound (IPPC) was administered to dogs naturally infected with this parasite. IPPC is composed of 68.0, 136.0 and 272.0 μg of ivermectin and 57.0, 114.0 and 227.0 mg pyrantel pamoate for small, middle, and large animals. Ivermectin has activity against nematodes and ectoparasites in dogs. Pyrantel pamoate is also effective against nematodes in dogs. Our results showed that this drug combination has good efficacy in *D. immitis* infected dogs.

Keywords : *Dirofilaria immitis*, ivermectin, ivermectin and pyrantel pamoate compound, pyrantel pamoate

Introduction

Companion animals are very important to families, as they provide many comfortable, relationships. However, dogs infected with zoonotic parasites can infect humans. Military and police dogs in Korea are frequently infected with parasites, such as *Toxocara canis* (8.2%), *Toxascaris leonina* (2.0%), and *Ancylostoma caninum* (17.1%) [15]. The major parasites in dogs are round-worm (*Toxocara canis*), whip-worm (*Trichuris vulpis*), and heart-worm (*Dirofilaria immitis*) as helminths, *Isospora canis* and *Giardia canis* as protozoa, and sarcoptic mites [13]. The prevalence of *D. immitis* in Korea is 2.3~40.0% in dogs [2, 5-8, 11, 12].

We conducted a study on the anti-parasitic efficacy and safety of an ivermectin and pyrantel pamoate compound (IPPC) against *D. immitis* in dogs. After the anti-parasitic activities of IPPC were evaluated in stray dogs, they were re-evaluated in dogs that presented at the private animal clinics.

Materials and Methods

Animals and feed

The experimental animals were companion animal dogs and stray dogs infected with *D. immitis*. All had detectable *D. immitis* microfilaria. Feed and water were supplied *ad libitum*.

Drugs and parasites

The components and dosages of the IPPC were as follows. This experiment used the drug formulation of 136.0 μg of ivermectin and 114.0 mg of pyrantel pamoate in 1 tablet for medium-sized animals and the H drug as control drug. For small animals, the effective components of IPPC are 68.0 μg of ivermectin and 57.0 mg of pyrantel pamoate in 1 tablet. And for large animals, those are 272.0 μg of ivermectin and 227.0 mg of pyrantel pamoate in 1 tablet. The drugs were evaluated for anti-parasitic activity against *D. immitis* in the stray dogs and the companion animal dogs from private animal clinics.

Methods

After *D. immitis* microfilaria verified in stray dogs and dogs from private animal clinics, the infected dogs were used in the following experiment. The experimental groups and investigated items are shown in Table 1.

Experimental groups

Forty-five dogs infected with *D. immitis* were divided

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Table 1. Experimental groups and items investigated to evaluate the anti-parasitic activities of ivermectin and pyrantel pamoate compound (IPPC) against *Dirofilaria immitis*

Groups	No. of animals	Replication	Treatment	Investigated items		
				Reduction rates of larva		Side effects
				2 weeks	4 weeks	
Infected control	5	3	N	1.6 (0.0)	0.0 (0.0)	No
A	5	3	Y	77.7 (46.7)	97.7 (86.7)	No
B	5	3	Y	75.0 (46.7)	93.5 (80.0)	No
Total	45					

Groups	Items	No of microfilariae (Weeks after treatment)		
		0	2	4
Control	**Total**	**124 (15/15)**	**122 (15/15)**	**124 (15/15)**
Control	**Mean**	**8.27**	**8.13**	**8.27**
Control	**SD**	**5.36**	**3.55**	**4.71**
IPPC	**Total**	**130 (15/15)**	**29 (8/15)**	**3 (2/15)**
A	**Mean**	**8.67**	**1.93**	**0.20**
A	**SD**	**4.47**	**2.12**	**0.56**
H	**Total**	**108 (15/15)**	**27 (8/15)**	**7 (3/15)**
B	**Mean**	**7.20**	**1.80**	**0.47**
B	**SD**	**3.43**	**1.90**	**0.99**

A: IPPC, B: H control drug.

Table 2. Experimental groups and items investigated to evaluate the anti-parasitic activities of IPPC against *Dirofilaria immitis* in a private animal hospital

Groups	No. of animals	Treatment	Investigated items		
			Reduction rates of microfilaria in blood		Symptoms
			2 weeks	4 weeks	
Infected control	10	N	31.7 (0.0)	5.0 (0.0)	No
RNL drug	10	Y	88.6 (70.0)	98.2 (90.0)	No
Total	20				

Groups	Items	No of microfilaria (Weeks after treatment)		
		0	2	4
Control	**Total**	**120 (10/10)**	**82 (10/10)**	**114 (10/10)**
	Mean	**12**	**8.2**	**11.4**
	SD	**6.60**	**4.89**	**5.60**
IPPC	**Total**	**114 (10/10)**	**13 (3/10)**	**2 (1/10)**
	Mean	**11.4**	**1.3**	**0.2**
	SD	**6.93**	**2.21**	**0.63**

into three groups, such as IPPC (1D, 2D and 4D) treated groups, a control drug (H) group and an infected control group (Table 1). Twenty dogs from private animal clinics were selected and also used in the experiment. One group compromised the control group and the other group was the IPPC-treated group (Table 2).

Investigated items

D. immitis microfilarial infections were investigated in the peripheral blood at 0, 1, 2, and 4 weeks before and after treatment.

Statistic analysis

We used Student's *t* test and SigmaPlot software (ver.

5.0, Jandel Scientific, USA) to compare the group results.

Results

Anti-parasitic efficacy of IPPC against *D. immitis*

The larval reduction rate in the IPPC-treated group was 77.7%, and it was 75.0% in the H control group at 2 weeks post treatment. The individual larval reduction rate of IPPC treated and H groups was 46.7%. The larval reduction rate in the IPPC-treated group was 97.7%, and it was 93.5% in the H control group at 4 weeks after treatment. The individual larval reduction rates in the IPPC-treated and H control groups were 86.7 and 80.0%, respectively (Table 1).

The anti-parasitic activities of IPPC against *D. immitis*

The microfilarial reduction rate of *D. immitis* in blood was 88.6% in the IPPC-treated group. The individual microfilarial reduction rate of *D. immitis* in the blood was 70.0% in the IPPC-treated group at 2 weeks after treatment. The microfilarial reduction rate of *D. immitis* in the blood was 98.2% in the IPPC-treated group at 4 weeks after treatment. The individual microfilarial reduction rate of *D. immitis* in the blood was 90.0% in the IPPC-treated group at 4 weeks after treatment (Table 2).

Discussion

The major canine parasites are round-worm (*Toxocara canis*), whip-worm (*Trichuris vulpis*), and heart-worm (*D. immitis*), protozoa-such as *Isospora canis* and *Giardia canis*, and arthropods-mites [13]. In this experiment, the anti-parasitic activity of IPPC was evaluated against *D. immitis.*

Clark *et al.* [3] reported that the anti-parasitic activity of ivermectin (6 mg/kg body weight) and pyrantel pamoate (5 mg active pyrantel/kg) supplied in a beef-based chewable formulation was 100% against larvae of *D. immitis*. McCall *et al.* [9] reported that the anti-parasitic reduction rates of ivermectin and milbemycin were 97.7 and 41.4% against *D. immitis*, respectively. Clemence *et al.* [4] found that ivermectin (Avermectin) and selamectin also prevented 100% of *D. immitis* infections.

Blagburn *et al.* [1], Rawlings *et al.* [10], and Takahashi *et al.* [14] reported the anti-dirofilarial drug, such as ivermectin and milbemycin.

The anti-parasitic activity of IPPC that we found was similar as that determined by other researchers for drugs such as ivermectin and pyrantel pamoate, and ivermectin, milbemycin, and selamectin.

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