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Comparable efficacy of topical eprinomectin and permethrin for treatment of sarcoptic mange in dogs

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ABSTRACT

The present study was conducted to evaluate the comparative efficacy of topically applied eprinomectin and permethrin for treatment of naturally occuring sarcoptic mange in dogs. A total of 24 dogs of various breeds, age and of both sexes were enrolled. Diagnosis of naturally occuring sarcoptic mange in dogs was made by identifying skin scrapings. All cases were subjected to scoring of the relevant significant clinical signs of scabies such as erythema, pruritis, alopecia, hyperpigmentation and crusting for the whole duration of the study. Dogs in group I (n = 9) received 0.5 mg/kg eprinomectin (5 mg/mL) topically once a week, and group II (n = 8) permethrin at a dosage of 20 mg/kg (100 mg/mL) topicallly once a week, both for a total of 4 weeks. Dogs in group III (n = 7) did not receive any treatment and were left as the control. All the scoring results were statistically evaluated on day 0 and 70, and revealed eprinomectin as the most effective group for evaluating clinical recovery ($P<0.05$). Evaluation of clinical signs and scoring results suggested complete clinical cure of 100% of dogs in the eprinomectin group, while permetrin was not effective where cure was evident in 2 out of 8 cases. In conclusion, topically applied eprinomectin was highly effective against naturally acquired infestation of *S. scabiei* by combined assessment of skin scrapings, scoring of skin lesions and clinical signs in comparison to permethrin.

Key words: eprinomectin, permethrin, sarcoptic mange, dogs

Introduction

Canine scabies is a severely contagious, nonseasonal and intensly pruritic skin disease caused by *Sarcoptes scabiei var. canis* (SCOTT et al., 2001). Molecular analysis has revealed that *Sarcoptes* mites belong to a genus consisting of a single heterogeneous species (ZAHLER et al., 1999). Sarcoptic mange may be transferable to other species (ARLIAN et al., 1984; FOLZ et al., 1984).

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The ease of administration of avermectin compounds makes them an effective option for controlling scabies. Several avermectins and other classes of drugs are used for treatment of sarcoptic mange in dogs, such as: ivermectin (SCOTT et al., 2001), selamectin (SHANKS et al., 2000; PIN et al., 2006), fipronil (CURTIS, 1996; CURTIS, 2004), imidaclopride and moxidectine combination (KRIEGER et al., 2005), lime sulfur (GHUBASH, 2006), milbemycin oxime (CARLOTTI and BENSIGNOR, 2002; CURTIS, 2004; GHUBASH, 2006) and amitraz (FOLZ et al., 1984; CURTIS, 2004; GHUBASH, 2006). Most of those therapy options should be reserved for early stage cases, and they are preferred when other treatments are contraindicated. Besides, there are anectodal reports of treatment failure (GHUBASH, 2006), and despite encouraging results, the potential side effects and poor efficacy may be observed for most of those drugs.

Eprinomectin is a macrocyclic lactone parasiticide, belonging to the avermectin subclass (SHOOP and SOLL, 2002). It possesses excellent insecticidal and miticidal efficacy against a wide range of external parasites in cattle (SHOOP et al., 1996; REHBEIN et al., 2005). The activity of eprinomectin in a 0.5% formulation for topical administration against *Sarcoptes* mite infestations has been reported in previous studies and under field conditions (BARTH et al., 1997; REHBEIN et al., 2003). Effective treatment of scabies is quite important in an attempt to control the disease in dogs, and probably for prevention of zoonotic spread. Therefore the aim of the present study was to compare the efficacy of topical eprinomectin *versus* topical permethrin for the treatment of naturally occuring Sarcoptic mange in dogs.

Materials and methods

Study design and subjects. Twenty-four dogs were included, referred with histories of pruritus, alopecia, erythema, hyperpigmentation scaling and crusting, with a diagnosis of naturally occuring sarcoptic mange, of both sexes (14 male, 10 female), of various breeds (1 Siberian Huskey, 1 Terrier, 1 Anatolian shepherd, 3 hunting dogs, 1 Labrador retriever, 1 Boxer, 1 Çoban and 15 crosbreds), aged 1-9 years. The study protocol was approved by the institutional laboratory animals ethics committee of Adnan Menderes University HADYEK (with no: B.30.2.ADU.0.00.00.00/050.04/2010/017) and informed written consent was obtained from all of the dogs' owners prior to enrolment of the dogs participating in study. For wellfare reasons and ethical conditions, the dogs involved in the control group were treated in a similar way to the eprinomectin protocol following the completion of the study.

None of the dogs had been treated with any ectoparasiticidical or steroidal anti-inflammatory drugs in the 30 days before the study. Throughout the study period, each dog was kept in its normal housing conditions and given its normal feed.

Scoring of skin lesions. All dogs enrolled were subjected to scoring for relevant clinical signs of sarcoptic mange (erythema, pruritus, alopecia, hyperpigmentation and crusting). All animals were clinically scored, similar to the scoring obtained for horses with Chorioptic mange (RENDLE et al., 2007), for severity of infestation on a scale of 0-3. Blinded clinical dermatological assessments (severity of the lesions and recovery degree) were made on days 0, 7, 14, 21, 42 and 70 for the treatment groups. For the control group scoring was performed at the beginning (day 0) and at the end of the study (day 70). Clinical evaluation scores were recorded as follows: 0: no clinical signs, 1: mild signs, 2: moderate signs and 3: severe signs.

Parasitological examination. Prior to enrollment in the study, the dogs had to have existing *S. scabiei* infestation, as assessed by the determination of live mites (larva, nymph and adult) within skin scrapings of at least 3-4 sites. Scrapings were performed (on days 0, 28 and 70) at those sites adjunctive to healthy tissues, believed to be most likely to yield mites and to those of visible suspected lesions. Hair was clipped throughly and then the lesion was scraped until capillary bleeding was evident. The obtained scraping material was mounted in paraffin liquid and microscopically examined for live mites, and when necessary the samples were cleared with potassium hydroxide. The data were recorded on the presence or absence of live mites.

Therapy protocoles. The dogs were divided and randomly assigned by coin toss into 3 groups. Dogs in group I (n = 9) received eprinomectin (Eprinex® pour on, Merial, France) at a dosage of 0.5 mg/kg topically in a spot on the skin on each animal's back, at the base of the neck in front of the scapulae, once weekly for a total of 4 applications. Dogs involved in group II (n = 8) received permetrin (Kwellada® lotion, Ali Raif, Turkey) at a dosage of 20 mg/kg topically in the same manner onto the skin on each animal's back at the base of the neck in front of the scapulae once weekly for a total of 4 applications respectively. Group III (n = 7) were left as control and no treatment was applied.

Statistical analysis. The ordinal data subjected to scoring were evaluated using the Wilcoxon test, for intragroup comparison, and by the Kruskal Wallis test between groups. When significance was evaluated with the Kruskal-Wallis test, differences among gorups were evaluated with the Mann-Whitney U test, using the Bonferroni correction. Results were deemed statistically significant if $P \leq 0.05$. Results for quantitative and ordinal data were given as mean ± standard error and median, respectively.

Results

Clinical examination results. Lesion localisations were variable, determined in every case enrolled. Mild to severe lesions were detected on the ears, periocular area, face, nasolabial area, chin, neck, flank, abdominal skin, elbow, legs and tail. Lesions were observed localised to 1-2 areas of the body in some cases, whereas generalized lesions were observed in others (Table 1).

Table 1. Localisations of skin lesions among naturally infected dogs with Sarcoptic mange

Eprinomectin Group I	Face	Periocular Area	Ear	Chin	Neck head	Supranasal	Trunk abdomen	Front feet	Hind feet	Bottom leg	Upper leg	Elbow	Hip	Tail	Generalized
1-			+	+	+		+	+	+	+					
2-			+						+	+	+			+	
3-		+	+			+	+	+	+	+		+			
4-							+	+	+	+	+	+		+	
5-						+			+	+					
6-															+
7-		+		+			+		+			+		+	
8-			+			+						+			
9-		+	+					+	+	+	+	+	+		
Permethrin Group II															
1-			+				+		+		+	+	+	+	
2-			+		+							+		+	
3-	+	+	+		+		+	+		+	+	+			
4-	+	+	+		+		+				+	+	+	+	
5-					+				+		+	+	+	+	
6-					+										+
7-	+		+				+	+	+	+	+	+			
8-	+		+		+			+	+	+	+	+		+	
Control Group III															
1-	+	+		+		+									
2-	+		+	+	+	+	+	+	+	+	+		+		
3-		+	+									+	+	+	
4-															+
5-			+				+	+	+		+				
6-			+					+	+	+	+			+	
7-			+					+				+			

Clinical efficacy. In the group I the dogs were treated with topical eprinomectin weekly for 1 month interval, 6 (66%) out of 9 cases by day 42, and all of them (100%) by day 70 showed complete clinical remission of clinical signs. In the dogs involved in group II, that received topical permethrin weekly for 1 month, by day 42 no clinical remission was observed, whereas by day 70 2 (25%) out of 8 dogs showed recovery, due to regression of clinical signs. Dogs enrolled in the control group appeared to show no degree of self-cure. Based on clinical examination, scoring and parasitological cure after day 42, eprinomectin brought about complete clinical and parasitological cure of naturally occuring sarcoptic mange in dogs. There were clear reductions in the severity of the clinical signs for the eprinomectin treated dogs, compared to those of permethrin treated and control dogs. In contrast, permethrin showed very limited efficacy for therapy. There was no adverse drug experience nor adverse treatment related mortality during the study in any of the groups.

Table 2. Descriptive statistics of median scoring values before (day 0) and after therapy (day 70) in groups

Group	N	Therapy and recovery period (day)		Wilcoxon test results	Kruskal-Wallis test results	
		0. day	70. day	P value	P value (day 0)	P value (day 70)
		Median Alopecia Score				
Eprinomectin	9	2.00	0[c]	0.007	0.703	<0.001
Permethrin	8	1.75	1.00[b]	0.018		
Control	7	1.75	2.00[a]	0.078		
		Median Erythema Score				
Eprinomectin	9	1.75[a]	0[a]	0.008	0.011	0.007
Permethrin	8	1.40[b]	0.70[b]	0.051		
Control	7	1.00[b]	1.13[b]	0.080		
		Median Hyperpigmentation Score				
Eprinomectin	9	1.00	0[c]	0.018	0.383	<0.001
Permethrin	8	1.42	0.46[b]	0.028		
Control	7	1.63	1.75[a]	0.180		
		Median Puriritus Score				
Eprinomectin	9	2.00	0[c]	0.007	0.119	<0.001
Permethrin	8	1.77	0.80[b]	0.038		
Control	7	1.85	2.16[a]	0.042		
		Median Crust score				
Eprinomectin	9	1.66	0[c]	0.012	0.075	<0.001
Permethrin	8	1.14	0.20[b]	0.017		
Control	7	1.00	1.00[a]	0.593		

Values referred as median. [a,b,c]: refers to statistical differences among groups on same days. Different superscripts in the same column indicate significant differences (according to Mann-Whitney U test using Bonferroni correction $P<0.05$).

Scoring results over the study period. All scores were presented as median values (Table 2). In terms of clinical recovery, eprinomectin ($P<0.01$) was the most effective group, as shown in Table 2, after therapy on day 70. The median scores of various signs/symptoms, including alopecia, hyperpigmentation, crusting and pruritus after treatment, on day 70, showed statistically significant differences compared to the baseline values in the eprinomectin and permethrin groups ($P<0.05$). However for median erythema scores significantly lower scores were observed only in the eprinomectin group after therapy when compared to baseline values ($P<0.01$), whereas insignificant changes ($P>0.05$) were detected in the other groups. Intragroup evaluation of control cases did not reveal significant changes among the median scores ($P>0.05$).

Table 3. Efficacy of eprinomectin against naturally acquired infestation of *Sarcoptes scabiei* on dogs: presence or absence of mites in skin scrapings

		Day 0		Day 28		Day 70	
Group	Case No.	Present	Absent	Present	Absent	Present	Absent
Eprinomectin	9	9	0	1	8	0	9
Permethrin	8	8	0	6	2	4	4
Control	7	7	0	5	2	6	1

Parasitological findings. At the pre-treatment assessment on day 0, live mites (adult mites, egg etc.) were recovered from all animals. No other parasitological agent (Demodex, Cheyletiella or Pelodera larvae) was observed. On day 28 only one case presented live mites in the eprinomectin group, whereas on day 70 no live mites were recovered. Six out of 8 cases were diagnosed with live mites on scrapings in the permethrin group, and moreover on day 70, four cases still demonstrated live mites (Table 3). Live mites were still recovered from 6 out of 7 animals in the control group on day 70.

Discussion

The ease of administration of avermectin compounds makes them an effective option for controlling scabies. Several avermectins and other classes of drugs are used for treatment of sarcoptic mange in dogs, such as selamectin (SHANKS et al., 2000; CARLOTTI and BENSIGNOR, 2002; GHUBASH, 2006; PIN et al., 2006). Most of those therapy options should be reserved for early stage cases, and they are preferred when other treatments are contraindicated. Besides there are anectodal reports of treatment failure, and despite encouraging results, potential side effects may be observed with most of those drugs (GHUBASH, 2006). Therefore, there is clearly an almost continuous need to evaluate new treatment regimes.

Eprinomectin at a dosage of 0.5 mg/kg weekly for 1 month maintained effective and safely clinical remission in hunter/jumper horses with *Psoroptes equi* (URAL et al., 2008). Six rabbits naturally infested with *Psoroptes cuniculi* received topical eprinomectin at a dosage of 0.5 mg/kg and it was partially effective in the treatment (ULUTAŞ et al., 2005). In cattle with sarcoptic mange, eprinomectin therapy was the subject of previous studies (BARTH et al., 1997, WARNICK et al., 2002). Available evidence suggested in the literature prompted the present study, as the efficacy of topically applied eprinomectin was comparatively evaluated with permethrin for treatment of naturally occuring sarcoptic mange in dogs.

The combined assessment of the clinical, parasitological and scoring results showed that weekly topical application of eprinomectin for 4 weeks yielded 100% clinical remission and parasitological cure on day 70, in all of the 9 eprinomectin treated dogs in the present study. Comparatively, permethrin only resulted in clinical and parasitological recovery in 2 out of 8 cases, whereas in the other dogs enrolled in the latter group clinical signs continued and no parasitological cure was evident.

There was a significant reduction in the severity of median alopecia scores in 8 out of 9 cases in the eprinomectin group on days 14 and 21. In terms of clinical recovery, median hyperpigmentation, pruritus and crusting scores showed statistically significant differences ($P<0.001$) among groups. Taking into account the clinical remission on day 70 after therapy, the eprinomectin group was the most effective. After day 28 no live *S. scabiei* mites were recovered from skin scrapings in 100% of the eprinomectin treated dogs. Clinical recovery rates were 100% and 25% for eprinomectin and permethrin, respectively, whereas no clinical or parasitological cure was observed among the control dogs.

Data on the life cycyle of *Sarcoptes scabiei var. canis'* presume that development from egg to adult may require 9-13 days (ARLIAN, 1989; ARLIAN et al.,1989). Maturation of the egg takes 3-4 days, following which the larva hatches from the egg (WALL and SHEARER, 2001). It is also known that survival off the host is up to 10 days or less, and greatly dependent on moderate conditions (ARLIAN, 1989; ARLIAN et al.,1989). Taking into consideration that, similar to the other avermectin compounds, eprinomectin has no ovicidal activity on the eggs of mites (PAN et al., 2006), the 4 dose regime within 7 day intervals between topical applications, permitted the development of both mites (derived from eggs either present at the time of therapy or laid after therapy by unaffected mites) and clinical signs in the present study. It was therefore possible to kill adult mites, besides killing any larvae hatching from eggs, as well as to prevent re-infection of mites off the host.

Eprinomectin has been tested and shown to be safe and effective against endo- and ecto-parasites in several animal species. The results of the present study presented here

indicate that weekly administration of eprinomectin for a month is highly effective against natural infestation of *S. scabiei* in dogs, with no adverse effects or recurrence after the last administration, when compared to permethrin. The combined assessment of the severity of mite infestation by skin scrapings, scoring of skin lesions and clinical signs have shown that eprinomectin may be safely and effectively used as a treatment protocole in dogs of a variety of ages and breed.

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SAŽETAK

Istraživanje je provedeno radi procjene usporedne učinkovitosti primjene eprinomektina i permetrina na koži u liječenju sarkoptoze pasa. Provedeno je na 24 psa različitih pasmina, dobi i spola. Bolest je dijagnosticirana na temelju nalaza parazita u strugotinama kože. Promatrani su klinički znakovi šuge poput crvenila, svrbeža, alopecije, hiperpigmentacije te pojave krasti. Psi u prvoj skupini (n = 9) liječeni su dozom od 0,5 mg (5 mg/mL) eprinomektina jednom tjedno. Permetrin je bio primijenjen u pasa druge skupine (n = 8) u dozi od 20 mg/kg (100 mg/mL) jednom tjedno. Liječenje je trajalo 4 tjedna. Psi u trećoj skupini (n = 7) nisu liječeni i služili su kao kontrola. Postignuti rezultati bili su statistički obrađeni uzimajući u obzir nalaze nultoga i sedamdesetoga dana. Rezultati su pokazali potpuno izlječenje u svih pasa u kojih je rabljen eprinomektin. Primjena permetrina bila je učinkovita u svega 2 od 8 slučajeva. Lokalna primjena eprinomektina bila je učinkovita kod prirodne infestacije grinjom *Sarcoptes scabiei* što se može zaključiti na osnovi pretraga strugotina kože, određivanja kožnih lezija i kliničkih znakova.

Ključne riječi: eprinomektin, permetrin, sarkoptoza, psi