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Short communication: Behavioral evaluation of the analgesic effect of flunixin meglumine in lame dairy cows

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ABSTRACT

The objective of this study was to evaluate the effect of flunixin meglumine treatment on lameness pain in dairy cows. Twenty-four lactating Holstein cows were enrolled in the study based on visual observation of abnormal locomotion. The primary measurement endpoint was weight-shifting between the rear limbs. Weight-shifting was calculated as the standard deviation of the weight borne on the rear limbs over a 15 min period; this value correlates directly with lameness pain in dairy cows. After collecting baseline weight-bearing data, we randomly assigned cows to 1 of 2 treatment groups: 2.2 mg/kg body weight flunixin meglumine (2 mL/45 kg) or an equivalent volume of isotonic sterile saline solution. Weight-bearing data were collected from each cow at 2, 6, 12, and 24 h after a single intravenous drug treatment. Mean locomotion scores over the 2 d before treatment were 2.38/5 in the flunixin-treated group and 2.43/5 in the saline-treated control group; these values were not significantly different. Weight-shifting values were also not significantly different on either pretreatment day. Cows treated with flunixin meglumine showed significantly less weight-shifting between the rear limbs at 6, 12, and 24 h after treatment compared with saline-treated controls, providing evidence that flunixin meglumine alleviates lameness-associated pain.
Key words: analgesia, flunixin, lameness, pain

Short Communication

Lameness is a common painful condition in dairy cows; recently published studies of North American dairy herds have returned estimates between 9.6% and 15% for the prevalence of lameness (Adams et al., 2017; Cook et al., 2016; King et al., 2016; Westin et al., 2016). Alleviating the pain of lameness can improve animal welfare, but no drugs have been approved by the United States Food and Drug Administration for the relief of pain in cattle. In horses, the non-steroidal anti-inflammatory drug (**NSAID**) flunixin meglumine is approved to treat pain due to musculoskeletal conditions and visceral pain due to colic (Intervet/Merck Animal Health, 2011). Flunixin meglumine is approved for use in cattle to treat inflammation and pyrexia associated with certain conditions, and NSAIDs such as flunixin meglumine are often used as extra-label therapy for pain relief in cattle (Fajt et al., 2011).

In a previous study, flunixin meglumine was administered to lame and non-lame dairy cows at the time of hoof trimming, and this combination of treatments did not affect lameness, as measured by visual observation (i.e., locomotion scoring) or by weight distribution (Chapinal et al., 2010a). The objective of this study was to evaluate the efficacy of flunixin meglumine treatment without concurrent hoof trimming for the alleviation of lameness pain in lactating dairy cows.

We selected lactating Holstein dairy cows for the study based on the presence of abnormal locomotion consistent with lameness and the absence of other health issues. Cows were enrolled weekly in cohorts of 2 or 4 and randomized to treatment groups blocked on enrollment cohort. Within each enrollment cohort, cows were randomly assigned to a treatment group, with equal allocation to each group (n = 12 per group) using SAS (SAS Institute, Inc., Cary, NC).

Cows in the drug treatment group (**FLU**) received a single intravenous injection of 2.2 mg/kg BW (2 mL/45 kg BW) flunixin meglumine (Banamine; Merck Animal Health, Madison, NJ). Cows in the placebo treatment group (**SAL**) received a single intravenous injection of isotonic sterile saline solution at the same volume dosage as the FLU group.

On each of the 2 d before treatment, we recorded baseline locomotion and weight-shifting data. A digital camera (Canon Power Shot; Canon USA, Melville, NY) was used to record each cow walking at least 5 paces, and these recordings were used by a masked, trained observer to assign a locomotion score of 1 to 5, as de-

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scribed by Flower and Weary (2006). A score of 1 was associated with no lameness, and a score of 5 indicated severe lameness. Scores were assigned in intervals of 0.5 points.

We recorded weight distribution using a 4-platform scale (Pacific Industrial Scale, Richmond, BC, Canada) with a standard head catch, which independently records the weight borne on each limb approximately 11 times per second, using procedures described by Chapinal et al. (2010b). Cows were acclimated to the 4-platform scale before data collection. At each data-collection point, cows stood on the scale for 3 sessions of 5 min each. Between sessions, cows were walked off the scale from the front, and then walked back onto the scale from the rear. Data recorded during defecation, urination, or placement of any hoof on the wrong platform were deleted from the analyses. We calculated the mean and standard deviation (**SD**) of the weight borne on each limb during each 5 min session, and averaged the SD values for the rear limbs. We then averaged the average SD values further across the 3 sessions to determine the overall weight-shifting value (**SHFT**) for that data-collection time point.

Then, 24 h after the second collection of baseline data as described above, cows received their assigned treatments. Immediately after morning milking, each cow was treated with flunixin meglumine or isotonic sterile saline solution. Treatment was followed by collection of weight-distribution data 2, 6, 12, and 24 h after treatment. Each cow was examined by a professional hoof trimmer 24 h to 48 h after the final data collection, and observed lesions were recorded.

We developed the summary and conducted the data analysis using SAS (SAS Institute, Inc.). As described above, the primary outcome variable was the SD of the mean weight borne on the rear limbs averaged over three 5-min sessions (SHFT). We analyzed the SHFT data using a general linear mixed model with repeated measures. The model included the fixed effects of treatment, time, and the treatment × time interaction. Random effects included block, animal within block and treatment, and error. A repeated effect with subject cow was included in the model. Different covariance matrices were tested and evaluated. We chose the best covariance matrix based on Akaike's and Bayesian information criteria. If the effects of treatment or treatment × time interaction were significant ($P < 0.05$), we performed treatment comparisons at each time point at the 5% level of significance (2-sided).

Locomotion scoring data are presented in Figure 1. Mean baseline locomotion scores 48 h before treatment were 2.33 ± 0.14 in the FLU group and 2.46 ± 0.14 in the SAL group. The day before treatment, mean locomotion scores were 2.42 ± 0.13 in the FLU group and 2.42 ± 0.12 in the SAL group. Locomotion scores were not significantly different between groups on either pretreatment day ($P > 0.05$ both days).

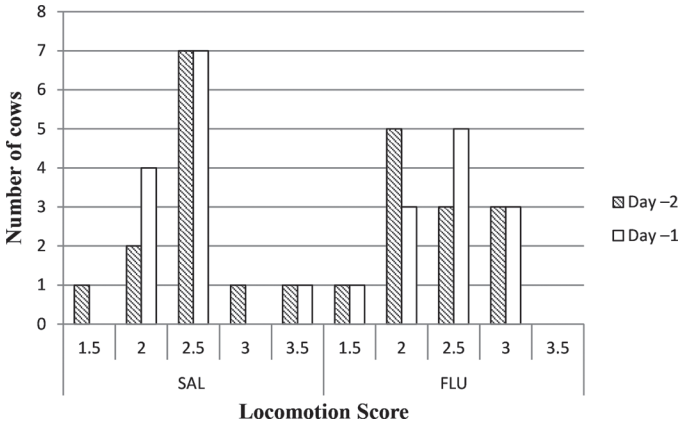

Figure 1. Distribution of pretreatment (d −2 and −1) locomotion scores. SAL = cows treated with 2 mL of isotonic saline solution/45 kg of BW (n = 12); FLU = cows treated with a single dose of 2.2 mg of flunixin meglumine/kg of BW (2 mL/45 kg; n = 12).

Weight-shifting data, measured as SHFT, are shown in Figure 2. Values for SHFT on days −2 and −1 before drug treatment were 27.1 ± 2.5 kg and 28.0 ± 3.0 kg in the SAL group and 24.7 ± 1.9 kg and 25.2 ± 2.4 in the FLU group. These values were not significantly different between groups on day −2 ($P = 0.52$) or day −1 ($P = 0.46$). Although SHFT values were not statistically different between groups before treatment, they were numerically different; therefore, they were included as a cofactor in post-treatment statistical analyses. At 2 h after treatment, SHFT values in the SAL and FLU groups were not different (29.6 ± 2.5 kg and 23.7 ± 2.5 kg, respectively, $P = 0.13$). At 6 h, 12 h, and 24 h, SAL cows exhibited more weight-shifting behavior than FLU cows. The SHFT after treatment in the SAL and FLU groups were 31.6 ± 2.6 kg and 23.4 ± 2.1 kg, respectively, 6 h after treatment ($P = 0.01$); 33.9 ± 2.7 kg and 25.1 ± 2.0 kg, respectively, 12 h after treatment ($P < 0.01$); and 32.3 ± 3.4 kg and 22.6 ± 2.6 kg, respectively, 24 h after treatment ($P < 0.01$).

In both treatment groups, the 2 daily pretreatment SHFT values were not different ($P > 0.05$ for both). In the FLU group, differences in weight-shifting behavior were not significant among days ($P > 0.05$ for all between-day comparisons). In the SAL group, SHFT values were not different between baseline and 2 h ($P > 0.05$), but weight-shifting was significantly greater at 6, 12, and 24 h after treatment than at baseline or 2 h after treatment ($P < 0.05$ for all comparisons).

Lesions observed in enrolled cows are described in Table 1. In both treatment groups, the most common lesions were sole lesions, including sole/toe hemorrhage,