J. Dairy Sci. 100:1–6
https://doi.org/10.3168/jds.2016-11747


# The effects of periparturient administration of flunixin meglumine on the health and production of dairy cattle

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## ABSTRACT

Research on the assessment and management of pain in cows following difficult or assisted calving is still limited, especially on the effects of analgesics intended to mitigate this pain. The purpose of this study was to assess the effects of flunixin meglumine on the health and production of Holstein cows after calving. In total, 34 flunixin-treated and 38 placebo-treated animals were enrolled in a precalving treatment trial. A total of 633 animals given flunixin and 632 animals administered a placebo were enrolled in a postcalving treatment trial. In both cases, animals were randomly assigned to treatment, and researchers were blind to treatment condition until after analysis. A total of 1,265 animal records were analyzed for milk production for the first 14 d in milk and health outcomes for the first 30 d in milk. Animals treated with flunixin meglumine before calving had a significantly increased risk of stillbirth. Animals treated immediately after calving had increased odds of having a retained placenta and, in turn, increased risk of a high temperature, decreased milk production, and an increased risk of developing metritis. The administration of flunixin meglumine within 24 h of parturition is not recommended in dairy cattle.
**Key words:** dystocia, nonsteroidal anti-inflammatory drug (NSAID), retained placenta, metritis

## INTRODUCTION

Calving can cause stress and pain for the cow. Calving is more likely to be painful when calving is assisted, and Holstein calvings commonly require some assistance, particularly for primiparous animals (Mee, 2008). Bruising and lacerations of the vagina and uterus because of dystocia likely cause pain for several days after calving. The concentration of the inflammatory protein haptoglobin is elevated for a 2-wk period after parturition (Bionaz et al., 2007), indicating tissue damage and suggesting that inflammatory pain may affect cattle for this period.

Little research to date has addressed pain management after calving. Newby et al. (2013) administered meloxicam 24 h after assisted calving and found that treated animals visited the feed bunk more often and spent more time at the feed bunk compared with their placebo counterparts. Pain may also have secondary effects; for example, reducing milk production after calving and increasing the risk of some diseases. Newby et al. (2013) assessed the effect of meloxicam on DMI, milk production, blood parameters, and health events after calving but found no effects. Richards et al. (2009) administered ketoprofen immediately after calving and again 24 h later, and found that ketoprofen-treated cows were less likely to incur a retained placenta compared with untreated cows.

To our knowledge, no study has yet assessed the effects of the nonsteroidal anti-inflammatory drug (**NSAID**) flunixin meglumine on the health and production of cows after calving. Our hypothesis was that flunixin meglumine would mitigate the pain, resulting in a faster recovery, as evidenced by improved milk production and reduced disease in treated animals.

## MATERIALS AND METHODS

This study was conducted at a large commercial dairy farm (study site 1) and at a dairy research facility (study site 2). The trial period was from June 2006 to June 2007.

### *Study Site 1: Large Commercial Dairy Farm*

Approximately 1,260 Holstein transition primiparous and multiparous animals were enrolled 3 wk before their expected calving date. Complete data were available for

Received July 15, 2016.
Accepted September 30, 2016.
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1,174 cows. Study animals were housed and managed at Green Meadow Farms (**GMF**; Elsie, MI). The cattle were housed in a freestall facility during all phases of this trial except during the parturition process, when they were housed in box stalls. After calving, cows were milked twice daily in a milking parlor. Feeding procedures were conducted according to GMF standard management procedures, using a prefresh TMR ration and a milking herd TMR. All rations were balanced by the herd nutritionist to meet or exceed National Research Council requirements for Holstein dairy cows according to stage of lactation and production. Data on production, health events, reproductive performance, and removal from the herd were recorded using DairyComp 305 (Valley Ag Software, Tulare, CA).

The enrollment period was from June to November 2006. Any prepartum Holstein primiparous or multiparous animals at Green Meadow Farms that was clinically normal at the time of enrollment and at calving were eligible for inclusion in this study. Any primiparous or multiparous animals that were currently being treated for systemic illness or had an ongoing clinical disease were not enrolled. Enrolled subjects were randomly assigned via a random number generator and blocked by parity to receive either 2 doses of flunixin meglumine (50 mg/mL, Banamine, Merck Animal Health, Madison, NJ) or placebo (sterile saline). The volume of either flunixin meglumine or saline placebo solution was 25 mL for multiparous cows and 22 mL for primiparous animals, administered via intravenous injection into the jugular vein. The calculated doses of flunixin meglumine were based upon average cow and primiparous animal weights for GMF and, in this manner, all treated animals received a USDA-approved label dose of flunixin meglumine (1.1 to 2.2. mg/kg of BW).

### *Change of Study Protocol*

For the first 72 animals (flunixin meglumine n = 34, placebo n = 38, from June 1 to June 11, 2006), the first treatment occurred when the animal was moved to the calving box stall immediately precalving and again 18 to 36 h later during the morning lockup. Trial personnel were notified by the herd veterinarian after about 1 wk on the trial that there was an increase in the herd rate of stillbirths. Following unblinding of the enrolled animals, it was discovered that the stillbirth rate was greater in the flunixin-treated group compared with the placebo group (26.5% vs. 5.3%; Fisher's exact test, $P = 0.02$). Consequently, the treatment protocol was adjusted so that treatment occurred following parturition (when the animal was restrained for milking and the calf was removed from the calving pen). The administration of the treatments occurred at approximately 1 h postcalving and again during the next day's milking lockup at approximately 24 h postpartum.

The close-up dry pen was monitored every 2 h, 24 h/d. When evidence of impending parturition in the study subjects was visible (i.e., amnion, feet, elevated tail head with straining), the animal was moved to a maternity box stall. Management of the calving event was according to documented GMF standard operating procedure. Calving difficulty was scored from 1 to 4 (1 = unassisted, 2 = easy pull with one person and no mechanical assistance, 3 = difficult pull with 2 or more people and (or) mechanical assistance, 4 = caesarian/fetotomy). For assisted calvings, repositioning of the calf was recorded as a dichotomized variable. Daily milk production, daily rectal temperature (taken in the morning at first milking), and periparturient disease [i.e., left displaced abomasum, mastitis, metritis, retained placenta (**RP**), ketosis] were recorded for the first 30 d after calving. Standard case definitions for each periparturient disease, including high temperature, were developed and used in accordance with the standard operating procedures at GMF (Table 1).

### *Study Site 2: University of Guelph Research Dairy*

The study animals (n = 148 Holstein transition primiparous and multiparous animals) were housed and managed at the Elora Dairy Research Station (**EDRC**) of the University of Guelph (Elora, ON, Canada). The animals were housed in the individual maternity pen around calving and then in a tiestall housing facility 2 d after calving. They were eligible to be enrolled only if they were clinically normal at the time of enrollment and at calving. In addition, these animals were managed using a milking parlor system and milked 2 times per day. Feeding procedures were conducted according to EDRC standard management procedures, using a prefresh TMR ration and a milking herd TMR. All rations were balanced by the herd nutritionist to meet or exceed National Research Council requirements for Holstein dairy cows according to stage of lactation and production.

Animals were randomly assigned to receive either flunixin meglumine or saline placebo at a volume of 25 mL for multiparous cows and 22 mL for primiparous animals, via intravenous injection into the jugular vein. The calculated doses of flunixin meglumine were based upon average cow and primiparous animal weights, and in this manner all treated animals received a label dose of flunixin meglumine (1.1 to 2.2. mg/kg of BW Banamine, Merck Animal Health) within 1 h postcalving or after finding the cow with a calf in the pen (d 0), and again the following morning (d 1, approximately