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Comparative evaluation of different therapy for canine demodicosis

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Abstract

Canine generalised demodicosis is a common noncontagious parasitic dermatosis caused by demodicosis spp. mite, It can be one of the most frustrating skin diseases of canine. For therapeutic study, a total of 12 dogs having generalised Demodicosis were divided randomly into two groups i.e. group I and group II, each group comprising of 6 dogs. Groups I and II which were treated with Tab ivermectin and topical amitraz 12.5% solution, respectively. Tab ivermectin with supplements has shown 100% recovery after 45 days, compared to amitraz 12.5% solution application which showed 66.6% recovery after 45 days and 83.4% recovery after 60 days. No adverse affects were found during the ivermectin therapy. Canine demodicosis with mild pyoderma could be successfully treated with a combination of miticidal therapy and antibiotics. During the monitoring period of two months no recurrence was found in the group treated with ivermectin. Oral ivermectin found to be more effective in comparison to weekly use of topical amitraz.

Keywords: Amitraz, canine generalised demodicosis, ivermectin, mite, parasitic dermatosis

Introduction

Cutaneous ectoparasitosis is one of the important skin manifestation of dogs and in some instances, they cause a nuisance and debilitation or even prove to be life threatening. Demodectic mange is a very common ectoparasitic infestation, caused by *Demodex canis* and considered as parasites that can act as opportunistic pathogens in certain circumstances. (Ferrer *et al.*, 2014) ^[1]

It is assumed that immunosuppression or a defect in the skin immune system allows mites to proliferate in hair follicles. (Mueller *et al.*, 2011) ^[2] Canine demodicosis is categorized as localized and generalized according to the area of skin covered by the disease. Localized demodicosis occurs most commonly in young dogs of less than one year of age, and spontaneous remission occurs in most patients. (Mueller *et al.*, 2004) ^[3] Lesions can occur anywhere on the body, although the face and feet are most commonly affected. A common complication of canine generalized demodicosis is a secondary bacterial folliculitis and furunculosis.

The diagnosis of canine demodicosis is usually done by identifying mites in skin scrapings, hair pluck, tape impression and histopathology may also be used depending upon the lesion and nature of location of lesion, (Tater *et al.*, 2008) ^[4] (Mueller *et al.*, 2009) ^[5] skin scraping is the most common method, and considered as the gold standard. There are only few studies that have evaluated and compared the various diagnostic techniques for canine demodicosis. (Pereira *et al.*, 2012) ^[6]

Canine demodicosis remains a very challenging disease to treat effectively because of acaricide in-efficacy and consecutive recurrences (Paterson *et al.*, 2009) ^[7] and difficult to manage because of the length of treatment. Reports on amitraz-resistant generalized demodicosis cases increasing nowadays. (Choudhary *et al.*, 2011) ^[8] (Zivicnjak *et al.*, 2005) ^[9] Hence the present study was taken with the objective to compare therapeutic efficacy of ivermectin oral and amitraz topical in canine suffering from canine demodicosis.

Material and method

The proposed research work was carried out during the period under study from September 2018 to February 2019 in cases presented with dermatological problems at Veterinary Clinical Complex (VCC), College of Veterinary and Animal Science, Bikaner.

The criteria for including dogs were history of pruriginous dermatitis and lesions characterised by erythema, papules, pustule, epidermal collarettes, crusts, alopecia, lichenification and hyperpigmentation. All the cases were screened for dermatological disorders by deep skin scrapings and bacterial culture. The lesions were categorised in to localized and generalized based upon the number of lesions and the

extension of infection process. The disease was considered to be generalized when a dog has five or more localized lesions, when an entire body region is involved.

All dogs suffering from canine generalised demodicosis were divided randomly into two groups (Group I and Group II) consisting of six dogs in each group. These dogs were subjected to the following treatment regimen (Table 01)

Table 1: Experimental design for therapeutic trial

Group	No. of animals	Drugs and dosage
I	6	Tablet Ivermectin (Neomec [®] , Intas Pharmaceuticals Pvt. Ltd.) @ 500 mcg / kg body wt, once daily (Verde <i>et al.</i> , 2005) ^[10] Topical application of benzoyl peroxide shampoo 2.5%, weekly
II	6	Amitraz (12.5%) (Ridd [®] , Pet Care Pvt. Ltd.) topical, weekly, Topical application of benzoyl peroxide shampoo 2.5%, weekly

All the dogs of both the groups were given Himalaya Immunol syrup containing tinospira gulanha (Guduchi) and Petcare's Nutricoat syrup (containing essential fatty acids such as Linoleic (Omega 6) and Linolenic (Omega 3) acids with zinc and vitamins) orally twice daily and antibiotics tablet Lixen (Virbac Pvt. Ltd.) containing cephalixin @30mg/kg Bwt bid PO for 10 days for treatment of secondary bacterial infection. The therapy was continued till two negative scrapings at 2 weeks apart in all the dogs.

Results and Discussion

Microscopic examination of deep skin scraping revealed the presence of a cigar shaped *Demodex canis*. The dogs suffering from canine demodicosis revealed a wide variety of clinical manifestations. Clinical examination of all dogs with canine generalised demodicosis revealed symptoms of alopecia, scales, erythema, pustules, pruritus, hyper pigmentation, seborrhea, lichenification, papules and scabs. (Attri *et al.*, 2005) ^[11] Alopecia is a consistent and remarkable clinical sign exhibited by almost all the affected dogs which might be resulted due to inflammations and irritations caused by the mites in the hair follicles. (Mullar *et al.*, 1989) ^[12]

A. Evaluation of therapeutic response

The therapeutic response of different treatments was evaluated on the basis of clinical signs and microscopic examination of skin scraping. Cases were monitored after every 15 days for clinical and laboratory examination. Treatment was continued till the two negative skin scrapings report obtained.

Group I (Oral Ivermectin tablet)

On clinical examination after '45th' day of treatment in group I all the dogs showed recovery from pruritus, erythema, pustules, scales, scabs, seborrhea and papules whereas alopecia, hyperpigmentation and lichenification were still present in one dog. On '45th' day of treatment skin scrapings of all the dogs in group I were found negative for demodex mites, showing 100% recovery. (Table 2), (Figure 1 to 4) Similar findings were found by (Paterson *et al.*, 2009) ^[7], (Nambi *et al.*, 2010) ^[13] and (Maravi *et al.*, 2018) ^[14] who reported that ivermectin was the most effective treatment in canine demodicosis.

The mode of action of this drug involves an inhibitory neurotransmitter, namely gamma-aminobutyric acid (GABA), which leads to paralysis and death of the parasites. (Prapasarakul *et al.*, 2001) ^[15]

Table 2: Clinical recovery and skin scrapings results in group I dog at various intervals of treatment

Oral Ivermectin (group I) (n=6)														
Days of observation	Total number of cases													
	Clinical recovery										Skin scrapings			Mites in skin scrapings
	Pruritus	Alopecia	Erythema	Pustule	Hyperpigmentation	Scales	Scabs	Seborrhoea	Lichenification	Papules	Positive	Negative	% recovery	
0 th day	6	6	6	6	4	5	2	3	4	5	6	0	0	Live
15 th day	4	5	4	4	4	4	2	2	3	2	5	1	16.6	Live+Dead
30 th day	1	3	2	1	3	2	1	1	2	0	2	4	66.6	Live+Dead
45 th day	0	1	0	0	1	0	0	0	1	0	0	6	100	Negative

Group II (Amitraz (12.5%) Topical)

On '45th' day of treatment in group II, skin scrapings of 4 dogs out of 6 were found negative for demodex mites, showing 66.6% recovery, so treatment was continued for 60 days. On clinical examination after '60th' day post treatment in group II all the dogs showed recovery in pruritus,

erythema, pustules, scales, scabs, seborrhea and papules whereas alopecia and hyperpigmentation were still present in '1' dog and lichenification was still present in '2' dogs. On '60th' day skin scrapings examination one case was still positive for demodectic mite, showing 83.4% recovery. (Table 3), (Figure 1 to 4)

Table 3: Clinical recovery in dogs by Amitraz 12.5% topical application

Amitraz 12.5% external use (group II) (n=6)														
Days of observation	Total number of cases													Mites in skin scrapings
	Clinical recovery										Skin scrapings			
	Pruritus	Alopecia	Erythema	Pustule	Hyperpigmentation	Scales	Scabs	Seborrhoea	Lichenification	Papules	Positive	Negative	% recovery	
0 th day	6	6	6	6	4	5	1	2	4	4	6	0	0	Live
15 th day	5	5	6	4	4	5	1	2	4	3	6	0	0	Live
30 th day	3	4	4	3	3	4	1	1	3	1	4	2	33.3	Live+Dead
45 th day	1	2	1	1	2	2	0	1	2	0	2	4	66.6	Live+Dead
60 th day	0	1	0	0	1	0	0	0	2	0	1	5	83.4	Live

In group I all the six dogs has shown recovery after 45 days of study with oral ivermectin treatment. In group II one dog has shown no improvement with amitraz 12.5% @4ml/l of water weekly application till 60 days of treatment, so on the basis of clinical signs and positive skin scrapping even after 60 days of treatment we can say amitraz resistance was present in this dog which also playing a important role in treatment of canine

demodicosis. The response to therapy was excellent in Group I compared to group II.

Similar findings were also observed by Ramprabhu *et al.*, 2010 [16] and Choudhary *et al.*, 2011 [8] who have found and reported amitraz resistance in their clinical study in which canine demodicosis dog not responded with external application of amitraz after 2 months of therapy.



Fig 1: to 4 Pre and Post treatment (group I and II)

B. Hematological analysis

Post treatment haemoglobin and PCV values were significantly increased, compared to pre treatment values of haemoglobin and PCV. According to Boda 2016 [17] the post therapy increase in the values of haemoglobin might be due to resolution of infection and improved appetite.

The post treatment values of neutrophil, TLC and eosinophil

were significantly decrease compare to pre treatment value, were similar to healthy control group, may be due to resolution of infection by using miticidal therapy as observed by Boda 2016 [17].

The post treatment values of TEC, lymphocyte and monocyte were significantly increased compare to pre treatment value, similar to healthy control group. (Table 4)

Table 4: Comparison between haematological values (Mean±S.E) of Group I, Group II animals (pre and post treatment)

Parameters	Group	Pre-treatment (0 th day)	Post-treatment (45 th day)
Hb (g/dl)	Healthy (n=6)	13.93 ^{bx} ±0.22	13.95 ^{bx} ±0.46
	Group 1 (n=6)	9.59 ^{ax} ±0.46	12.02 ^{ay} ±0.22
	Group 2 (n=6)	10.29 ^{ax} ±0.35	12.27 ^{ay} ±0.59
PCV (%)	Healthy (n=6)	40.67 ^{bx} ±1.2	40.5 ^{by} ±0.95
	Group 1 (n=6)	26.17 ^{ax} ±0.95	37.84 ^{ay} ±1.43
	Group 2 (n=6)	28 ^{ax} ±1.06	33.67 ^{ay} ±1.02
TEC (10 ⁶ /μl)	Healthy (n=6)	6.4 ^{bx} ±0.2	6.4 ^{ax} ±0.17
	Group 1 (n=6)	5.05 ^{ax} ±0.17	6.09 ^{ay} ±0.21
	Group 2 (n=6)	4.82 ^{ax} ±0.2	6.34 ^{ay} ±0.31
TLC (10 ³ /μl)	Healthy (n=6)	11.3 ^{ax} ±0.82	11.52 ^{ax} ±0.65
	Group 1 (n=6)	15.53 ^{bx} ±0.65	13.17 ^{ay} ±0.74
	Group 2 (n=6)	15.9 ^{bx} ±0.67	11.95 ^{ay} ±0.24
N (%)	Healthy (n=6)	71 ^{ax} ±2.29	72.5 ^{ax} ±0.89
	Group 1 (n=6)	84.5 ^{bx} ±0.89	74.17 ^{ay} ±1.84
	Group 2 (n=6)	82.5 ^{bx} ±1.52	71.17 ^{ay} ±1.08
L (%)	Healthy (n=6)	21.83 ^{bx} ±2.34	20.67 ^{ax} ±0.67
	Group 1 (n=6)	9.67 ^{ax} ±0.67	19 ^{ay} ±1.99
	Group 2 (n=6)	8.5 ^{ax} ±0.87	21.34 ^{ay} ±0.76
M (%)	Healthy (n=6)	5.83 ^{bx} ±0.92	5.67 ^{ax} ±0.48
	Group 1 (n=6)	1.84 ^{ax} ±0.52	5.34 ^{ay} ±0.88
	Group 2 (n=6)	3 ^{ax} ±0.58	6 ^{ay} ±0.73
E (%)	Healthy (n=6)	1.17 ^{ax} ±0.31	1 ^{ax} ±1.03
	Group 1 (n=6)	4 ^{bx} ±1.03	1.17 ^{ay} ±0.26
	Group 2 (n=6)	5.67 ^{bx} ±0.8	1.17 ^{ay} ±0.31
B (%)	Healthy (n=6)	0.17±0.17	0.17±0.21
	Group 1 (n=6)	0.3	0.33±0.17
	Group 2 (n=6)	0.33±0.21	0.5±0.34

means having different superscript in a row(x,y) differ significantly ($P<.05$)

means having different superscript in a column(a,b,c) differ significantly ($P<.05$)

C. Biochemical analysis

In demodectic dogs there was significant hypoproteinemia, hypoalbuminaemia and hyperglobulinaemia was found similar findings was also noted by previous workers Dadhich *et al.*, (2008) [18], Sakina *et al.*, (2012) [19] and Pradhan *et al.*, (2012) [20]. Decreased levels of serum albumin in the present study might be the result of excessive breakdown of proteins due to trauma to skin and proliferation of mites. Elevated globulin level might be indicator of immune response following severe mite infestation in canine demodicosis (Sakina *et al.*, 2012 and Haleem *et al.*, 2015) [19, 21].

The post treatment values of protein, albumin, A:G ratio and glucose were significantly increased compare to pre treatment

value which was similar to healthy control group might be due to resolution of infection and improved appetite.

The post treatment values of globulin, SGPT and SGOT were significantly decrease compare to pre treatment value might be due to resolution of infection and improved appetite therefore liver condition of dog improved. Decrease level of hepatic enzyme like SGPT and SGOT could be due to the decreased hepatic damage because of control on mites proliferation and toxic products release from mites.

The post treatment values of BUN and creatinine were non significantly decrease compare to pre treatment value, and was similar to healthy control group. (Table 5)

Table 5: Comparison between Biochemical values (Mean±S.E) of Group I, Group II animals (pre and post treatment)

Parameters	Group	Pre-treatment	Post-treatment
Total protein (g/dl)	Healthy (n=6)	6.63 ^{bx} ±0.16	6.17 ^{ax} ±0.16
	Group 1 (n=6)	5.8 ^{ax} ±0.16	6.37 ^{ay} ±0.23
	Group 2 (n=6)	6.1 ^{ax} ±0.23	6.42 ^{ay} ±0.19
Albumin (g/dl)	Healthy (n=6)	3.17 ^{bx} ±0.12	3.12 ^{ax} ±0.08
	Group 1 (n=6)	1.99 ^{ax} ±0.08	2.97 ^{ay} ±0.14
	Group 2 (n=6)	1.97 ^{ax} ±0.17	2.94 ^{ay} ±0.22
Globulin (g/dl)	Healthy (n=6)	3.48 ^{bx} ±0.09	3.22 ^{ax} ±0.12
	Group 1 (n=6)	3.87 ^{ax} ±0.12	3.4 ^{ay} ±0.03
	Group 2 (n=6)	4.14 ^{ax} ±0.17	3.49 ^{ay} ±0.11
A:G ratio	Healthy (n=6)	0.92 ^{bx} ±0.04	0.97 ^{ax} ±0.02

	Group 1 (n=6)	0.52 ^{ax} ±0.02	0.89 ^{ay} ±0.05
	Group 2 (n=6)	0.48 ^{ax} ±0.05	0.86 ^{ay} ±0.08
Glucose (mg/dl)	Healthy (n=6)	98.34 ^{bx} ±2.03	98 ^{ax} ±2.06
	Group 1 (n=6)	84.17 ^{ax} ±2.06	94.17 ^{ay} ±1.84
	Group 2 (n=6)	82.5 ^{ax} ±1.98	92.5 ^{ay} ±1.61
	Healthy (n=6)	20.67 ^{ax} ±0.49	20.84 ^{ax} ±1.28
ALT/SGPT U/L	Group 1 (n=6)	25.67 ^{bx} ±1.28	21 ^{ay} ±0.48
	Group 2 (n=6)	27.67 ^{bx} ±0.76	20.34 ^{ay} ±0.67
AST/SGOT U/L	Healthy (n=6)	23.5 ^{ax} ±0.43	23.5 ^{ax} ±0.95
	Group 1 (n=6)	29.17 ^{bx} ±0.95	22.34 ^{ay} ±0.62
	Group 2 (n=6)	30.5 ^{bx} ±0.43	22.17 ^{ay} ±0.79
	Healthy (n=6)	12.5±0.56	12.17±0.76
BUN (mg/dl)	Group 1 (n=6)	13.67±0.76	11.34±0.48
	Group 2 (n=6)	13.84±0.4	12.5±0.43
Creatinine (mg/dl)	Healthy (n=6)	0.85±0.08	0.57±0.11
	Group 1 (n=6)	1.14±0.11	0.75±0.07
	Group 2 (n=6)	1.24±0.09	0.89±0.12

means having different superscript in a row(x,y) differ significantly ($P<.05$)

means having different superscript in a column(a,b,c) differ significantly ($P<.05$)

D. Mineral parameter analysis

In the present investigation the values of serum zinc, copper and iron concentration was significantly low in canine demodicosis affected dog compared to healthy control group dogs.

As reported by Nath *et al.* (1984) [22] the observed lower concentration of copper and zinc could be attributed to their over utilization in the synthesis of antioxidant enzymes to

counter oxidative stress.

The post treatment values of zinc, copper and iron were significantly increased compare to pre treatment value, were significantly similar to healthy control group. The improvement in serum zinc, copper and iron levels in animals following therapy might be due to cure of inflammatory condition of skin improvement in the health of the animal and reduction in oxidative stress.

Table 6: Comparison between Mineral values (Mean±S.E) of Group I, Group II animals (pre and post treatment)

Parameters	Group	Pre-treatment	Post-treatment
Zn (µg/ml)	Healthy (n=6)	1.42 ^{bx} ±0.1	1.42 ^{ax} ±0.05
	Group I (n=6)	0.75 ^{ax} ±0.05	1.36 ^{ay} ±0.09
	Group II (n=6)	0.7 ^{ax} ±0.07	1.27 ^{ay} ±0.05
Cu (µg/ml)	Healthy (n=6)	1.13 ^{bx} ±0.1	1.13 ^{ax} ±0.03
	Group I (n=6)	0.5 ^{ax} ±0.03	1.15 ^{ay} ±0.1
	Group II (n=6)	0.53 ^{ax} ±0.03	1.04 ^{ay} ±0.09
Fe (µg/ml)	Healthy (n=6)	1.27 ^{bx} ±0.23	1.25 ^{ax} ±0.02
	Group I (n=6)	0.28 ^{ax} ±0.02	1.22 ^{ay} ±0.17
	Group II (n=6)	0.3 ^{ax} ±0.02	1.09 ^{ay} ±0.07

means having different superscript in a row(x,y) differ significantly ($P<.05$)

means having different superscript in a column(a,b,c) differ significantly ($P<.05$)

Conclusion

Based on the findings of present study, it was concluded that the use of tablet ivermectin @ 500 µg/kg b. wt along with supportive therapy for 45 days was found to be effective in terms of elimination of clinical signs and rapid reduction of mite in comparison to weekly application of 12.5% amitraz.

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