Evaluation of ivermectin tablets in the treatment of generalized canine demodicosis

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SUMMARY

Sixteen privately owned dogs with generalized demodicosis included in this study. For the treatment of generalized demodicosis, tablet form of ivermectin (Efektin tablet® 10 mg, Sanovel) at a dose of 600 µg kg^{-1} daily was used in study dogs for 6-22 weeks. Ivermectin was used at least for 2 weeks more after no mites (dead or alive) seen. All dogs had significant reduction in the in clinical signs and number of mites on skin scrapings during re-evaluations. All dogs became skin scrapings negative. After no mites were seen, treatment was continued for 2 more weeks and then stopped. But three dogs relapsed 5, 8 and 9 months after the therapy lasted. Remained 13 dogs were negative for skin scrapings and clinically normal after 12 months. Oral ivermectin, at a dosage of 600 µg kg^{-1}, PO, daily, was found to be effective in resolving generalized demodicosis in 13 of 16 dogs (82,25 %.) in one year follow-up after discontinuing of therapy. Although, there were some literatures evaluating the efficacy of the use of injectable formula of ivermectin, to the present authors' knowledge these is the first report evaluating tablet form of ivermectin in the treatment of canine demodicosis.

Keywords : Dog, demodicosis, ivermectin tablets.

RÉSUMÉ

Évaluation de l'efficacité de comprimés d'Ivermectine dans le traitement de la demodécie canine généralisée

Seize chiens présentant des démodécies généralisées ont été utilisés pour cette étude. Pour le traitement de ces démodécies généralisées, de l'ivermectine formulée en comprimé (Efektin tablet® 10 mg, Sanovel) a été administrée à une dose journalière de 600 µg kg^{-1} pendant 6-20 semaines. Tous les chiens traits ont présenté une réduction significative des signes cliniques ainsi que du nombre des acariens observés sur des raclages de peau pendant le suivi. Tous les chiens sont devenus négatifs aux contrôles effectués par grattage de la peau. L'ivermectine a été administrée au moins 2 semaines supplémentaires après la disparition des parasites. Trois chiens ont rechuté 5, 8 et 9 mois après le traitement. 14 chiens étaient toujours négatifs lors des contrôles cutanés effectués après 12 mois. L'ivermectine administrée par voie orale, à un dosage de 600 µg kg^{-1}, quotidiennement, est avérée efficace pour traiter des démodécies canines généralisées dans 13 cas sur 16 (82.25 %) à un an. À la connaissance des auteurs, il s'agit de la première évaluation de l'efficacité de comprimés d'ivermectine dans le traitement de la démodécie canine.

Mots-clés : Chien, démodécie, comprimés d'ivermectine.

Introduction

Canine demodicosis (demodectic mange, follicular mange, red mange) is a frequent parasitic skin disease resulting from excessive proliferation of the mite *Demodex canis* within the hair follicles [27]. They are normal commensals on canine skin but are able of producing generalized disease if mite numbers proliferate [29]. Two clinical forms of the disease, localized and generalized, have been recognized [16, 27]. The disease is considered to be generalized when a dog has five or more localized lesions, when an entire body region is involved, or where the complete involvement of two or more feets occurs [27, 29]. Lesions are most common on the face, but they can be anywhere on the body. Usually, patchy, regional, multifocal, or diffuse alopecia is observed with variable erythema, grayish scaling, papules or pruritus [11, 27]. Affected skin may become lichenified, hyperpigmented, pustular, crusted, or ulcerated from secondary superficial or deep pyoderma. Lesions are not usually pruritic unless they are secondarily infected [9, 27].

Amitraz is one approved drug for the treatment of canine demodicosis [27], although this therapy sometimes fails [26]. Also amitraz has a foul smelling, the use has poor owner compliance, and adverse reactions may affect both owner and dog especially when used in a poor ventilated area [15]. To date, interests have been focused on oral use of alternative drugs such as ivermectin and milbemycine oxime [16]. Treatment with milbemycin oxime has given good results [8] but it is much expensive than ivermectin and also not readily available in Turkey. Long term oral treatment of the disease with orally used injectable formula of ivermectin has also been reported [14, 20, 23]. However, because of its bitter taste, injectable formula of ivermectin needs flavouring before application.

Tablet form of oral ivermectin became available in Turkey primarily for treatment of endo and ectoparasites in the sheep. The aim of this study was to evaluate the efficacy of tablet form of ivermectin at a dose 600 µg kg^{-1} for the treatment of generalized demodicosis.

Material and Methods

Method of this study was adopted from a previous study [23]. Sixteen privately owned dogs with generalized demodi-

cosis included in this study. Four dogs had been treated unsuccessfully with amitraz rinses. Criteria for the diagnosis of generalized demodicosis were five or more localized disease or involvement of 50 % of body area. Breeds, age, sex, and treatment protocols from study dogs is shown in table I. Fourteen dogs were pure breeds, 2 dogs were mixed-breed. There were 6 females (3 spayed, 3 intact) and ten males (all intact). The median age at the time of diagnosis was 3 years (1.5-7 year, mean 2.9 year). All dogs were vaccinated annually and free of endoparasites and microfilaria defined by Knott's test. Blood samples for haemogram and serum biochemistry profile were obtained from all dogs at initial treatment started and 4 weeks intervals at the course of therapy. Bacterial cultures, antibiotic susceptibility tests, fungal culturing, skin scrapings were performed on all dogs. Dogs with endocrinopathies (hormonal diseases) were not selected for the trial. Dogs diagnosed to have an underlying disease that may lead to the development of demodicosis excluded from the study. Multiple skin scrapings from at least 3 different areas were performed. Affected skin was scraped with a dermal curette until blood oozed. Laboratory data were based on direct microscopy of skin scrapings demonstrating many adult, larval or egg forms of *Demodex canis*. Skin scrapings performed 2 weeks interval during the course and at the end of therapy.

Case no.	Breed	Sex	Age (Year)	Weight	Previous treatment for demodicosis	Concurrent pyoderma	Duration of treatment	Outcome
1.	Boxer	M	2	21 kg	-	+	12 weeks	Successful
2.	Boxer	M	3	19 kg	-	+	10 weeks	Successful
3.	Pointer	M	2	17 kg	+	+	10 weeks	Successful
4.	American Cocker	SF	4	17 kg	-	+	8 weeks	Successful
5.	German shepherd	F	2	28 kg	+	+	8 weeks	Relapsed 5 months after treatment discontinued
6.	Anatolian shepherd	M	7	42 kg	+	-	14 weeks	Successful
7.	Terrier	SF	3	13 kg	-	-	12 weeks	Successful
8.	Pointer	M	2	21 kg		-	10 weeks	Relapsed 9 months after treatment discontinued
9.	Mixed	SF	3	14 kg	+	+	22 weeks	Successful
10.	Mixed	M	5	20 kg	-	+	8 weeks	Successful
11.	Pitbull Terrier	M	1.5	27 kg	-	-	6 weeks	Successful
12.	German shepherd	M	3	30 kg	-	+	16 weeks	Successful
13.	German shepherd	M	4	27 kg	-	+	10 weeks	Relapsed 8 months after treatment discontinued
14.	Terrier	F	1.5	9 kg	-	-	10 weeks	Successful
15.	English Bulldog	M	1.5	15 kg	-	+	18 weeks	Successful
16.	Anatolian shepherd	F	4	28 kg	-	-	16 weeks	Successful

M: Male, F: Female, SF: Spayed Female

TABLE I: Data of 16 dogs with generalized demodicosis

In the present study owners were informed about the extra-label use of oral ivermectin. For the treatment of generalized demodicosis, tablet form of ivermectin (Efektin tablet® 10 mg, Sanovel, Turkey) at a dose of 600 µg kg^{-1} daily was used in study dogs. To avoid and monitor any adverse effects due to individual sensitivity, the dose was gradually increased from 50 µg kg^{-1} body weight on day one, 100 µg kg^{-1} on day two, 150 µg kg^{-1} on day three, 200 µg kg^{-1} on day four, 300 µg kg^{-1} on day five and to the final dose of on day six. At sensitivity monitoring stage, as calculated dosages were very small to adopt, tablets were fractionated and weighted by use of an electronic balance to adjust to the weight of treated dogs. After no mites were seen (dead or alive), treatment was continued for 2 more weeks and then stopped. All dogs had followed up for 12 months after treatment stopped. During that time the owner was told to observe any skin lesions on their dog and if so return to the clinic for skin scrapings. Systemic antibiotics (e.g Amoxicillin-Clavulanic acid, Cephalexin) were given concurrently with ivermectin to dogs with pyoderma.

Treatment was considered as successful after complete resolution of clinical signs and skin scrapings from three different sites where mites had been previously identified were negative and remain negative for 12 months. Treatment was considered as failure if the disease is persisted despite therapy or if the dog relapsed within 12 months after ivermectin therapy lasted.

Results

Sixteen dogs with adult onset generalized demodicosis studied. Two was mixed-breed dog, 14 were pure breeds from 8 different breeds. Ten were sexually intact males, 3 were spayed, 3 were sexually intact females. Concurrent pyoderma was diagnosed 10 out of 16 dogs. No pododemodicosis was diagnosed.

All dogs had significant reduction in the in clinical signs and number of mites on skin scrapings during re-evaluations. Median treatment time was 10 weeks (6-22 weeks, mean 11.9 weeks). But three dogs relapsed 5, 8 and 9 months after the therapy lasted. Remained 13 dogs were negative for skin scrapings and clinically normal after 12 months. Relapsed 3 dogs received a second ivermectin therapy protocol and cured.

In the present study efficacy of oral ivermectin in the treatment of generalized demodicosis was found as 82,25 %. All dogs were well tolerated oral ivermectin therapy. No adverse reactions associated with ivermectin therapy seen. In haemogram and biochemistry panels no abnormal findings were noted.

Discussion

Ivermectin was first introduced as an antiparasitic drug in 1981. In small animals the sole indication of ivermectin is heartworm therapy. But effective extra-label use in sarcoptic mange, cheyletiellosis and other parasitic diseases were reported [5, 19, 24, 28]. Weekly parenteral administration protocol was found ineffective in the treatment of canine demodicosis [26, 30]. Ivermectin is not licensed for the treatment of generalized demodicosis. However the unregistered use of daily oral ivermectin is an effective alternative therapeutic for generalized demodicosis. The use of ivermectin in the treatment of canine demodicosis was first reported in 1985 [26]. There are reports evaluating the effectiveness of ivermectin at 300-600 µg kg^{-1} daily orally for the treatment of generalized demodicosis in the dog [4, 7, 14, 17, 23]. However, these studies were all conducted with the use of oral injectable formula of ivermectin. The present authors observed that amitraz rinses has poor owner compliance. The authors also have some experience about the difficulty of administering the bovine injectable formula of ivermectin due to its bitter taste; however this study showed that application difficulties prevented by using tablet form of ivermectin.

Two studies [2, 10] demonstrated that administration of oral tablet form of ivermectin at three dose level (6, 27 and 100 µg kg^{-1}) yielded linear increased peak plasma concentrations. Similar results were obtained by use of oral injectable formula of ivermectin [6]. These reports showed that plasma concentration of ivermectin does not influenced by the formulation when given orally.

When given per os daily with various dosage regiments, injectable formula of ivermectin found to be effective up to % 85 of adult dogs with generalized demodicosis [4, 7, 14, 23, 26]. In the present study, the administration of tablet form of ivermectin was resulted in resolving generalized demodicosis in 13 of 16 dogs (82,25 %.) in one year follow-up after discontinuing of therapy.

MEDLAU *et al* (1996) [14] had reported that 600 µg kg^{-1} ivermectin is more successful than other dose regiments. Fondati (1996) [4] also reported that the effectiveness of ivermectin is dose dependent. Because of its better success the present authors also decided to use the dosage of 600 µg kg^{-1}. It has been reported that generalized demodicosis may relapse even after 11 months following clinical remission [1, 26]. In the present study, three dogs relapsed 5, 8 and 9 months after the therapy lasted. These relapses were considered as failure.

Ivermectin has a wide safety margin. The highest single oral dose without adverse effects was reported as 2 mg kg^{-1}. In a study conducted with Beagles, approximate median lethal dose LD50 was found to be 80 mg kg^{-1} [22]. Adverse effects due to ivermectin are rare and included lethargy, tremor, ataxia, stupor, mydriasis, coma and death. These reactions are rarely occurs in most breeds. Purebred and mixed-bred Collies, Old English Sheepdogs, Shetland Sheepdogs and Australian Shepherd dogs are more sensitive to ivermectin toxicosis [12]. Signs of acute toxication may be seen in 4 to 12 hours after oral administration. More severe symptoms may be seen in earlier toxicosis [21]. Because of the relatively long half-life of ivermectin [13], chronic toxicity associated with therapy may develop with prolonged daily ivermectin treatment [12, 16, 22]. To avoid any adverse effects due to individual sensitivity, one report recommended to gradually increasing the dose of ivermectin administered from 50 µg kg^{-1} to 100, 200 and 300 µg kg^{-1} during the first days of treatment to monitor sensitive animals [18]. No any adverse effects were noticed at the beginning and during the course of the study that attributed to use of oral ivermectin. In the pre-

sent study the authors had used the dosage regimen as mentioned above, however the difficulty of dosage for small amounts, as it was the case in the present study, raises the need to develop more adapted drugs to the treatment of small animals.

Conclusion

Oral ivermectin, at a dosage of 600 µg kg^{-1}, PO, daily, was found to be effective in the treatment of generalized demodicosis in dogs. Tablet form of ivermectin is also more tolerable than the oral use of injectable formula.

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