THERAPEUTIC TRIALS OF PYODERMA IN DOGS WITH CLINDAMYCIN AND IN COMBINATION WITH A TOPICAL ANTIBACTERIAL COMBINATION OF CHLORHEXIDINE GLUCONATE AND SILVER SULPHADIAZENE

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[Received: 16.7.2014; Accepted: 30.11.2014]

Fifty dogs with pyoderma were selected and divided into five groups of ten animals each.The animals of group I were treated with Clindamycin once daily. Animals of Group II & III were treated with a topical preparation containing Silver Sulphadiazene and Chlorhexidine Gluconate twice and once daily respectively. Animals of Group IV & V were treated with Clindamycin once daily along with the topical preparation twice and once daily, respectively. The animals treated with Clindamycin alone or in combination with topical cream showed good response to therapy whereas animals treated with only topical cream showed moderate response showing that clindamycin is an effective drug in the treatment of pyoderma and topical therapy with chlorhexidine gluconate and silver sulphadiazene can be used as an adjunct therapy when prolonged antibacterial therapy is required.

Introduction

Pyoderma is one of the most common dermatological disorders encountered in small animal (Put the Reference). Which requires a higher dosage of antibiotics and a longer duration of therapy. Several antibiotics are used with varying degrees of efficacy and there are reports of resistance to the commonly used antibiotics (Schwarz *et al*, 1989). Cephalosporins like cephelexin, cefadroxil and fluoroquinolones like enrofloxacin, marbofloxacin are reported to be effective and are being widely used in the treatment of pyoderma (Mason, 1997; Carlotti *et al,* 1999; Craig, 2003). However, of late methicillin resistant staphylococci are being reported and these organisms are resistant to most of the commonly used drugs and therefore, it are essential for an appropriate therapeutic approach to control this problem. Rifampicin and Amikacin are some of the antibiotic options but shows hepatotoxicity and nephrotoxicity, while Clindamycin is another safer alternative

Materials and Methods

Therapy of pyoderma is frustrating and challenging to the clinician because of the prolonged duration of therapy required, frequent recurrences and development of resistance towards the antibacterial drug by the primary causative agent. In order to select a suitable therapeutic regimen, clinical trials were undertaken.

Dogs presented to Veterinary College Hospital, Bangalore were used for this study. Dogs showing primary clinical signs of pyoderma such as papules, pustules, epidermal collarettes, alopecia (localized and generalized), erythema, pruritus and presence of erosive lesions / draining tracts / ulcers were selected and subjected to bacterial culture of material from lesions in Mannitol Salt Agar and coagulase testing to detect the presence of Staphylococcus species, the primary agents implicated in pyoderma i.e *S intermedius* and *S aureus.* Thus the fifty confirmed cases of pyoderma were randomly selected and divided into 5 groups of 10 animals each for clinical trials using different therapeutic regimen.

Animals of Group I were given the conventional therapy with an antibiotic i.e. Clindamycin @ 11 mg / kg body weight once daily. Animals of Group II and III were treated with a topical cream containing 1% w/w Silver Sulphadiazene and 0.2% w/w Chlorhexidine Gluconate applied on the lesions twice daily and once daily, respectively. Animals of Group IV and V were treated with Clindamycin at 11mg / kg body weight once daily along with the above

topical cream twice and once daily, respectively.

The animals of all the five groups were treated for 2 weeks and were further monitored for a period of 2 months from the initiation of therapy. The response to therapy was monitored based on the disappearance of clinical signs and the lesions at the end of 2 weeks and at the end of the 2 months period. A detailed study of the clinical signs was made on these animals prior to treatment and the lesions observed were listed. Based on the disappearance of the lesions, a grading was done with scores ranging from1 to 5 for each of the lesions. The lesions or the clinical signs noted were papules, pustules, epidermal collarettes, alopecia (localized and generalized), erythema, pruritus, erosive lesions and ulcers etc. which correspond to Manon, (1998); De Boer (1995). A score of 5 was allotted if the recovery was excellent with complete disappearance of the sign in 15 days. A score of 3 was given if the recovery was good with disappearance of lesions by 2 months and a score of 2 was given if there was moderate progress with a few lesions persisting even at the end of 2 months. A score of 1 was given if the response observed was only marginal and some of the lesions still persisting at the end of two months and score of 0 was given if no response was observed or if there was worsening or recurrence of lesions noted. The scores for individual lesions were then totaled and the average for each animal was taken for grading the response to treatment and also for comparison between groups.

Results and Discussion

The group-wise classification of pyoderma of the 50 dogs utilized for therapeutic trials are depicted in Table I. Scores were allotted depending on response to therapy as excellent (5) Good (4), Moderate (3), Marginal (2) and Poor (1) based on resolution of clinical signs/lesions and animals were evaluated within the groups as depicted in Table II and III and Fig 1 and between the groups as indicated in Table IV & Fig 2.

TABLE I: GROUP-WISE CLASSIFICATION OF PYODERMA*FOR THERAPEUTIC TRIALS DURING THE STUDY

		Group I n=10	Group II n=10	Group III n=10	Group IV n=10	Group V n=10	Total n=50
I	**Superficial Pyoderma**	**5**	**7**	**5**	**7**	**5**	**29**
	1.Skin fold pyoderma	-	-	-	1	-	1
	2.Impetigo	-	1	-	-	-	1
	3.Folliculitis	5	6	5	6	5	27
II	**Deep Pyoderma**	**5**	**3**	**5**	**3**	**5**	**21**
	1.Furunculosis	3	2	4	3	2	14
	2.Cellulitis	-	-	-	-	-	-
	3.Interdigital pyoderma complex	2	1	1	-	3	7

*Classification as per Fourrier *et al.* (1996)

TABLE II : MEAN ± SE OF SCORES AS RESPONSE TO THERAPY BASED ON RESOLUTION OF CLINICAL SIGNS IN THE 5 GROUPS OF DOGS WITH PYODERMA (N=50)

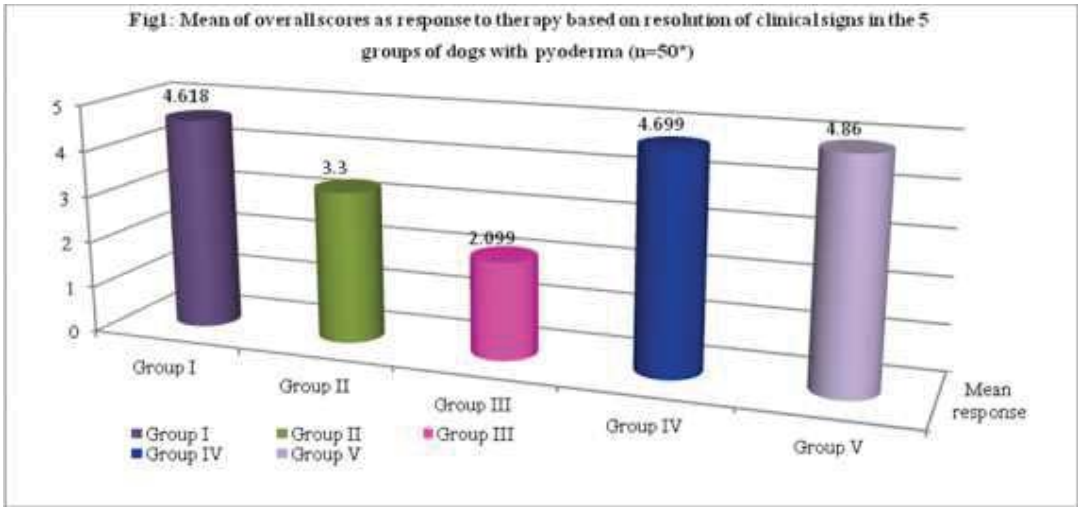
	Group I n=10	Group II n=10	Group III n=10	Group IV n=10	Group V n=10
After 15 days	4.170 ± 0.2195 [a]	3.140 ± 0.4129 ™	2.864 ± 0.4352 ™	4.401 ± 0.2167 [a]	4.094 ± 0.2318 [a]
After 2 months	4.618 ± 0.1501 [a]	3.300 ± 0.4808 ™	2.099 ± 0.6622 ™	4.699 ± 0.1099 [a]	4.860± 0.0991 [a]

Note: Scores were given on the basis of resolution of clinical signs. Different superscripts indicate statistically significant difference between groups

TABLE III: RESPONSE TO THERAPY IN PERCENTAGE BASED ON MEAN SCORES AND RESOLUTION OF CLINICAL SIGNS IN THE 5 GROUPS OF DOGS WITH PYODERMA

	Per cent response to therapy (N=50)

	Group I	Group II	Group III	Group IV	Group V
At 15 days	83.14%	62.80%	57.20%	88.02%	81.88%
At 2 months	92.40%	66.0%	41.98%	93.98%	97.20%

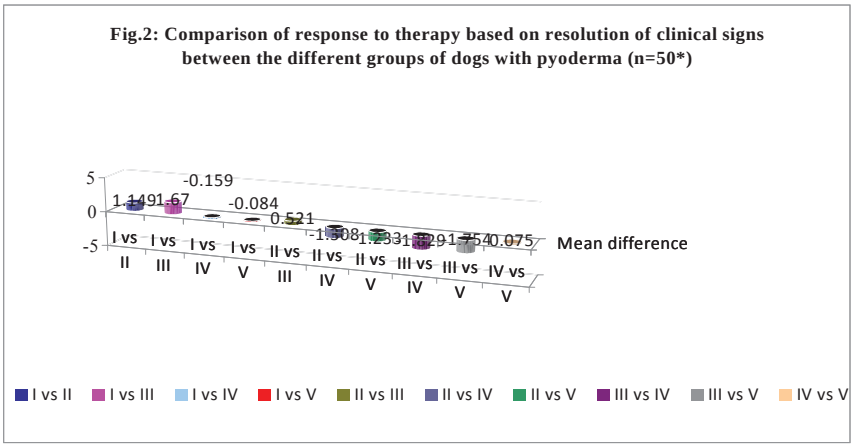


* 10 dogs in each group

TABLE IV: COMPARISON OF RESPONSE TO THERAPY BASED ON RESOLUTION OF CLINICAL SIGNS BETWEEN THE DIFFERENT GROUPS OF DOGS WITH PYODERMA (N=50*)

Groups	Mean difference ± SE of difference	Significant (S**) / Nonsignificant (NS)
I vs II	1.149 ± 0.4258	**S****
I vs III	1.670 ± 0.4258	**S****
I vs IV	-0.1590 ±0.4258	**NS**
I vs V	-0.0840 ± 0.4258	**NS**
II vs III	0.5210 ± 0.4258	**NS**
II vs IV	-1.308 ± 0.4258	**S****
II vs V		**S****
III vs IV		**S****
III vs V	-1.233 ± 0.4258	**S****
IV vs V	-1.829 ± 0.4258	**NS**

10 dogs in each group



Overall comparison of the Mean ± SE scores of the 5 groups at the end of the 2 months period showed significant differences (P≤0.05) between the Group I & II, Group I & III, Group II & IV, Group II & V, Group III &IV and Group III & V.

Group I, IV and V did not reveal any significant differences and the response to therapy between these groups varied from a minimum of 81.88% to a maximum of 97.20%. However, Group II and Group III did not differ significantly between them but differed significantly (P≤ 0.05) from all other groups i.e. Group I, IV and V and the response to therapy between the groups II & III varied from a minimum of 41.98% to a maximum of 66%.

The Table II shows that the percentage of response to treatment varied between a minimum of 41.98% (Group III) to a maximum of 97.2% (Group V).There was no statistically significant difference in the responses between Groups I, IV and V (92.40%, 93.98% and 97.20%, respectively) all of which had Clindamycin as the primary drug. It can therefore be concluded that Clindamycin at 11 mg / kg once daily for 2 weeks is a very effective systemic antibiotic for treatment of pyoderma. This is in agreement with the report of Harvey *et al.* (1993) who found 94% response to Clindamycin at 11 mg / kg orally once daily for 3 weeks in dogs with superficial pyoderma. In the present study cure was observed in 2 weeks though earlier workers have suggested that therapy should be continued for 6-10 weeks (De Boer, 1995) or for periods long enough to ensure complete cure (Ihrke, 2005). The findings of the present study are in accordance with that of Bloom and Rosser (2001) who studied the efficacy of once daily treatment of superficial pyoderma with Clindamycin at 11 mg / kg orally and obtained a clinical score of excellent (complete remission) in 71.4% (i.e. 15/21) of dogs within 14-28 days. Similarly, Scott *et al.* (1998) in a study on efficacy of Clindamycin at 11 mg / kg in the treatment of deep pyoderma reported the response to therapy as 100%. However the duration of therapy was 21-91 days unlike in the present study where it was restricted to 15 days. Further, since no no statistically significant difference between groups II and III (topical preparation) whereas there statistically significant differences between the groups I, IV and V was observed the response to therapy can be attributed to a large extent to be due to Clindamycin .

The response to therapy in the groups II and III which involved the use of topical Silver sulphadiazene and Chlorhexidine cream alone either twice daily or once daily varied from a minimum of 41.98% (Group III) to a maximum of 66% (Group II- Table III). This indicated that the topical preparation is moderately effective even when used alone without concurrent use of a systemic antibiotic. There was were statistically significant differences (P≤ 0.05) between Groups II & I, II & IV and II & V as well as between groups III & I, III & IV and III & V thus suggesting that the topical preparation alone is moderately effective when used singly and far more effective when used along with Clindamycin. Chlorhexidine gluconate is said to be an effective antibacterial agent when used topically in pyoderma as an adjunct therapy (Buerger, 1989, Frazer *et al*, 2004, Loeffler, 2011, Young *et al*, 2012). In addition to rapid antibacterial activity it has good residual effect and emollient action. Silver sulphadiazene is an antibacterial which is specifically used for treatment of burn injuries in human beings (Frazer *et al,* 2004). It is effective against *Pseudomonas aeruginosa* and *Staphylococcal* infections (Snelling & Roberts, 1988, Frazer *et al* , 2004,). No definite study has been made on the combination of Chlorhexidine gluconate and Silver sulphadiazene in the treatment of pyoderma. In the present study the combination of Chlorhexidine gluconate and Silver sulphadiazene was found to be moderately effective in the treatment of pyoderma in dogs when used as a topical agent and more effective when used in combination with the systemic antibacterial agent Clindamycin. However it was not

possible to distinguish whether the increased response was due to Clindamycin alone or Clindamycin with the topical agent combination as there was no statistically significant differences in response to therapy between groups I, II and III though a slight increase in response was observed when topical preparation was used with Clindamycin. Snelling and Roberts (1988) compared the efficacy of 1% Silver Sulphadiazene with and without Chlorhexidine digluconate for its antibacterial effect in the treatment of burn injury, and found that Chlorhexidine digluconate increased the antibacterial efficacy of Silver Sulphadiazene. Frazer *et al.* (2004) also similarly found the combination of 1% Silver sulphadiazene and 0.2% Chlorhexidine digluconate cream to be more effective than either of the agents used singly. Thus, as per the current study, the combination of Silver sulphadiazene and Chlorhexidine gluconate appears to be moderately effective when used topically without a systemic antibacterial agent.

It can be concluded that Clindamycin is an effective systemic antibacterial agent for treatment of pyoderma and that the efficacy can be increased if the therapy is customized to the requirement of each case based on the severity. Topical therapy with Silver Sulphadiazene and Chlorhexidine gluconate was found to be moderately effective and can be considered as an useful adjunct to systemic therapy and also as a follow-up therapy after initial systemic antibiotic therapy in long standing cases of pyoderma requiring prolonged therapy. Further, since this is the first of its kind study using this combination for topical therapy of pyoderma, more investigations are warranted.

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