SHORT COMMUNICATION

Efficacy of Ivermectin and Combination of Eprinomectin with Fipronil against Demodicosis in Cats

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Abstract

Parasitic skin diseases are important part of feline dermatology in general. Feline demodicosis is caused by *Demodex cati*, *Demodex gatoi* and an unnamed species. The present investigation was conducted to diagnose and study the haemato-biochemical alterations and therapeutic efficacy of ivermectin and eprinomectin with Fipronil in feline demodicosis. Clinical examinations of gross lesions and microscopic examination of deep skin scrapings were used for diagnosis. Haematological study revealed microcytic hypochromic anaemia, leucocytosis with neutrophilia, lymphopenia and eosinophilia in most of cats with demodicosis which improved significantly following 28 days of treatment. No significant change in plasma AST-ALT activity was noted in cats affected with demodicosis. The efficacy of different therapeutic regimens was assessed based on disappearance of clinical symptoms and restoration of altered haemato-biochemical parameters. It was found that both the regimen were effective for treatment of demodectic cats, however, the recovery rate was faster in group treated with spot on containing two acaricide drug eprinomectin and fipronil.

Key words: Cat, Demodicosis, Eprinomectin, Ivermectin.

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Introduction

The cat (*Felis catus*) is a domestic small carnivorous mammal. It is the only domesticated species in the family Felidae and is often referred to as the domestic cat to distinguish it from the wild members of the family. There are several types of mange in the cat including *Otodectosis, Notoedrosis, Cheyletiellosis,* and *Demodicosis* (Lliev *et al.,* 2019). *Demodicosis* is a skin condition caused by *Demodex* genus mites (Acariformes: Demodecidae). Feline demodicosis is uncommon to a rare condition, and it is caused by three species of *Demodex* mites (*D. cati, D. gatoi,* and an unnamed species). These mites show high host specificity and their location can vary according to species. Thus, *D. gatoi* is identified in the epidermal layer, as opposed to *D. cati,* which is found within the hair follicle (Ilie *et al.,* 2021).

In most cases, deep skin scraping is the diagnostic tool of choice. Also, therapeutic diagnosis can be performed by assessing the patient's response to miticidal treatment (Mueller *et al.,* 2020). Several drugs have been used to treat feline demodicosis, including organophosphate baths, rotenone, lime sulfur dips, amitraz rinses, ivermectin orally and injectable, selamectin, milbemycin oxime and a moxidectin/imidacloprid spot-on. This study was aimed to evaluate the haemato-biochemical alterations and compare the efficacy of ivermectin and a combination of eprinomectin with fipronil against Demodicosis in cats.

Materials and Methods

In the present study, a total number of 140 cats, presented at the Veterinary Clinical Complex, College of Veterinary Science and Animal Husbandry, Mhow (M.P.), and at Government Veterinary Hospital, and private pet clinics at Indore were screened. Clinical examinations of the affected cats revealed significant itching, alopecia, redness, hyper-keratinization, and crustation. Out of 140 cats examined 12 cats were positive for *Demodex* infestation. For haematological tests, 2 mL of blood samples were obtained in EDTA vials from 12 infected cats. Using an auto-haemo-analyzer (Model Abacus 380, make Diatron), haemoglobin (Hb), total erythrocytes count (TEC), packed cell volume (PCV), total leukocytic count (TLC) and

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differential leukocyte count (DLC) were determined. Plasma biochemical parameters, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were evaluated by a biochemical analyzer (Model SB-501, make Sinduri Biotech) using commercial kits (Erba Mannheim manufactured by Transasia Biomedicals Ltd).

For the therapeutic assessment, 12 cats positive for *Demodex* infestation were divided into two groups with each group having six cats. The demodectic cats were monitored before treatment and for four weeks after treatment. The weekly assessment was done post-treatment by deep skin scraping examinations in 10% potassium hydroxide solution, as per routine technique for microscopic analysis (Soulsby, 1982). The cats in group I were administered Ivermectin @ 0.2 mg/kg b.wt. subcutaneously at weekly intervals and the cats in group II were administered Spot-on combination of Fipronil 8.3% and Eprinomectin 0.4% single application. All the cats in the treatment groups were given Tab Enrofloxacin @ 5 mg/kg b.wt. orally for 5 days, and supplemented with liquid containing Omega-3 and Omega-6 fatty acids for a month. Treatment was continued until the cats were completely recovered. After therapy, two consecutive negative skin scrapings were regarded as confirmation of recovery from *Demodex* infestation. The data on haemato-biochemical profiles were analysed by one way ANOVA and DNMRT for treatment effect and by 't' test for group effect within the period (Snedecor and Cochran, 1994).

Results and Discussion

Clinical Findings

Clinical examination revealed the presence of erythematous patches, papules, severe crusting, scaling, alopecia, hyperpigmentation, and lichenification along with itching. The lesions were mostly distributed on-ear, face, nose, neck, peri-orbital, legs, and trunk region. The skin became thickened, grey, easily bled, and lost its elasticity, thereby sagging and forming folds. The same clinical findings were also observed in mites' infestation in cats by Sofyan *et al.* (2018) and Fular *et al.* (2019). The signs associated with the condition are attributable to irritation and inflammatory reactions caused by mites in the hair follicles resulting in damage of the epidermal cells and exudation produced by secondary bacterial and fungal infection. In the present study the lesions like alopecia, redness, hyperpigmentation and scratching subsided gradually with both the treatment regimen at day 14 and day 28, and the clinical effect was better with regimen II (Table 1).

In the present study the rectal temperature, pulse rate, and heart rate were recorded on day 0 (pre-treatment), 14^{th,} and 28th (post-treatment), respectively. The analysis of variance revealed non-significant ($p>0.05$) changes in rectal temperature, pulse rate, and respiration rate within and between groups affected with demodicosis. These findings corroborated with Tkacheva and Glazunova (2018).

Haemato-Biochemical Observations

The reduced levels of haemoglobin, PCV and total erythrocytes count in cats affected with demodectic mange were non-significantly improved following treatment in both the groups (Table 2). The significant decrease in haemoglobin and erythrocyte levels in demodecosis observed on day 0 has been reported earlier by Kano *et al.* (2012), Ozukum *et al.* (2019). The lower mean haemoglobin, PCV and erythrocytes concentration observed in demodicosis during the present study may be attributed to blood loss caused by the blood-sucking mites (Solanki and Hasnani, 2006), or due to stress arising from the disease (Sakina *et al.,* 2012). These values gradually improved and came to normal on the 28th day of treatment in both the groups (Table 2).

Total leucocyte count, neutrophils and eosinophils were significantly elevated, whereas lymphocyte values were significantly decreased in demodicosis affected cats on day 0, which improved significantly by day 14th and further improved towards normalcy by 28th day of treatment in both the groups. The mean values of monocytes were however not influenced by the demodicosis infection (Table 2). These altered TLC and DLC values were in accordance with the findings of Serieys *et al.* (2013). Neutrophilia is due to cell injury which in turn causes the release of substances such as leukotoxin and leucocytosis-promoting factors from the blood into the injured area resulting in the release of neutrophils in the bloodstream (Antipov *et al.,* 2017). The sharp increase of eosinophils in the blood of demodicosis affected cats is a sign of an allergic reaction because of intoxication by mites' metabolites (Ozukum *et al.,* 2019), which was resolved following both the treatment regimen.

In the present investigation there was a non-significant change in the plasma levels of ALT & AST values within

Table 1: Clinical presentation of cats with demodicosis on different days of treatment

Clinical observations	Groups of cats with demodicosis					
	Treatment I (n=6)			Treatment II (n=6)		
	0	14	28	0	14	28
Alopecia	6 (100%)	5 (83%)	2 (33%)	6 (100%	4 (66%)	2 (33%)
Redness	6 (100%	5 (83%)	2 (50%)	6 (100%	5 (83%)	1 (16%)
Hyper-keratinization	6 (100%	4 (66%)	2 (50%)	6 (100%	4 (66%)	1 (16%)
Scratching	6 (100%	5 (83%)	1 (16%)	6 (100%	3 (50%)	1 (16%)

Table 2: Haemato-biochemical values of demodicosis infected cats on different days of treatment

Parameters	Groups	0th Day	14th Day	28th Day
Hb (g/dL)	I	$8.59^{aA} \pm 0.27$	$11.70^{aA} \pm 0.31$	$12.07^{aA} \pm 0.11$
	II	$8.61^{aA} \pm 0.35$	$11.41^{aA} \pm 0.53$	$12.13^{aA} \pm 0.32$
PCV (%)	I	$32.83^{aA} \pm 1.35$	$34.16^{aA} \pm 0.87$	$34.83^{aA} \pm 0.40$
	II	$31.33^{aA} \pm 1.66$	$32.50^{aA} \pm 0.88$	$33.66^{aA} \pm 0.91$
TEC (10^6/mm^3)	I	$6.68^{aA} \pm 0.38$	$6.64^{aA} \pm 0.45$	$6.82^{aA} \pm 0.44$
	II	$6.56^{aA} \pm 0.15$	$6.53^{aA} \pm 0.14$	$6.97^{aA} \pm 0.24$
TLC (10^3/mm^3)	I	$26.90^{aA} \pm 0.7$	$22.75^{bA} \pm 0.47$	$20.15^{bA} \pm 0.61$
	II	$26.01^{aB} \pm 0.83$	$16.31^{bB} \pm 1.2$	$15.24^{bB} \pm 0.93$
Neutrophils (10^3/mm^3)	I	$73.16^{aA} \pm 2.42$	$62.16^{bA} \pm 1.35$	$57.16^{cA} \pm 0.60$
	II	$74.66^{aA} \pm 2.18$	$54.50^{bB} \pm 1.23$	$45.50^{cB} \pm 2.30$
Lymphocytes (10^3/mm^3)	I	$20.50^{aA} \pm 1.36$	$24.33^{bA} \pm 0.88$	$27.16^{cA} \pm 1.24$
	II	$18.16^{aB} \pm 0.70$	$26.00^{bB} \pm 0.68$	$30.50^{cB} \pm 1.17$
Monocytes (10^3/mm^3)	I	$0.33^{aA} \pm 0.21$	$0.33^{aA} \pm 0.21$	$0.33^{aA} \pm 0.21$
	II	$0.16^{aA} \pm 0.16$	$0.33^{aA} \pm 0.21$	$0.16^{aA} \pm 0.16$
Eosinophils (10^3/mm^3)	I	$15.16^{aA} \pm 0.94$	$7.83^{bA} \pm 0.47$	$4.00^{cA} \pm 0.63$
	II	$16.16^{aA} \pm 1.62$	$5.83^{bB} \pm 0.65$	$2.50^{cB} \pm 0.22$
ALT (IU/L)	I	$57.48^{aA} \pm 8.89$	$62.19^{aA} \pm 6.59$	$62.57^{aA} \pm 5.06$
	II	$61.23^{aA} \pm 4.17$	$62.33^{aA} \pm 5.64$	$58.30^{aA} \pm 0.99$
AST (IU/L)	I	$31.27^{Aa} \pm 0.94$	$29.58^{aA} \pm 1.66$	$30.94^{aA} \pm 1.44$
	II	$29.94^{Aa} \pm 0.67$	$29.7^{aA} \pm 0.16$	$29.76^{aA} \pm 0.94$

Mean values bearing uncommon superscripts within the row (a,b) or column (A,B) for a parameter differ significantly at $p<0.05$. Group I - Ivermectin @ 0.2 mg/kg b.wt. S/C at weekly interval, Group II- Spot-on (Fipronil 8.3% + Eprinomectin 0.4%) single application.

and between groups affected with demodicosis, and the treatments also did not cause any alteration (Table 2). These findings coincided with earlier research of Reddy *et al.* (2015).

Comparative Efficacy of Treatment

The therapeutic efficacies of two different groups were evaluated based on clinical signs and parasitological examinations. After 2 weeks of treatment, the skin scrapings were negative for mites and the therapy was considered successful, if the cat appeared clinically normal for 12 weeks after cessation of treatment.

The cats in group I were administered ivermectin @ 0.2 mg/kg b.wt. subcutaneously at weekly intervals. It inhibits the electric activity of nerve cells and causes paralysis and death of mites (Adams, 2001). Many workers have reported the therapeutic efficacy of ivermectin in demodicosis when used @ 0.2 mg/kg b.wt. subcutaneously at weekly intervals (Sivajothi *et al.,* 2015; Fular *et al.,* 2019).

The cats in group II were administered, Spot-on solution containing fipronil 8.3% and eprinomectin 0.4%, single application. Eprinomectin (eprinomectin B1), 4''-epiacetylamino-4''-deoxyavermectin B1, belongs to the macrolide class of parasiticides and the avermectin family. It is a semi-synthetic derivative of avermectin B1 or abamectin, which has a similar mechanism of action as ivermectin (Wolstenholme, 2012). Many workers have reported the therapeutic efficacy of topical eprinomectin in demodicosis when administered at 0.5 mg/kg body weight. Both groups were treated with supportive therapy as mentioned above. The recovery in terms of clinical signs, TLC, neutrophils, lymphocytes and eosinophils counts (Table 1, 2) was faster in group II treated with spot-on containing two acaricides like eprinomectin and fipronil and only one application was required in most cases of demodicosis. A complete recovery was observed after 28 days of treatment. The second application was required only in severe cases of demodicosis after 28 days of the first treatment. The recovery in group I treated by Inj. ivermectin was observed after 28 days of treatment, but most of the cases required 42 days for the complete recovery.

In general, it was found that the microscopic examination of deep skin scrapings is an effective method for the diagnosis of feline demodicosis, and the regimens comprising ivermectin as well as spot-on containing fipronil and eprinomectin were effective for treatment of demodectic cats. The recovery rate was faster in group treated with spot on containing two acaricide drug and brought the altered haemato-biochemical profile to normal within a month after single application.

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