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Therapeutic management of chronic generalized demodicosis in dogs

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Abstract
Present study was undertaken to compare the efficacy of two miticidal drugs for chronic generalized demodicosis in dogs. A total of 341 dogs were screened for chronic generalized demodicosis at TVCC, College of Veterinary Science and A.H., Jabalpur from August 2017 to April 2018. For therapeutic study, a total of 12 dogs having mange were divided randomly into two groups i.e. T_1 and T_2, each group comprising of 6 dogs. Groups T_1 and T_2 were treated with Tab Ivermectin and Inj Doramectin, respectively. Skin scraping examination was done on day 0 (pre treatment) and on days 15, 30, 45 (post treatment). On the basis of clinical recovery and presence of mite, Inj Doramectin @200 mcg/kg/week s/c (T_2) was found more effective.

Keywords: Demodicosis, Ivermectin, Doramectin, therapeutic response

1. Introduction
Demodicosis is a parasitic inflammatory skin disease of dogs caused by excessive proliferation of *Demodex canis*. Demodicosis is also referred as demodectic mange. These mites reside and feed in the hair follicles and oil glands of the skin [1]. Demodex mites are better considered as parasites that normally do not cause adverse effects on their host but sometimes that can act as opportunistic pathogens.

Chronic generalized demodicosis is characterized by five or more affected areas or by lesions covering an entire region of the body and/or pododemodicosis involving two or more paws [2]. Pathological changes include erythema, papules, lichenification, crusts in the feet, face, pinnae, abdominal skin, flank and/or in the lumbar area. Alopecia and scaling on the ventral aspects of the chest, all four limbs, ventral aspect of the neck and around the eyes may also be found [3]. Receptivity of dogs to demodicosis and progression of the clinical disease is influenced by factors like genetic predisposition, malnutrition and immunosuppression.

Demodicosis is diagnosed by performing skin scrapings. Scraping should be obtained from multiple areas and should be deep enough to produce capillary bleeding while squeezing the area being scraped which forces mites deep in the hair follicle to the surface. Microscopically, fusiform eggs, six-legged larvae, eight legged nymphs or eight-legged adult mites can be seen [4].

Currently available therapeutic options to treat generalized demodicosis entail daily, weekly, fortnightly or monthly treatments for periods of 2 months or more. The clinical cure is clearly associated with parasiticidal treatment and a reduction in the number of demodex mites. As with all macrocyclic lactones, ivermectin can cause severe neurologic adverse effects, from lethargy, tremors, mydriasis and ataxia up to coma and death in sensitive individuals. For this reason, it is strongly recommended to start with a dose of 0.05 to 0.1 mg/kg and increase the dose to 0.3 to 0.6 mg/kg in the first 4 days. Doramectin is a miticidal drug in the same group as ivermectin has been used for the treatment of canine demodicosis [5].

2. Materials and methods
The proposed work was conducted in the Department of Veterinary Medicine, College of Veterinary Science and Animal Husbandry, Nanaji Deshmukh Veterinary Science University, Jabalpur (M.P.). A total of 341 dogs having dermatological disorders were screened at TVCC, College of Veterinary Science and A.H., Jabalpur from August 2017 to April 2018. Complete history of the dogs was recorded including age, sex, breed and duration of illness.

All the dogs were thoroughly examined for the presence of any visible skin lesions like scab, erythema, pruritus, papules, alopecia and pigmentation. The skin scrapings of these dogs were examined microscopically as per the standard procedure [6] for the presence of *Demodex canis* mite. Out of 341 dogs, 67 were found positive for *Demodex canis* mite. For therapeutic study, a total of 12 dogs having mange due to *Demodex canis* were divided randomly into two groups i.e. T_1 and T_2, each group comprising of 6 dogs. These dogs were subjected to the following treatment regimen (Table 01).

To evaluate the efficacy of treatment, improvement in clinical parameters viz. alopecia, erythema, papaules, pruritus and hyperkeratosis were observed on days 0 (pre treatment) and on days 15, 30, 45 (post treatment). Moreover, to record the presence/absence of mites, deep skin scrapings of these dogs (so that capillary oozing occurs) were collected on day 0 (pre treatment) and on days 15, 30, 45 (post treatment).

Table 1: Experimental design for therapeutic trial

Group	No. of animals	Drugs and dosage
T_1	6	Ivermectin @ 0.05 mg/kg PO-1st,2nd day @ 0.1mg/kg PO-3rd,4th day @ 0.2mg/kg PO-5th, 6th day @ 0.3mg/kg PO-7th, 8th day @ 0.4mg/kg PO-9th, 10th day And thereafter continued upto 45 days
T_2	6	Doramectin @ 200 mcg /kg /week s/c for 6 weeks

3. Results and discussion

3.1 Clinical assessment

Various clinical symptoms were observed during the study period in 12 demodectic dogs. Affected dogs showed a combination of symptoms i.e alopecia, erythema, papaules, pruritus and hyperkeratosis. In the affected dogs the predominant symptoms were pruritus, alopecia and erythema i.e. 91.6 percent (11 out of 12) followed by papules and hyperkeratosis i.e. 41.6 percent (5 out of 12) (Table 02).

Table 2: Clinical picture of chronic generalized demodicosis in dogs (n=12)

Clinical signs	Frequency	Percentage
Pruritus	11	91.6
Alopecia	11	91.6
Erythema	11	91.6
Papules	05	41.6
Hyperkeratosis	05	41.6

Results of the present study are in accordance with the work of Janus *et al.* [7] who observed multifocal areas of alopecia, erythema and hyperpigmentation on head, trunk and legs in chronic generalized demodicosis affected dogs. Yatoo *et al.* [1] also noticed alopecia, crusting of skin and pustules around ventral abdomen, face, neck and back in the demodectic dog. Similarly Kumari *et al.* [8] recorded itching, alopecia, pustules, bad odour, erythema, hyper pigmentation, scales, lichenification, nodules, crusts, pododemodicosis and keratinization in demodectic dogs.

3.2 Evaluation of therapeutic response

The therapeutic response of different treatments was evaluated on the basis of clinical signs like pruritus, alopecia, erythema, papules and skin scraping examination of all the dogs under therapeutic trial on day 0 (pre treatment) and on days 15, 30, 45 (post treatment).

3.3 GroupT_1 (Tablet Ivermectin)

Results revealed that on clinical observation in chronic generalized demodicosis affected dogs on day '0', pruritus and erythema was observed in all 6 dogs whereas alopecia, hyperkeratosis and papules were seen in 5, 3 and 2 dogs, respectively. On day 45 (post treatment), all the dogs showed recovery in pruritus and papules whereas alopecia, erythema and hyperkeratosis were still present in 1 dog. No mites were seen on skin scraping examination on day 45 post treatment (Table 03).

Table 3: Evaluation of therapeutic response of dogs of group T_1 (n=6)

Parameters	Days			
Clinical observation	**0**	**15**	**30**	**45**
Pruritus	6	5	2	0
Alopecia	5	5	3	1
Erythema	6	4	2	1
Papules	2	2	0	0
Hyperkeratosis	3	3	3	1
Presence of mite	6	3	1	0

The incremental dose of ivermectin used in the present study was in accordance with Mueller *et al.* [9] who reported that a gradual increase of the ivermectin dose within the therapeutic ranges (50 mcg/kg b.wt. on day one to the final dose of 300 mcg/kg body weight from day five onwards until resolution for demodicosis) is recommended for generalized demodicosis in dogs. Similarly Reddy *et al.* [10] and Karakurum *et al.* [11] observed that the incremental doses of ivermectin for treating Demodex mite resulted in complete disappearance of mites and re-growth of hair.

Ivermectin selectively binds to glutamate- gated and gamma-aminobutyric acid (GABA)-gated chloride cannels in the mite's nervous system, resulting in cell hyper polarization, mite paralysis and finally death. The most worrisome aspect of treatment with ivermectin is the acute neurologic toxicity. Although, the toxicity is common in Collie and its related breeds but it can occur in any dog. So the safety of ivermectin treatment may be improved by gradual increasing the dose over several days until the desired dose is reached [12].

3.4 Group T_2 (Injection Doramectin)

Results in affected dogs revealed that on day 0, alopecia was observed in 6 dogs, pruritus and erythema in 5 dogs and papules, hyperkeratosis in 3 and 2 dogs, respectively. On day 45 post treatment, pruritus, erythema and papules recovered in all dogs. However, alopecia and hyperkeratosis was seen in only 1 dog. No mites were seen in all the dogs of this group from 30 day post treatment onwards (Table 04).

Table 4: Evaluation of therapeutic response of dogs of group T_2 (n=6)

Parameters	Days			
Clinical observation	**0**	**15**	**30**	**45**
Pruritus	5	4	2	0
Alopecia	6	5	3	1
Erythema	5	3	2	0
Papules	3	2	0	0
Hyperkeratosis	2	2	1	1
Presence of mite	6	2	0	0

Similar studies were conducted by Hutt *et al*. [13] who reported that doramectin @ 0.6 mg/kg body weight subcutaneously, once in a week was safe and effective for generalized demodicosis in dogs and the mean treatment duration was of 7.1 weeks.

Doramectin is an avermectin antiparasitic agent that is often used to treat endoparasites and ectoparasites in dogs. It is a miticidal drug and is neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in mites. Paralysis and death of the mite is caused by increased permeability to chloride ions and hyperpolarization of nerve cells.

The better efficacy of doramectin as compared to ivermectin might be due to the reason that there is a pharmacokinetic difference between doramectin and ivermectin. Doramectin has a lower clearance, lower volume of distribution and probably a higher bio-availability as compared to ivermectin and therefore doramectin may have a longer duration of preventive efficacy [14].

After completion of therapy on day 45 post treatment, the comparison of therapeutic response evaluation of treatment groups revealed that complete clinical recovery from pruritus, erythema and papules was observed in 100% dogs of group T_2 and no mites were seen on microscopic skin scraping examination. On the basis of clinical observation and presence of mite, Injection Doramectin @200 mcg/kg/week s/c (T_2) was found to be more effective than Tablet Ivermectin (T_1) (Table 05).

Table 5: Comparative evaluation of therapeutic response of treatment groups

Parameters	Percent Recovery	
Clinical observation	**T_1**	**T_2**
Pruritus	100	100
Alopecia	80	83
Erythema	83.3	100
Papules	100	100
Hyperkeratosis	66.6	50
Absence of mite	100	100

4. Conclusion

In the present study on the basis of percent recovery in the parameters of clinical observation, it can be concluded that Injection Doramectin @200 mcg/kg/week s/c was found to be more effective than Tab Ivermectin.

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