

INDIVIDUAL AND COMBINED ANTI-DEMODICOSIS EFFECT OF IVERMECTIN AND AMITRAZ IN THE TREATMENT OF NATURAL CANINE DEMODICOSIS- A CLINICAL STUDY

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ABSTRACT

The present study's essence was to determine the individual and combined anti-demodicosis effect of oral administration of ivermectin and application of amitraz rinse. Eighteen naturally affected canine were randomly divided into three groups of six animals each. Group I was administered with ivermectin tablet @ 0.4 mg/kg body weight, whereas group II was applied amitraz rinse @ 0.05% locally for six occasions on seven days interval. Group III was administered the combined ivermectin tablet @ 0.3 mg/kg body weight and amitraz rinse of 0.025% locally, allowing three days difference between the medication at one-week intervals six occasions. Cephalixin to guard secondary bacterial infection; skin tonic to boost the skin regrowth and benzyl peroxidase shampoo to remove dirt and crust of the skin was also advised for all groups. The combined therapy group with ivermectin and amitraz has better recovery in terms of total recovery of the animal without relapse, followed by the ivermectin and amitraz rinse groups.

Key words: Canine, demodicosis, ivermectin, amitraz

Introduction

Small animal veterinarians encounter many dermatological disorders, constituting up to 75 % as a major complaint from the pet owners (Shah *et al.*, 2017). Demodicosis or demodectic mange is one of the common contagious dermatopathic conditions encountered worldwide in canine. *Demodex canis*, a parasitic mite, has been identified as the primary cause of the disease; however other mites viz., *Demodex injai* and *Demodex cornei* are also responsible for similar conditions (Tater and Patterson, 2008). *Demodex canis* (D. canis), otherwise recognized as a demodectic mite or follicular mite or red mite, is a typical inhabitant of young dogs' hair follicle and sebaceous glands and is acquired during nurturing from its dam (Sharma and Pokharel, 2019). Clinical demodicosis occurs due to the severe proliferation of mites in the hair follicle due to immune suppression or any defects which can affect skin immunity. Elderly and young dogs from three months to a year mostly have clinical conditions (Sharma and Wadhwa, 2018). Demodicosis occurs in two forms viz. localized (Juvenile) and generalized. Localized (Juvenile) form is characterized by one or two bald spots chiefly around the eye, muzzle, face and leg self-limiting in most cases (Sharma and Wadhwa, 2018).

Contrary to it, generalized demodicosis involves more than five or more sites, characterized by erythematous, patchy lesion, scale and papule (Sharma and Wadhwa, 2018). Suppose unattended skin turns crusted and ulcerated due to secondary infections. In the present scenario, deep skin scrapings are the gold standard diagnostic test in the suspect (Mueller *et al.*, 2012). The therapeutic regime for canine demodicosis is multifocal (such as acaricidal therapy, secondary infections treatment, skin tonic). Conventional therapeutic regimes with

variable efficacy, such as amitraz rinse, ivermectin, doramectin, milbemycin, moxidectin, are already in use (Ranjan *et al.*, 2014). Amitraz, the first drug approved for canine demodicosis, was less efficacious in adult demodicosis and toxic for both pet and pet owner (Mueller *et al.*, 2012; Arsenovic *et al.*, 2015). Again macrocyclic lactones also have few demerits such as recurrence and toxicity in some breeds (Mueller *et al.*, 2012; Arsenovic *et al.*, 2015). The remission and recurrence depend on various factors such as used acaricides, duration of treatment, age of patients, and associated infection treatment (Arsenovic *et al.*, 2015). As per the author's information, no systemic study to ascertain the anti-demodicosis effect of the drug for canine in the north bank of Brahmaputra valley, Assam, was reported. Hence, this study essence was undertaken to ascertain the anti-demodicosis effect of ivermectin and amitraz each and together in the treatment of natural generalized canine demodicosis to find treatment with better efficacy and shorter duration.

Materials and Methods

Eighteen privately owned canines admitted to the Veterinary Clinical Complex at Lakhimpur College of Veterinary Science in Assam, India, for therapeutic consultation with clinical symptoms of generalized demodicosis as shown in (Fig. 1-4) (lesion size >2.5 cm and lesions at more than five sites) (Koch, 2017) and multiple positive skin scrapings for *D. canis* were enrolled in the present study for one and a half years between January 2019 and July 2020. Relevant data concerning age, sex, breed of the patients were recorded. Most dogs (n=12) were cross, while three Rottweilers, two Labrador retrievers, and one German shepherd. The patient's age was between 3 months to 2 years consisting of three females and nine males.

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Fig. 1: Mange lesion in a G. shepherd



Fig. 2: Mange lesion in a Rottweiler

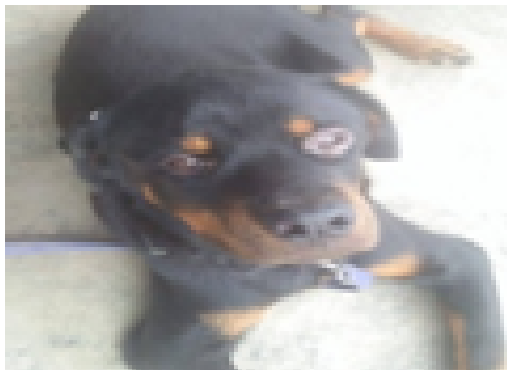


Fig. 3: Mange lesion around eye in Rottweiler

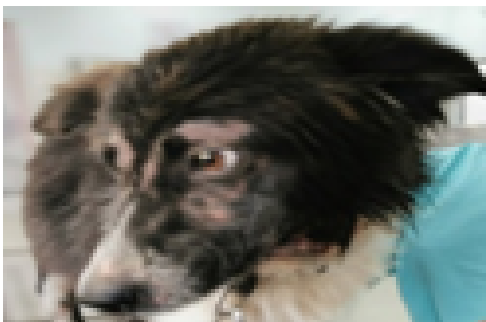


Fig. 4: Mange lesion around eye and face in Crossbred

Deep skin scrapings were collected at each visit initially at a two-week interval for eight weeks, followed by three months break for one and a half years. Skin scrapings were collected from six affected skin sites, in the parallel direction of hair growth using a sterilized scalpel blade until capillary bleeding occurred in 10% potassium hydroxide (KOH) solution (Sharma and Wadhwa, 2018). The collected skin sample was transferred to a slide, mixed with mineral oil, and examined microscopically at 10X magnification to determine whether the representatives were positive or negative for *D. canis* (Fig. 5). For all the animals before inclusion in the study protocol, a complete blood count, estimation of T3, T4, and TSH, fecal examination to rule out any underlying diseases. Patients suspected of other underlying conditions were not included in the present study.

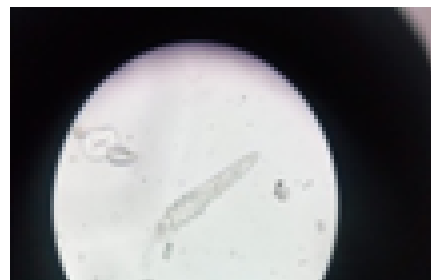


Fig. 5: Demodex canis under 10X resolution

Affected animals, irrespective of age, sex, breed, were divided into three equal treatment groups with six animals in each group viz. group I, group II, and group III. Each animal of the treatment groups was assigned an identification number i.e., AN1, AN2, AN3, AN4, AN5, AN6. As suggested by Singh *et al.* (2011), Mueller *et al.* (2012) and Arsenovic *et al.* (2015), the following treatment protocol was advised in the treatment groups.

Group I - Ivermectin

Neomec® tablet (Ivermectin, Intas pharmaceutical, India) @ 0.4 mg/kg body weight subcutaneous at a one-week interval for six occasions.

Group II- Amitraz rinse

Ridd® rinse (12.5 % liquid Ayurvet PVT.LTD.) @ 0.05 % at one-week interval for six occasions.

Group III- Ivermectin and Amitraz rinse

Neomec® tablet (Ivermectin, Intas pharmaceutical, India) @ 0.3 mg/kg body weight orally Ridd® rinse (Ayrvet PVT.LTD.) @ 0.025 % allowing three days interval between both the medication at the one-week interval for six occasions.

For all the treatment groups, the pet owners were advised to monitor for adverse effects closely. All the treatment groups were further advised with antibiotic Lixen® palatab (Cephalexin, Virbac Animal Health India Pvt. Ltd.) @15 mg per kg b.wt. twice daily orally for 14 days to guard the secondary bacterial infection, nutritional support for skin, Skin & Coat® (Omega 3 & 6 fatty acids, ascorbic acid, zinc, eicosapentaenoic acid, docosahexaenoic acid, Vit E, biotin, turmeric extract, green tea extract), Drools, Abis Exports India Pvt.Ltd) @ 5 ml twice daily orally for 60 days and PetBen® shampoo (Provimi Animal Nutrition India Pvt. Ltd.) as body a wash at weekly intervals for

six occasions was advised to remove the skin's crust and debris.

For group II and group III, before amitraz rinses, it was advised to clip the hairs for all the medium to long hair coat animals and be repeated for each application. The rinse should be applied carefully with a sponge on the skin and allowed to be air dry.

Treatment efficacy was witnessed based on the remission and recurrence of the demodicosis based on the clinical findings (Fig. 6-9) followed by skin samples positive or negative for *D. canis*. Affected pets were considered free only after two consecutive negative skin scrapping examinations for Demodex (Mueller *et al.*, 2012). The pet found positive for demodicosis after completing the treatment (42 days) and positive for the recurrence after recovery of *D. canis* were excluded from the study and shifted to other feasible conservative therapy.



Fig. 6: G.shepherd on post treatment 30th day

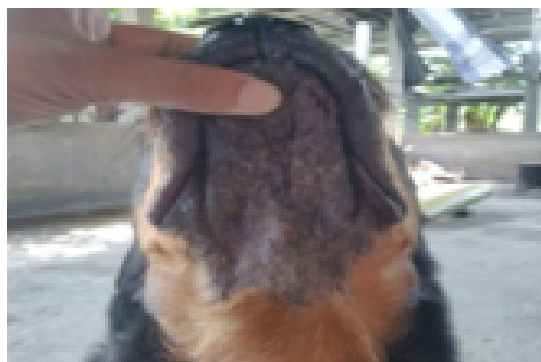


Fig. 7: Rottweiler on post treatment 30th day

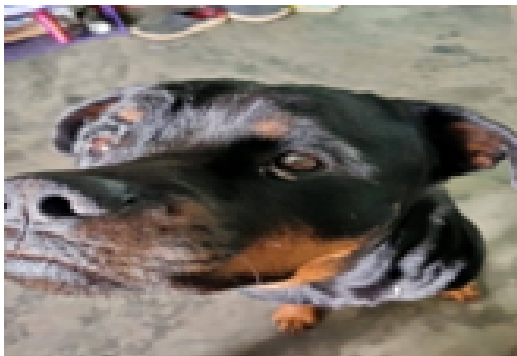


Fig. 8: Rottweiler on post treatment 30th day

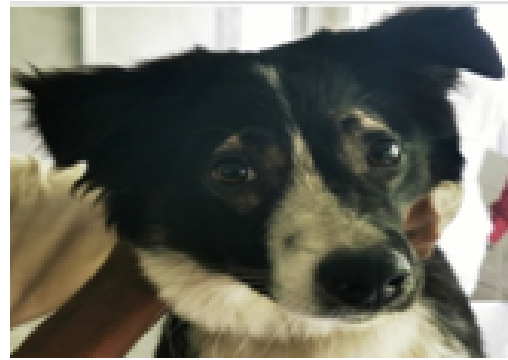


Fig. 9: Crossbred on post treatment 30th day

Results and Discussion

In group I, which was treated with oral ivermectin and other supportive therapy, four animals at the end of the study period (506th day) completely recovered from demodicosis. One animal (AN4) was excluded from the study on the 42nd day being positive for mite. One animal (AN2) was excluded from the study on 146th day for being positive for demodicosis after negative on the 56th day. Both the excluded pet were shifted to feasible conservative therapy.

In group II which was treated with amitraz rinse and supportive therapy, only three animals at the end of the study period completely recovered from demodicosis. One animal (AN2) at the end of 42nd day due to non-recovery and two animals (AN5 and AN6) on the 326th and 412th day for recurrence were excluded from the study and shifted to feasible conservative therapy.

In group III, treated with a combination of ivermectin orally and amitraz rinse along with other supportive therapy, all animals recovered with no relapse.

Ivermectin is not approved for canine demodicosis (Mueller *et al.*, 2012). However, it has been used with a variable and inconsistent efficacy as a subcutaneous injection @ 0.4 mg per kg on weekly intervals (Mueller *et al.*, 2012). Singh *et al.* (2011), Mueller *et al.* (2012) and Koch (2017) have also suggested good evidence with the oral ivermectin at the dose rate of 0.3-0.6 mg/kg orally every 24 hours. Amitraz is the approved drug for adult canine demodicosis in many countries for decades. Singh *et al.* (2011), Mueller *et al.* (2012), Arsenovic *et al.* (2015) and Koch (2017) reviewed and reported good efficacy of amitraz rinse with concentration ranging from 0.025 to 0.6 % with a frequency of weekly or once in two weeks. Mueller *et al.* (2012) reported better clinical efficacy with higher concentration and shorter intervals. Again Medleau and Willemse (1995) and Hugnet *et al.* (2001) advised daily rinse of 0.125 % and weekly rinse of 1.25% rinse of amitraz in refractory cases, respectively. Atipamazole (0.1 mg/kg body weight, IM) and yohimbine (0.1 mg/kg body weight for three days was also advised by Hugnet *et al.* (2001) to minimize the adverse effect of amitraz.

In the present study, neither of the individual therapeutic protocol was completely successful in the cure of all the animal without relapse. However, complete recovery was recorded in the combined therapy group. Our study corroborated the findings of Manu *et al.* (2019), where combination therapy (ivermectin 0.4 mg/kg body weight subcutaneous and amitraz

dip @ 0.05 %) on every five days for 45 days was successful in the treatment of generalized demodicosis. Our combined therapy cure result also corroborated the finding of Kumari *et al.* (2017) and Manjusha *et al.* (2018). The relapse of the cases in the present study can be supported by recent studies of Arsenovic *et al.* (2015) and Koch (2017). Arsenovic *et al.* (2015) concluded that recovery, remission and recurrence mostly depended on used acaricides, the average age of patients, and secondary infection treatment. Koch (2017) also suggested associated underlying health conditions can also be attributed as an important factor for the cure. No satisfactory result in individual therapy protocol was similar to the findings of Manu *et al.* (2019), where individual amitraz rinse and subcutaneous ivermectin injection was able to cure the demodicosis initially, but the occurrence was reported as drugs were discontinued.

In the present work, cephalixin was used to guard secondary bacterial infection, as suggested by Mueller *et al.* (2012), Singh *et al.* (2011), Arsenovic *et al.* (2015) and Manjusha *et al.* (2018). Benzyl peroxide treatment helps to control the amount of Demodex mites in the hair follicle through follicular flushing. Manjusha *et al.* (2018) and Sharma and Wadhwa (2018) have also suggested the use of benzyl peroxide shampoo for the synergistic effect of the drugs. Skin tonic use has also been suggested by Mueller *et al.* (2012), Singh *et al.* (2011), Arsenovic *et al.* (2015), Manjusha *et al.* (2018) and Sharma and Wadhwa (2018) as skin and coat® was used in the present study.

From this study, combination therapy along, with other supportive drugs can be suggested, provided all the associated adverse toxicity precaution and underlying disease conditions can be considered. Single therapy might take longer duration and might not be as effective as combination therapy. Veterinarians should try to follow the manufacturer label and also the instruction of the regulatory authority in their respective areas. This is an observational study. It warrants an extended detailed study on a larger group of patients. Further studies are required on large scale in this part of India.

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