J. Dairy Sci. 100:1–14
https://doi.org/10.3168/jds.2016-12257

Comparison of the efficacy of a commercial footbath product with copper sulfate for the control of digital dermatitis

C. Jacobs,*[1] K. Orsel,* S. Mason,*† K. Gray,* and H. W. Barkema*
*Department of Production Animal Health, Faculty of Veterinary Medicine, University of Calgary, Calgary, Alberta, Canada T2N 4N1
†Alberta Milk, Edmonton, Alberta, Canada T6X 1H1

ABSTRACT

Digital dermatitis (DD) is the most prevalent foot lesion affecting dairy herds worldwide. Its implications include production losses and decreased animal welfare. Footbathing is the most common herd-level prevention strategy for DD. Because many common footbath products have negative environmental and health consequences, replacement products expected to have improved safety but equal efficacy are being developed. Therefore, the aim of this study was to evaluate the efficacy of a new quaternary ammonium-based commercial footbath product (QAC) for reducing the prevalence of active DD lesions compared with an industry standard (copper sulfate; $CuSO_4$) and typical on-farm footbath practices. A controlled intervention trial was conducted on 19 Alberta dairy farms over 12 wk, with 9 farms allocated to the QAC group (1% QAC daily, 5 d/wk), 5 to the $CuSO_4$ group (5% $CuSO_4$ daily, 5 d/wk), and 5 to a noninterference group (maintained typical footbath practices). A total of 22,285 observations on 3,465 lactating cows were assessed for DD lesions and leg cleanliness in the milking parlor. Five farms discontinued use of the QAC product for various reasons. Noninferiority analysis was used to assess QAC ability to decrease the proportion of cows with 1 or more active DD lesions compared with $CuSO_4$ after 6 wk. Multilevel logistic regression models for repeated measures were used to evaluate efficacy of QAC compared with $CuSO_4$ and noninterference farms in reducing the prevalence of active DD lesions at the foot level over 12 wk. The noninferiority analysis determined that the proportion of cows with 1 or more active DD lesion decreased 2.19 (95% CI: 1.39–3.46) times less after 6 wk of study on the QAC farms compared with $CuSO_4$ farms, making QAC inferior to $CuSO_4$. The multilevel logistic regression models determined that the proportion of active DD lesions increased in the QAC herds, whereas this proportion decreased in the $CuSO_4$ and noninterference herds over 12 wk. Additionally, cows in mid- and late-lactation had a higher odds of having active DD compared with fresh cows. Older cows (parity 3 and ≥4) had a decreased odds of active DD compared with first-parity cows. At the farm level, a higher baseline active DD prevalence resulted in increased odds of active DD; however, this did not modify the effect of treatment or week of study. We concluded that QAC was inferior to $CuSO_4$ and typical on-farm footbath practices, and further development of novel footbath products is required to develop an ideal alternative.

Key words: digital dermatitis, footbath, intervention study, copper sulfate, foot lesion

INTRODUCTION

Digital dermatitis (**DD**) is an infectious disease causing erosive, ulcerative, often painful lesions on the heel bulbs of cattle. The consequences of DD in dairy cattle include lameness, hoof conformation changes, losses in milk production, and decreased cow comfort, longevity, and fertility (Holzhauer et al., 2008a; Gomez et al., 2015). Digital dermatitis affects 70 to 90% of North America dairy farms (Cramer et al., 2008; Elliott and Alt, 2009; USDA, 2009; Solano et al., 2016) and was the most common (40%) of all foot lesions recorded by hoof trimmers in Alberta, British Columbia, and Ontario dairy herds over a 3-yr period (Alberta Milk, 2013; Solano et al., 2016).

Digital dermatitis is a multifactorial disease related to various bacterial (Gomez et al., 2012; Krull et al., 2016), host (Rodríguez Lainz et al., 1999; Murray et al., 2002; Solano et al., 2016), and environmental characteristics (Rodríguez Lainz et al., 1996a,b; Solano et al., 2015) that play a role in disease manifestation and progression. Farm-level risk factors for high prevalence of DD include poor environmental and animal hygiene (Rodríguez Lainz et al., 1996a,b), inadequate use of footbaths (Solano et al., 2015), purchase of cattle (Rodríguez Lainz et al., 1996a; Wells et al., 1999), and herd size >100 cows (Solano et al., 2016). Animal-level risk

Received November 4, 2016.
Accepted February 24, 2017.
[1]Corresponding author: jacobs.casey@gmail.com

factors include low parity and mid to late lactation for primiparous cows and peak lactation for multiparous cows (Murray et al., 2002; Somers et al., 2005; Solano et al., 2016).

Control of DD typically focuses on improving hygiene to limit bacterial spread and using footbaths with various antibacterial or disinfecting products to prevent DD lesions and control infectious foot diseases (Laven and Logue, 2006). The most common footbath product currently used in Canadian provinces is copper sulfate ($CuSO_4$), followed by formalin (Solano et al., 2015). Compared with a negative control (no footbath), the use of $CuSO_4$ footbaths resulted in more cows with no lesions (45 vs. 30%) and fewer cows with active (M1 + M2) lesions (21 vs. 70%; Speijers et al., 2010) when used at a 5% solution, 4 consecutives milkings weekly for 5 wk. However, both $CuSO_4$ and formalin have undesirable characteristics. Formalin is carcinogenic (Doane and Sarenbo, 2014), whereas $CuSO_4$ has been linked to environmental residues resulting in toxicity of aquatic organisms as well as death in sheep (Flemming and Trevors, 1989; Hoff et al., 1998; Epperson and Midla, 2007). This has prompted development of alternative footbath products with equivalent effectiveness to $CuSO_4$ or formalin but without the negative repercussions for the environment and human health.

The experimental product (**QAC**, DeLaval Manufacturing, Kansas City, MO) is a formulation containing quaternary ammonium compounds, specifically didecyldimethylammonium chloride and alkyl (C12–C16) dimethylbenzylammonium chloride, acting as broad-spectrum bactericidal and fungicidal disinfectants for the prevention of DD. When evaluated in vitro on *Treponema* culture without the presence of manure after 30 s and 10 min exposure, MIC and minimum bactericidal concentration (**MBC**) measurements suggest that QAC was equal to $CuSO_4$ (equal MIC and MBC) but less effective (lower MIC and MBC) than formalin (Hartshorn et al., 2013). In the presence of 10% manure, QAC was more effective (higher MIC and MBC) than $CuSO_4$ and formalin; however, at 20% manure, the MIC and MBC of QAC were lower than $CuSO_4$ and formalin. Further testing on dairy farms was required, as in vitro models cannot replicate the complexity of situations in the field. Therefore, the aim of this study was to evaluate the efficacy of QAC for decreasing the prevalence of active DD lesions. This was completed using 2 methods: (1) comparison to $CuSO_4$ (active control) using a noninferiority hypothesis that QAC is at least as efficacious as $CuSO_4$, and (2) comparison of the prevalence of active lesions in QAC to those in $CuSO_4$ and a noninterference group (no change in footbath protocol), therefore accounting for farm- and animal-level factors.

MATERIALS AND METHODS

Study Design

The study was designed as a randomized noninferiority intervention study with farms enrolled in 2 different footbath intervention groups. However, the parameters for a noninferiority study should ideally be determined using a meta-analysis or large studies, and results were only available from a single trial, with a small sample size and a relatively short duration of 6 wk (Speijers et al., 2010). Therefore, in addition to the 6-wk noninferiority study, a further evaluation over a 12-wk period was carried out to determine the efficacy of QAC compared with both $CuSO_4$ and a noninterference group for reducing the prevalence of active DD lesions. A noninterference group of farms was added to compare QAC to typical farm footbath protocols.

The objective of noninferiority trials is to demonstrate that an experimental treatment is at least as effective as an established treatment within a pre-specified margin of noninferiority (∂; Freise et al., 2013). The margin of noninferiority is determined as the smallest reliable effect size based on prior experience with an active control compared with no treatment and further determining the clinically relevant margin of indifference (Δ). This is the margin used in the null hypothesis that a 1% QAC protocol is inferior compared with a 5% $CuSO_4$ protocol in terms of the proportion of cows with active DD lesions over 6 wk expressed as a risk ratio (**RR**). The ∂ was determined by the smallest reliable effect size of $CuSO_4$ based on the one reported superiority study (Speijers et al., 2010). This effect size corresponded to the lower boundary of the 2-sided 95% confidence interval of the risk reduction of $CuSO_4$ relative to no treatment (a risk reduction of 25.1%), resulting in a $\partial = 1.335$ [RR calculated by dividing the $CuSO_4$ effect versus no treatment (0.749) into 1 ($1 \div 0.749 = 1.335$)]. Thereafter, Δ was calculated to maintain at least 50% of the smallest reliable effect of $CuSO_4$ (50% retention of 25.1% risk reduction; Freise et al., 2013), calculated by taking 50% of the natural logarithm of RR and converting it back to a RR ($e^{[\ln(1.355) \times 0.5]}$). Thus, Δ was defined as $\Delta = 1.155$. Noninferiority of QAC compared with $CuSO_4$ was concluded if the upper bound of the 2-sided 95% CI of the RR between QAC and $CuSO_4$ was smaller than Δ.

Farm Selection and Enrollment

Sample size was calculated based on the effect of the reference treatment ($CuSO_4$) from the trial comparing $CuSO_4$ to a negative control (Speijers et al., 2010) and an assumption of a 20% difference between the standard