STUDY REPORT

Some observations on the treatment of superficial pyoderma in dogs with totarol

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Superficial bacterial skin infection (superficial pyoderma) is common in dogs, being one of the most common conditions seen in veterinary practices in New Zealand especially in the summer. The major bacterial commensal and pathogen is *Staphylococcus pseudintermedius* but other bacterial pathogens are identified including *Staphylococcus aureus* (Schmidt 2017). Antibiotic resistant organisms including methicillin resistant *S. pseudintermedius* have been identified in dogs in New Zealand (Schmidt 2017; Bell *et al.* 2016).

Surface and superficial pyoderma include fold pyodermas (lip, face, vulva), impetigo, bacterial folliculitis, superficial spreading pyoderma and combinations of folliculitis and spreading pyoderma (Gross *et al.* 2005). Bacterial folliculitis is the most common pyoderma seen in dogs and has many clinical presentations: a follicular papule or pustule progressing to epidermal collarettes characterised by a circular area of hair loss with variable erythema, exudation, crusting and pigmentation. Pruritus may be present especially in atopic dogs where pyoderma is a co-factor that promotes itching.

Veterinary treatment of superficial pyoderma has included the administration of systemic and/or topical antibiotics or the application of local antiseptic agents. While a number of biocides have been used, 2–4% chlorhexidine is currently the most effective topical agent and the treatment of choice of many veterinarians based on trial evidence (Murayama *et al.* 2010; Loeffler *et al.* 2011; Mueller *et al.* 2012).

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Totarol, an aromatic diterpenoid phenol, is a natural organic extract of the tōtara tree (*Podocarpus totara*) which has potent antibacterial action against gram positive organisms *in vitro* (Kubo *et al.* 1992). Totarol was first isolated in 1937 (Short and Stromberg 1937) but the medicinal properties of totara tree extracts were known to Māori for many years before. Totarol has been used as an antibacterial agent for skin infections and in other medications for people but there are no equivalent clinical data to support claims for the treatment of superficial pyoderma in dogs. Nevertheless, there are anecdotal reports of its use to treat skin infections in dogs.

The purpose of this pilot study was to confirm the efficacy of totarol applied in a vehicle of sodium bentonite clay (1% w/v) or as a 0.2% aqueous spray for the treatment of superficial bacterial skin infections in dogs. A positive control group of dogs was treated with 3% chlorhexidine wash, an accepted topical biocide treatment for dogs.

Materials and methods

Massey University ethics approval applied to the study (AEC/18 amended 04/17) and owner consent was obtained for all cases.

Animals

Eighteen client-owned dogs of mixed age and breed were recruited from three veterinary practices in the North Island. The dogs were presented for examination of their skin condition and a clinical diagnosis of superficial bacterial skin infection was made by the attending veterinarian based on the history and the characteristic clinical signs of superficial bacterial skin infection (Figure 1).

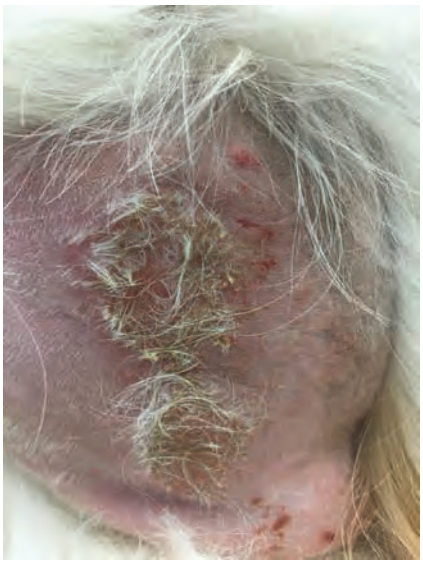


Figure 1. A typical "hot spot" with moderate erythema, sparse papules, moderate exudate and fine crusts on a 9-year-old Maltese Terrier crossbreed dog at visit 1 (pre-treatment). Note: hair over the lesion has been clipped.

Skin lesions

Lesion(s) were scored for the presence of each of the following: erythema, pruritus, exudation, hair loss, and depth of the lesion, according to a linear scale) where 0=none, 1= mild, 2=moderate, 3=severe.

The same veterinarian scored the skin lesions for each dog at days 1, 7 and 28.

Cytology

An impression smear of the exudate was taken from the lesion(s), air dried, stained with Diff Quick and examined (AGB).

Microbiology

A swab taken from the lesion was sent to a veterinary diagnostic laboratory for bacterial culture and antibiotic sensitivity determination.

Treatment

The selection of a treatment was randomly selected by dice throw. Based on the dice throw each dog was allocated to a treatment group:

1. Six dogs were treated daily for 7 days with 3% chlorhexidine wash (Pyoderm^{R}S; Virbac, Sydney, Australia)
2. Six dogs were treated daily for 7 days with topical 0.2% totarol aqueous spray (Totarol; Vetcarevets, Masterton, NZ)
3. Six dogs were treated daily for 7 days with topical 1% w/v totarol in medical grade sodium bentonite clay (Pet Putty; Vetcarevets, Masterton, NZ)

If necessary, hair was clipped from over and around the lesion and the owners were shown how to apply the topical medications to the lesion(s). A treatment sheet was provided for each owner which contained a full explanation of how treatment should be undertaken each day until the next visit.

Revisits

Each dog was examined 7 days after the first visit (Figure 2). Medications were withdrawn and the dogs then re-examined 28 days after the first visit. Owners were asked to complete a short questionnaire on their experience using the prescribed products.

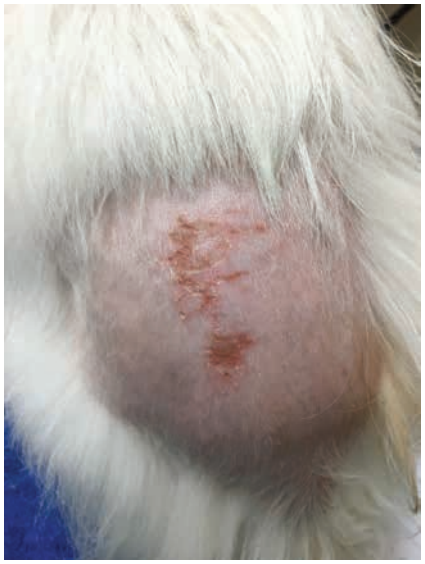


Figure 2. The same dog as in Figure 1 after 7 days of treatment with Pet putty. There is superficial ulceration, resolution of papules and mild erythema. The hair over the lesion was clipped.

Data analysis

Score difference was defined as the difference between day 1 scores and day 7 scores for the measures; erythema, pruritus, exudation, hair loss, depth and total score. Mean score differences for the three treatment groups were compared using the non-parametric Kruskal-Wallis test. The Dunn test (Dunn, 1964) was applied for multiple comparisons. The p-values were adjusted for type I and type II errors using the Benjamini-Hochberg method. P-values <0.05 were considered significant. All analyses were carried out using R statistical software version 3.6.3 (R Development Core Team 2020; R Foundation for Statistical Computing, Vienna, Austria).

Results

One dog from the totarol group was excluded from the final results as it was bitten by another dog 4 days after treatment started. The bite injuries to this dog required antibiotic treatment

Cytology

Surface cytology revealed cocci and neutrophils in 15/17 dogs. Yeast-like organisms, rod bacteria, melanosomes and red blood cells were seen infrequently and in very low numbers. The findings in all dogs supported a diagnosis of superficial bacterial infection.

Microbiology

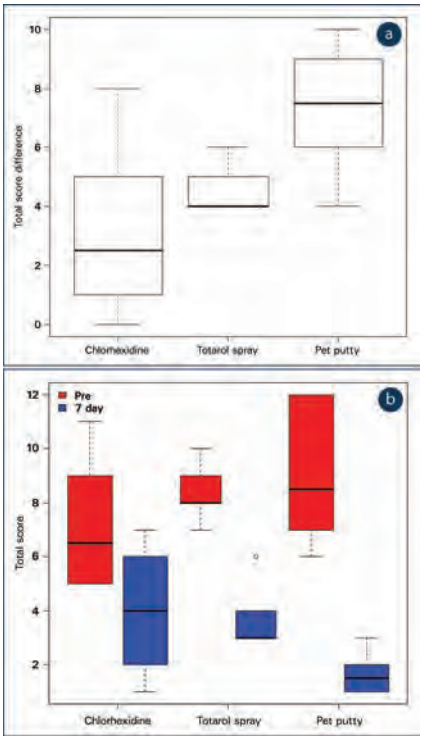
Staphylococcus pseudintermedius was recovered from the lesion(s) of 15 dogs including the two which had negative cytological results. All isolates were sensitive to antibiotics in common use by veterinarians. No isolate was multi-antibiotic resistant. *Streptococcus dysgalactiae* and *Klebsiella* spp. were recovered from the lesions in two dogs. Other bacteria recovered from some dogs were regarded as contaminants or of questionable significance.

The two dogs with negative cultures had evidence of bacterial infection on cytology. The transport delay in submission to the laboratory was considered the reason for a negative culture.

Outcome of treatment

All remaining dogs in each treatment group improved, with resolution of most of their clinical signs and a reduction in their severity scores by day 7 (Table 1). By day 28 the severity scores were zero for 15/17 dogs. One dog in the chlorhexidine group and one dog in the totarol spray group still showed some signs both with a severity score of 2. The dog receiving totarol spray resisted application by the owners. It had a score of 10 before treatment began and 6 after 7 days.

The appearance of the lesions 7 days after treatment and the score differences for each clinical sign showed all products were effective but the improvement in the totarol/clay group was significantly better than that of the chlorhexidine group (p=0.031) (Table 2). There was no evidence of a difference in the score reductions for each clinical sign in any group except for hair loss. Figure 3 shows box plots of the reduction in total score between days 1 and 7 for each treatment group.



Figures 3. Box plots showing distribution of (a) the difference in total scores between day 1 (pre-treatment) and day 7 and (b) total scores on days 1 and 7, for dogs treated with 3% chlorhexidine wash (n=6), 0.2% totarol spray (n=5) and Pet putty (1% totarol in bentonite clay; n=6).

Table 1. Age, breed and sex of dogs included in a study comparing the effect of totarol with chlorhexidine for treatment of superficial pyoderma and the scores allocated to each dog for the clinical signs of erythema, exudation, pruritus, hair loss, depth of lesion before treatment (pre) and at day 7 after treatment for each treatment group.

				Clinical sign					
Treatment groups			**Time**	**Erythema**	**Itch**	**Exudate**	**Hair loss**	**Depth**	**Total**
Chlorhexidine group (age, sex, breed)									
12 years	FS	Bichon	Pre	2	3	2	3	1	11
			7 day	1	1	0	3	1	6
5 years	FS	Mastiff	Pre	3	3	1	1	1	9
			7 day	0	0	0	0	1	1
5.5 years	FS	Huntaway	Pre	3	1	0	0	1	5
			7 day	1	0	0	0	1	2
4.5 years	FS	Mastiff X	Pre	2	2	0	0	1	5
			7 day	1	1	1	0	1	4
1.6 years	MN	Labrador X	Pre	1	2	1	1	1	6
			7 day	1	2	0	0	1	4
3 years	MN	Mastiff X	Pre	1	2	2	1	1	7
			7 day	2	2	2	1	0	7
Totarol spray group (age, sex, breed)									
3 y	M	Labrador	Pre	2	0	3	3	0	8
			7 day	0	0	0	3	0	3
15 years	M	Fox Terrier X	Pre	2	1	2	3	0	8
			7 day	1	0	0	3	0	4
3 years	F	Labrador	Pre	2	3	3	1	1	10
			7 day	1	2	3	0	0	6
2 years	MN	Ridgeback X	Pre	3	3	2	0	1	9
			7 day	1	0	0	1	1	3
1 years	M	Labrador	Pre	2	1	1	2	1	7
			7 day	0	0	0	2	1	3
Pet Putty group (age, sex, breed)									
4 years	MN	Maltese	Pre	3	3	2	2	2	12
			7 Day	0	0	0	1	1	2
5 years	M	Cairn X	Pre	1	2	1	1	1	6
			7 day	1	0	0	0	1	2
8 years	FS	Maltese X	Pre	1	2	2	3	1	9
			7 day	1	0	0	0	0	1
9 years	MN	Labrador	Pre	3	3	2	3	1	12
			7 day	1	0	0	1	1	3
3 years	F	Ridgeback	Pre	2	2	2	1	1	8
			7 day	0	0	0	0	1	1
9 years	MN	Shih Tzu	Pre	2	2	1	1	1	7
			7 day	0	0	0	0	1	1

Owner questionnaire

All owners followed the requested treatment protocol and were positive about the result of treatment for their dog. Three dogs tried to lick off the totarol/clay preparation after the first application, but this did not affect the outcome for these dogs and further applications in the following days were tolerated well. One dog in the totarol spray group did not accept the spray application and the owners found application difficult.

Table 2. Comparison of mean differences in the total pyoderma lesion score between pre-treatment to day 7 for dogs with superficial pyoderma treated with 3% chlorhexidine wash (n=6), Pet putty (1% totarol in bentonite clay; n=6) or 0.2% totarol spray (n=5).

		P-value[a]	
Groups compared	**Z**	**Unadjusted**	**Adjusted[b]**
Chlorhexidine vs. Pet putty	–2.5644	0.010335	0.031
Chlorhexidine vs. Totarol spray	–0.8022	0.42437	0.422
Pet putty vs. Totarol spray	1.642863	0.100411	0.150

[a] Significance of difference between groups based on Kruskal-Wallis
[b] P-values adjusted using the Benjamini-Hochberg method

Discussion

The antibacterial action of totarol is established (Kubo *et al.* 1992; Muroi and Kubo 1996; Guo *et al.* 2015). The results of this study show that when applied topically for 7 days to dogs with superficial pyoderma 1% w/v totarol in bentonite clay achieved a greater reduction in lesion scores than chlorhexidine wash. There was no evidence of a difference in efficacy between 0.2% totarol aqueous spray and chlorhexidine wash. The two preparations containing totarol were both effective.

The reason two dogs, one in the totarol spray group and one in the chlorhexidine group, still showed signs at day 28 was not established. The score for the dog in the totarol spray group at day 7 improved from day 1 but the dog resisted application and we suspect it received inadequate treatment; more prolonged treatment might have resulted in a better outcome. The dog in the chlorhexidine group that did not improve had equivalent scores at days 1 and 7 and although improved by day 28 the lesions had not resolved fully. The significance of hair loss between the totarol/clay and spray groups was confounded by clipping the hair over and around the lesion(s) in some dogs thus no weighting should be given to this finding.

The effectiveness of totarol in this study is claimed due to its antibacterial properties but there is also evidence that totarol has anti-inflammatory properties (Young *et al.* 1989), and also inhibits lipid peroxidation (Harraguchi *et al.* 1997). These properties were not investigated in this study but may have contributed to its effectiveness.

No methicillin resistant *Staphylococcus* spp. were recovered from any of the dogs but there is evidence to support totarol's antibacterial properties and efficacy against methicillin resistant *Staphylococcus* spp. (Kubo *et al.* 1992; Kubo *et al.* 1994; Muroi *et al.* 1996; Smith *et al.* 2007; Guo *et al.* 2015) which is an additional advantage if resistant strains are suspected or recovered.

Veterinarians involved in this study did not identify underlying predisposing causes for the pyoderma in any dog in the study population but the authors acknowledge that identification of predisposing causes of pyoderma e.g. atopy is important to assist recovery.

The role of topical antibacterial biocides is important and while chlorhexidine is the current biocide of choice for the treatment of superficial pyoderma in dogs, the effectiveness of totarol in this study gives practitioners the choice of a biocide which could be prescribed instead of chlorhexidine.

The sample size for each group in this study is very small and as such there is the risk of type I and II error. However, we believe there is sufficient preliminary evidence to support the use of topical totarol as a 0.2% aqueous spray or as a 1% w/v totarol/clay preparation for the successful treatment of localised superficial pyoderma in dogs.

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