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Changes in feeding, social, and lying behaviors in dairy cows with metritis following treatment with a nonsteroidal anti-inflammatory drug as adjunctive treatment to an antimicrobial

J. Lomb,* H. W. Neave,* D. M. Weary,* S. J. LeBlanc,† J. M. Huzzey,*¹ and M. A. G. von Keyserlingk*²

*Animal Welfare Program, Faculty of Land and Food Systems, University of British Columbia, 2357 Main Mall, Vancouver, BC, V6T 1Z4, Canada
 †Population Medicine, Ontario Veterinary College, University of Guelph, ON, N1G 2W1, Canada

ABSTRACT

Dairy cows with metritis display sickness behaviors, and nonsteroidal anti-inflammatory drugs (NSAID) have the potential to reduce these responses. The objective of this study was to investigate changes in feeding, social, and lying behaviors in dairy cows with metritis that had been treated with the NSAID meloxicam. After parturition, cows were housed in a dynamic, mixed-parity group of 20 animals with access to 12 electronic feed bins, 2 electronic water bins, and 24 lying stalls in a freestall pen. Every third day after parturition, vaginal discharge was evaluated to diagnose metritis based on the presence of foul smell and characteristic visual appearance. When diagnosed with metritis, animals ($n = 87$) were randomly allocated to receive either a single dose of meloxicam (0.5 mg/kg of body weight subcutaneously) or a placebo solution. All metritic animals received an antimicrobial (ceftiofur) for 5 d. We measured feeding and social behaviors at the feed bunk, as well as lying behaviors, and assessed within-cow changes from the day before to the day of (d 0) NSAID treatment, and from the day before to d 1 to 5 after treatment. Generally, behaviors changed around the day of diagnosis of metritis. Compared with the placebo group, cows that received meloxicam had a greater increase in the number of visits to the feeder, but tended to show less of an increase in dry matter intake and feeding time. These differences did not persist beyond 24 h after NSAID treatment. We observed no differences in changes in number of meals and feeding rate on d 0, but from d 1 to 5 cows treated with meloxicam had a lesser decrease in the number of meals and tended to have a greater decrease in feeding rate than did placebo-treated cows. In multiparous cows

on d 0 and from d 1 to 5, meloxicam treatment was associated with decreased lying times. In primiparous cows, lying time changes were similar between treatments on d 0, but lying times increased more on d 1 to 5 for meloxicam than for placebo cows. Overall, cows changed the number of lying bouts on d 0, and this increase tended to be smaller for the meloxicam cows. There were no treatment differences in changes of social behavior. In summary, we observed inconsistent and generally small effects of a single dose of meloxicam in addition to antimicrobial therapy on the behavior of cows with metritis.

Key words: analgesic, sickness behavior, meloxicam, pain, disease, welfare

INTRODUCTION

Cows diagnosed with postpartum disease show sickness behaviors, including reduced feed intake, shorter feeding times, changes in social behavior (Huzzey et al., 2007; Goldhawk et al., 2009), and changes in lying behavior (Medrano-Galarza et al., 2012; Itle et al., 2015). Metritis—an illness caused by uterine infection and characterized by fetid vaginal discharge with or without concurrent fever—is common in dairy cows, with a reported incidence of 10 to 30%, depending on the intensity and means of detection (Dubuc et al., 2010; Giuliadori et al., 2013; Pohl et al., 2016). Metritic cows are at risk of reduced milk production and impaired reproduction (Dubuc et al., 2011; Wittrock et al., 2011; Mahnani et al., 2015) and likely experience visceral pain (Stojkov et al., 2015). A wide range of bacteria can result in inflammation of the uterus (Azawi, 2008), with treatment strategies including systemically and locally administered antimicrobials (Haimerl and Heuwieser, 2014).

Only 2 nonsteroidal anti-inflammatory drugs (NSAID), flunixin meglumine and ketoprofen, have been studied in metritic cows. Drillich et al. (2007) treated cows with acute puerperal metritis with antimicrobials (ceftiofur at 1 mg/kg) either alone or in combi-

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¹Present address: Department of Animal Science, California Polytechnic State University, San Luis Obispo, CA.

²Corresponding author: marina.vonkeyserlingk@ubc.ca

nation with a single dose of flunixin meglumine (2.2 mg/kg i.v.), and found no beneficial effects of the NSAID on body temperature, reproductive performance, or milk yield. Pohl et al. (2016) found no differences in milk yield or reproductive performance between cows with acute puerperal metritis treated with ketoprofen (3 mg/kg per day for 3 d) or an antimicrobial treatment (ceftiofur, 1 mg/kg per day for 3 d). However, Amiridis et al. (2001) reported that when metritic cows treated with an antimicrobial and supportive fluid therapy were also provided flunixin meglumine, they showed a reduced fever, faster involution of the uterus, and improved reproductive performance.

Nonsteroidal anti-inflammatory drugs primarily act through inhibition of the enzymes cyclo-oxygenase (COX)-1 and COX-2. Through synthesis of prostaglandins, COX-2 promotes a pain and inflammatory response to infection, as well as a range of sickness behaviors (Pecchi et al., 2009), including reduced feed intake, reduced social interactions, and prolonged resting, which are thought to support pathogen elimination by the host (Hart 1988; Dantzer and Kelley, 2007). In contrast, sickness is thought to be associated with a feeling of malaise (Weary et al., 2009). Further, it has been argued that a sickness response may become maladaptive when expressed out of proportion or for a prolonged period (Pecchi et al., 2009). Provision of an NSAID mitigates these sickness behaviors in mice (Crestani et al., 1991; Swiergiel and Dunn, 2001; Soncini et al., 2012), pigs (Johnson and Von Bore, 1994), and dairy calves (Todd et al., 2010), but it is not clear whether provision of an NSAID would reduce sickness behaviors in adult dairy cows.

In contrast to flunixin meglumine and ketoprofen, meloxicam inhibits COX-2 more selectively and has a longer elimination half-life (>17 h in lactating dairy cows; EMEA 2009), so fewer treatments may be necessary to gain therapeutic benefits. A single dose of meloxicam has been shown to reduce local inflammation (Fitzpatrick et al., 2013) and increase cure, milk production, and reproductive performance (McDougall et al., 2009, 2016) in dairy cows with mastitis. In cows with dystocia, meloxicam improved some measures of feeding behavior (Newby et al., 2013).

This paper describes work that was done as part of a larger study that addressed multiple objectives including effects of parity on behavior (Neave et al., 2017) and changes in behavior in the days before diagnosis of metritis (Neave et al., 2018). The specific objective of this study was to determine whether providing meloxicam to cows with metritis, in conjunction with antimicrobial treatment, reduces the expression of sickness behaviors, including changes in feeding, social, and lying behaviors. We hypothesized that cows treated with

meloxicam would show reduced sickness behaviors, and that the positive effects of meloxicam would be most pronounced during the first 24 h after treatment when plasma concentrations of the drug are highest.

MATERIALS AND METHODS

The study was conducted at the University of British Columbia (UBC) Dairy Education and Research Centre in Agassiz, British Columbia, Canada. Animals were cared for following the guidelines of the Canadian Council on Animal Care (2009) and all procedures were approved by the UBC Animal Ethics Committee (protocols A10-0163 and A14-0040).

Animals, Housing, and Diet

From July 2013 to October 2014, all healthy, nonlame cows in the herd were monitored from approximately 21 d before calving to 21 d after calving. In total, health and behavior data from 105 primiparous (cows that had never calved before enrollment in the study) and 232 multiparous (cows that had at least 1 lactation before enrollment in the study) cows were collected by the end of the study (see Neave et al., 2017, 2018). From these animals, cows diagnosed with metritis and no other clinical disease, as described in detail below, were included in the study presented here.

In summary, cows were housed in a prepartum pen beginning 3 wk before their expected calving date and moved to the calving pen when imminent signs of calving were visible (e.g., relaxation of tail ligament, milk let-down). To maintain stocking density at 20 cows in the pen, we moved 1 cow into the prepartum pen every time 1 cow was removed. Within 24 h after parturition, cows were moved from the calving pen to the postpartum pen. To maintain stocking density at 20 cows, this addition coincided with the removal from the pen of the cow with the highest DIM. In both pens, cows had access to 12 electronic feed bins and 2 electronic water bins (Insentec, Marknesse, the Netherlands) and 24 lying stalls equipped with mats (Pasture Mat, Promat Inc., Woodstock, ON, Canada) covered with approximately 5 cm of sand. The adjacent maternity pen, a sawdust-bedded pack, housed at most 2 cows at a time and was equipped with 1 Insentec water bin and 6 Insentec feed bins; the number of feed bins filled with feed was equal to the number of cows in the pen.

Cows in all pens had ad libitum access to a TMR mixed according to NRC (2001) requirements and fed twice daily at 0700 and 1530 h. Details on feed composition are reported in Neave et al. (2017). After calving, cows were milked twice daily at approximately 0700 and 1700 h.

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