RESEARCH ARTICLE

Comparative Efficacy of Different Treatment Regimens of Miticidal Drugs in the Clinical Management of Canine Generalized Demodicosis

Mayank Parwari*, Ghanshyam C. Mandali, Jignasha M. Parmar

Abstract

The present study compared the efficacy of amitraz, doramectin, imidacloprid + moxidectin, test product (Green clean), and its combinations in the clinical management of canine generalized demodicosis. A total of 48 positive cases of generalized demodicosis were selected for the therapeutic trial. The affected dogs were divided into 6 groups, *viz*., A, B, C, D, E, and F; each group comprised 8 dogs. Six healthy dogs negative for demodectic mites were also used as control (group G) for comparison. The response to treatment was assessed by conducting a clinical examination and parasitological examination of cases at weekly intervals included in the therapeutic trial till clinical recovery (4-7 weeks) or treatment failure. Treatment regimens comprising of a combination of systemic miticidal drugs (doramectin @ 600 µg/kg b.wt. s/c weekly) and a topical miticidal compound (amitraz @ 500 ppm spray weekly or test product 5% spray twice daily) with supportive therapy were more efficacious in resolving the lesions and eliminating the mites than the treatment regimens having single drug (doramectin/amitraz/test product). The combination therapy, along with supportive therapy with benzyl peroxide shampoo, produced appreciable therapeutic results. There was no significant difference between different treatment groups, except Group D (test product), which took a long time for clinical cure.

Keywords: Amitraz, Canine generalized demodicosis, Doramectin, Imidacloprid + Moxidectin, Test product, Treatment regimen.

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Introduction

Demodicosis, also named as demodectic mange, is a common but exigent, inflammatory, non-contagious parasitic dermatosis caused by over population of the host-specific follicular mites of various *Demodex* species (Ravera *et al.,* 2015; Shrestha *et al*., 2015). Canine generalized demodicosis (CGD) may be a severe and potentially life-threatening disease. Treatment for canine generalized demodicosis includes amitraz, ivermectin, milbemycin oxime, moxidectin and doramectin (Paterson *et al.,* 2009; Singh *et al.,* 2011; Perego *et al.,* 2019). Macrocyclic lactones include two groups of molecules: avermectins (ivermectin, doramectin, selamectin, abamectin, and eprinomectin), and milbemycins (milbemycin oxime and moxidectin). All of these molecules have a similar mode of action (Mueller, 2012). Amitraz is an inhibitor of monoamine oxidase and prostaglandin synthesis and acts as an α-2 adrenergic agonist. It is a member of the formamidine family and is a broad-spectrum miticide (Hugnet, 2001 and Cerundolo, 2017). Test product (Green clean, Table 1) is a recent nanotechnology-based formulation containing alkyl polyglycosides of herbs (Nauriyal, 2015), claimed to be effective against generalized demodicosis. Therefore, the present study was aimed to investigate the comparative efficacy of different treatment regimens of miticidal drugs in the clinical management of canine generalized demodicosis.

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Materials and Methods

The dogs with clinical manifestations of different dermatological afflictions brought to Veterinary Clinical Complex (VCC) of the College of veterinary sciences and A.H., Anand and VCARE, Vadodara were taken into consideration for the study. Forty-eight dogs found positive for *Demodex canis* were selected for the therapeutic trial. These dogs were divided in six groups consisting of eight animals each group. Each dog was examined at weekly intervals by deep skin scrapings during the treatment course of 4 to 7 weeks for *Demodex* mites and

Table 1: Composition of test product (Green clean™)

Sr. No.	*Ingredient*	*Botanical name*	*Used part*	*Comp.(%)*
1	Processed coconut extracts	*Cocos nucifera*	Fruit rind	20.00
2	Processed corn extracts	*Zea maize*	Fruit	20.00
3	Processed extracts of sugarcane	*Saccharum officinarum*	Extract	26.00
4	Water	-	-	19
5	Citronella oil	*Cymbo pogon*	Oil	00.10
6	Cinnamon oil	*Cinnamom umverum*	Oil	00.10
7	Cedar oil	*Cedrus deodara*	Oil	00.10
8	Mint oil	*Menthe piperita*	Oil	00.10
9	Spear mint oil	*Menthe arvensis*	Oil	00.10
10	Geranium oil	*Geranium wallichianum*	Oil	00.10
11	Water lilly oil	*Nymphea alba*	Oil	00.10
12	Karanja oil	*Pongamia pinnata*	Oil	00.10
13	Neem oil	*Azadirachta indica*	Oil	00.20
14	Excipient	-	-	q.s.

clinical cure. Six healthy dogs negative for demodectic mites were also used as control (Group G) for comparison.

The dogs in Group A received inj. Doramectin @ 600 µg/kg b.wt. Subcutaneously at weekly intervals. The dogs in Group B received Liq. Amitraz @ 500 ppm as whole body spray at weekly interval. The dogs in Group C received Spot-on Advocate (imidacloprid 10 % + moxidectin 2.5%) at weekly intervals as per the animal's body weight. The dogs in Group D received a test product (Table 1) @ 5% solution whole body spray twice daily. The dogs in Group E were administered inj. Doramectin @ 600 µg/kg b.wt. subcutaneously at weekly interval together with amitraz as whole body spray @ 500 ppm at weekly interval. The dogs in Group F were administered inj. Doramectin @ 600 µg/kg b.wt. subcutaneously at weekly and test product as whole body spray @ 5 % sol twice daily. The dogs belonging to all six groups received supportive therapy in bathing with benzyl peroxide shampoo at weekly intervals and essential fatty acids with vitamin A, D, and E supplementation.

The response to treatment was assessed by clinical recovery or treatment failure. Skin scrapings were taken from approximately the same site on every examination. If any mites, dead or alive, were seen, treatment was continued. If no mites were seen, the treatment was continued for 2 weeks and then stopped. The therapeutic trial data was compiled into an Excel spreadsheet (Office 2010, Microsoft, India) and analyzed using statistical analysis in social science (SPSS) for Windows (Version 24.0, IBM India). One way ANOVA test was performed for therapeutic trial. The results were presented as mean ± standard error (SE) (Snedecor and Cochran, 1994).

Results and Discussion

The clinical and parasitological recovery recorded in the dogs of group A (doramectin @ 600 µg/kg b.wt. s/c) was in the range of 4 to 7 weeks with the mean of 5.75 ± 0.37 weeks (Table 2). One dog recovered after 4 weeks; two dogs after 5 weeks; three dogs after 6 weeks; and two dogs after 7 weeks of therapy. Many workers have reported the therapeutic efficacy of doramectin in demodicosis when used @ 600 µg/kg b.wt. weekly by subcutaneous or intramuscular route (Dimri *et al.*, 2009 and Hutt *et al.,* 2015).

In dogs in Group B treated with amitraz @ 500 ppm as whole body spray at the weekly interval, the clinical and parasitological recovery ranged from 5 to 7 weeks with a mean of 5.5 ± 0.60 weeks. In this group, one dog recovered after 5 weeks; two dogs after 6 weeks; three dogs after 7 weeks, and two dogs after 8 weeks of therapy. Recommended treatment protocols vary from 250 ppm amitraz rinses used every 2 weeks (Mueller, 2012 and Chansiripornchai and Chansiripornchai, 2017) to 500 ppm weekly (Patel, 2012; Kumar *et al.,* 2012). The success rate of amitraz therapy in canine demodicosis varies from 0 to 92.5% (Medlau and Willemse, 1995). We used amitraz @ 500 ppm as whole body spray at weekly interval and achieved good results at par with doramectin, spot-on approach, and its combination (Table 2).

Dogs in the Group C treated with the topical formulation (2.5% moxidectin + 10% imidacloprid) as spot-on at weekly interval showed clinical and parasitological recovery in 4 to 6 weeks with the mean of 5.38 ± 0.26 weeks (Table 2). One dog of this group recovered after 4 weeks; three dogs recovered after 5 weeks, and four dogs after 6 weeks of therapy. Many workers have reported therapeutic efficacy of a combination of imidacloprid 10% + moxidectin 2.5% spot-on approach in demodicosis (Paterson *et al.,* 2014 and Fourie *et al.*, 2015). Fourie *et al.* (2009) compared the efficacy of two treatment regimens using an imidacloprid 10 % plus moxidectin 2.5% topical formulation (Advocate®, Bayer) on dogs with generalized demodicosis at 7 and 28 days intervals and observed a consistently greater reduction in mite numbers for the weekly treatment regimen as compared to 28-day intervals.

Table 2: Summary of clinical improvement after multiple treatments of canine demodicosis

Treatment group	*Drug used*	*No. of dogs*	*Recovery time (weeks)*
Group-A	inj. Doramectin @ 600 µg/kg b.wt., weekly	8	5.75 ± 0.37[a]
Group-B	liq. Amitraz @ 500 ppm as body spray, weekly	8	5.50 ± 0.60[a]
Group-C	Spot-on (imidacloprid 10%+ moxidectin 2.5%), weekly	8	5.38 ± 0.26[a]
Group-D	Green Clean™ @ 5% solution whole body spray twice daily	8	7.25 ± 0.60[b]
Group-E	Combination of Gr A + Gr B	8	4.50 ± 0.33[a]
Group-F	Combination of Gr A + Gr D	8	5.00 ± 0.38[a]

Means with the same superscript in a column do not differ significantly ($p > 0.05$).

In Group D, dogs treated with test product (Green Clean™) @ 5% solution as whole body sprays twice a day had the clinical and parasitological recovery in 5 to 9 weeks with the mean of 7.25 ± 0.60 weeks, being significantly longer than all other approaches (Table 2). In this group, two dogs recovered after 5 weeks; one dog after 6 weeks; three dogs after 8 weeks, and two dogs after 9 weeks of therapy. Nauriyal (2015) evaluated *in vivo* efficacy of Green Clean™ (2.0% twice a day, twice a week and 3.0% twice a day, twice a week) in clinical cases of canine dermatological infections/infestations and reported a higher concentration of the product being more effective.

Dogs in Group E were treated with the combination of doramectin @ 600 µg/kg b.wt. weekly by the subcutaneous route, amitraz @ 500 ppm weekly as a whole body spray and immune modulators, revealed the clinical and parasitological recovery in 3-6 weeks with a mean of 4.50 ± 0.33 weeks, being the lowest among all approaches (Table 2). Here one dog recovered after 3 weeks; 3 dogs recovered after 4 weeks; three dogs recovered after 5 weeks, and one dog after 6 weeks of therapy. Chansiripornchai and Chansiripornchai (2017) reported recovery of two dogs with chronic generalized demodicosis using doramectin @ 600 µg/kg b.wt. s/c at weekly interval and amitraz @ 250 ppm weekly as whole body spray for 6 weeks.

Dogs belonging to Group F were treated with the combination of doramectin @ 600 µg/kg b.wt. s/c at weekly interval and test product (Green Clean™) @ 5 % solution as whole body sprays twice a day showed the clinical and parasitological recovery in 4 to 7 weeks with a mean of 5.00 ± 0.38 weeks. Three dogs of this group recovered after 4 weeks; three dogs recovered after 5 weeks; one dog after 6 weeks, and one dog after 7 weeks of therapy. In our study, none of the treated dogs with any approach showed adverse reactions, and there was no relapse in any case. Doramectin, amitraz, moxidectin + imidacloprid, and test product (Green Clean™) were found safe and efficacious in the treatment of canine demodicosis. It is assumed that the combination of avermectin (doramectin) and formamide compound (amitraz) produces better results and early recovery in canine demodicosis.

Conclusion

Based on the severity of lesions and the time taken for the clinical and parasitological cure of dogs with canine demodicosis following different approaches. It can be concluded that all treatment regimens comprising combinations of systemic (doramectin) and a topical (amitraz/ test product) miticidal compound along with benzyl peroxide shampoo and supportive therapy of Vit ADE are efficacious in resolving the lesions and eliminating the mites than the regimens having single drug (doramectin/ amitraz/ test product). Though efficacious, the test product ((Green Clean™) took a longer time than other approaches in curing the patients.

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