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Research

Effect of meloxicam administration after calving on milk production, acute phase proteins, and behavior in dairy cows

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ABSTRACT

Calving is an intrinsically risky process that can cause welfare and economic problems. The objective of this study was to assess the effect of the nonsteroidal anti-inflammatory drug meloxicam on various physiological and behavioral measures which can be related to pain in cattle. Sixty Friesian dairy cows from first to sixth parity were studied around calving and were randomly allocated into 2 homogeneous groups relative to parity and treated with either meloxicam or a placebo after calving. Treatments were administered on average 3.4 hours after calving, within a maximum of 6 hours. Calf positions at calving and calving assistance (unassisted or easy manual pull) were recorded. Milk production, rectal temperature, and activity (calculated as the number of steps per hour) were measured on each cow. From a subsample of 20 cows, haptoglobin (Hp) and serum amyloid A (SAA) concentrations were also obtained. The following behaviors were observed on video recordings: posture, changing posture, location of cow in pen, feeding, and tail up behaviors 2 days before and after calving. Statistical analysis was carried out with the SAS software using MIXED or GENMOD procedures. Most variables showed a parity and/or time effect around calving. This study did not demonstrate any significant effect of meloxicam on milk production or on acute phase responses of Hp and SAA. However, postcalving activity was significantly increased in meloxicam-treated heifers.

Introduction

It is widely accepted that calving causes acute pain with at least 2 dimensions, a sensory and an affective component (Chapman and Nakamura, 1999). Calving is an intrinsically risky process for both mother and young, and this risk increases in dystocic calving. Maternal health problems that have their origin in the peripartum period can extend far into lactation. Perinatal mortality represents half of all preweaning calf mortality. Both cause welfare problems and economic losses (e.g., Berglund et al., 2003; Farhoodi et al., 2000). Consequently, the periparturient or transition period is the most critical period in dairy cows, in terms of health status and production (Tóthová et al., 2008). Optimizing pain management during the periparturient period can have an important effect on health, welfare, and productivity in dairy cows. Measures of physiology, behavior, and food or water intake may be useful for the assessment of pain during calving (Weary et al., 2006). A greater immune or inflammatory response during parturition may indicate calving conditions associated with pain such as active infection or physical trauma (e.g., vaginal tears). Increased rectal body temperature and activation of the acute phase response may be used to study such immune and inflammatory activation. Anil et al. (2002) suggested that behavior is a more sensitive measure of pain than physiological indicators. Deviation from normal behavior is the most important single indicator of pain but may sometimes be difficult to interpret. For example, isolation from group members can be an early sign of pain (Anil et al., 2005) but also of impending parturition in herd animals. The most frequently described behavioral changes before calving are an increase in restlessness and a decrease in eating and/or ruminating time, perhaps due to discomfort associated with calving (e.g., Houwing et al., 1990; Huzzey et al., 2005). Behaviors such as scraping the floor with the forefeet (Wehrend et al., 2006) or raising the tail for longer (Barrier et al., 2012) before calving were more frequent in dystocic than eutocic calving. However, more efforts are needed to study behavior

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before and after parturition to indicate valuable and practical indicators for pain or discomfort during calving and during recovery from inflammation caused by parturition. Parturition is associated with activation of the inflammatory cascade (e.g., Romero et al., 2006) by an increase in the number of inflammatory cells and a higher production of proinflammatory cytokines in the cervix, myometrium, membranes, and amniotic cavity (Gotsch et al., 2008). The aim of treatment with steroids or nonsteroidal anti-inflammatory drugs (NSAIDs) is primarily to control pain by reducing inflammation and swelling (Short, 1998). Despite frequent use of NSAIDs by veterinarians in the postcalving period, published data on their effect use in the calving cow are very limited (Laven et al., 2012). Meloxicam, a preferential COX-2 inhibitor, has anti-inflammatory, antiexudative, analgesic, and antipyretic properties (EMEA, 2009). To our knowledge, only 1 work has been published on the effect of meloxicam following assisted calving (Newby et al., 2013). Although there was no significant difference in productive, physiological, or health indicators in this study, meloxicam administration 24 hours after dystocic calving resulted in increased feeding time and frequency of bunk visit.

This study aimed to investigate whether the administration of meloxicam after calving provided beneficial analgesic and anti-inflammatory effects that could be identified using physiological and behavioral measures. It was hypothesized that milk production, rectal temperature (RT), acute phase proteins, cow activity, and cow posture may be affected by meloxicam therapy.

Materials and methods

Animals and treatments

The experimental procedure was carried out on a commercial dairy farm (Torre Santa Maria, Vallfogona de Balaguer, Lleida, Spain) from September to December 2008. Each cow was studied from 5 days before the expected calving date (day 5) to 1 month after calving. The farm had 1000 Friesian dairy cows, and the mean $\pm$ standard error (SE) of environmental temperature was 13.22 $\pm$ 0.47°C. Although the farm did not calculate the prevalence of annual dystocic calvings, the veterinarian in charge did not consider dystocia to be a major problem.

Sixty Friesian dairy cows from first to sixth parity (mean $\pm$ SE, 2.25 $\pm$ 1.18 parities) were randomly selected on day −5. Cows with an acceptable body condition score (BCS) (BCS $\geq$ 2.5 and $\leq$ 3.5, using the 5-point scale from the study by Roche et al., 2009; Wildman et al., 1982) and without lameness (lameness was diagnosed in moving animals when a veterinarian observed uneven temporal rhythm between hoof beats and reluctance to bear weight on a foot) or any other clinical sign of illness were included in the study. Only calving that required no assistance or assisted calving by means of an easy manual pull applied only by 1 person (Mee, 2008) were studied. Dystocic calvings (13 cows that required hard rope pull and/or mechanical calf puller, and 1 cow that required caesarean section), stillbirths (9 cows), and twin calving (6 cows) were excluded.

Cows were randomly allocated into 2 groups according to parity and treated with either meloxicam (Metacam® 20 mg/mL solution injection; Boehringer Ingelheim) or placebo (excipient without pharmacologically active ingredient) as control, at a dosage of 0.5 mg/kg injected subcutaneously in the neck region. Twenty-five heifers (12 in the meloxicam group and 13 in the control group) and 35 multiparous cows (17 in the meloxicam group and 18 in the control group) were tested. In compliance with management practices on the farm, treatments were administered when cows entered the postcalving pen within a maximum of 6 hours. The time interval between calving and treatment was recorded in every cow (mean $\pm$ SE, 3.39 $\pm$ 0.26 hours). To ensure blinding, the meloxicam and control groups were labeled A and B, respectively, and producers and researchers were unaware of whether a given cow was in the treatment or the control group. In cases where an additional anti-inflammatory treatment was required, the cow was excluded from the study. Occurrence of retained placenta, metritis, mastitis, milk fever, and digestive or respiratory disorders diagnosed from the day of calving (day 0) to 15 days after calving (day +15) was documented.

Housing, feeding, and general management

In the pre- and post-calving pens, cows were fed *ad libitum*. The precalving pen was covered with fresh straw daily and cleaned once a month. Following management practices on the farm, cows were not permitted to eat from 1 PM to 6 PM in the precalving pen to increase the percentage of daylight calving (e.g., Gleeson et al., 2007). In the postcalving pen, however, cows had free access to food. About 5 days before expected parturition, cows were housed in the precalving pen. When clear indicators of calving were observed (i.e., enlargement of the udder, swelling of the vulva, and relaxation of the pelvic ligaments, Berglund et al., 1987), the cow was separated from its herd mates and taken to a different area in the same precalving pen, where it was visually supervised every 15 minutes from outside the pen. Cows were initially left to calve alone. However, if calving did not progress within 90 minutes, the farmer provided assistance via an easy manual pull, a hard rope pull, or a hard mechanical pull. In severe cases, veterinary intervention was required. Calves were kept with their dams for a minimum of 15 minutes and a maximum of 4 hours after calving, depending on milking time. Once the calf was removed, cows were milked and then moved to the postcalving pen. Cows were milked twice daily (at 9 AM and 7 PM), in a rotating parlor with 60 stalls.

Data collection

Calving difficulty

During calving, the following events were recorded: calf position (head forward, head back, or unknown), sex of calves (male or female), and level of calving assistance (unassisted or easy manual pull).

Milk production

Milk production (kilograms per cow per milking) was recorded for 1 month. Data were analyzed for each milking and as total production for the day.

Physiological measures

RT was measured using a single thermometer probe (Testo 110, Lenzkirch, Germany) and a consistent penetration depth of 10 cm for all measurements. RT was taken when cows were placed in the precalving pen (day −5), twice a day (at 10:30 AM and 8:30 PM) for 3 days after calving, and every time a blood sample was taken. In this study, fever was defined as RT $\geq$ 39.5°C (Smith and Risco, 2005). Just before administration of either treatment or placebo, blood samples were collected from the coccygeal vein of 20 cows (well balanced for parity and treatment) to determine serum amyloid A (SAA; μg/mL) and haptoglobin (Hp; mg/mL) on the day of calving (day 0) and on days +2, +4, and +15 after calving. Serum was obtained by centrifugation and frozen until analyzed. Hp was quantified by a spectrophotometric method (hemoglobin binding assay) with commercial reagents from Tridelta Development Limited (Ireland) on an automated analyzer (Olympus AU400, Hamburg, Germany). Concentration of SAA was quantified by a sandwich ELISA kit (Tridelta Development Limited, Kildare, Ireland).