Comparative pharmacokinetics of meloxicam between healthy postpartum versus mid-lactation dairy cows

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Introduction

Pain is a physiological response that cattle often experience as a result of pathological conditions or through implementation of common management procedures. There is a need for effective modalities of analgesia to manage pain and limit welfare concerns in lactating dairy cattle. Meloxicam has been shown to be an effective treatment to decrease lameness-associated pain related to udder edema in the postpartum period.[1] To date, transdermal flunixin meglumine is the only available labeled product for bovine pain control in the United States. Non-steroidal anti-inflammatory (NSAIDs) drugs, like meloxicam and flunixin meglumine, are commonly used by veterinarians. Previous work by our team has found differences in plasma and milk concentrations of oral meloxicam between postpartum and mid-lactation dairy cows.[2] This work displayed an increased relative bioavailability in postpartum cows and longer milk residue. Due to this discovery, longer withdrawal periods for meat and milk are necessary in the postpartum cow following meloxicam therapy. This prior work has precipitated a need to further characterize the bioavailability of oral administration of meloxicam in various stages of lactation and establishment of withdrawal periods in the postpartum dairy cow. We hypothesize that meloxicam will be more bioavailable in postpartum relative to mid-lactation dairy cows and therefore require longer withdrawal times.

Materials and Methods

To further characterize bioavailability, a parallel study design was implemented. In phase one, 24 healthy, lactating Holstein cows were enrolled. The postpartum group was enrolled within 24 hours of freshening and randomly assigned to meloxicam intravenous (0.091 mg/lb; 0.2 mg/kg) or oral (0.45 mg/lb; 1.0 mg/kg) administration. At the time of enrollment, the cow was paired to a mid-lactation (> 150 DIM) cow to receive the same treatment. Plasma was collected at 0, 5, 10, 15, 30, 60 minutes, 2, 4, 8, 16, 24, 48, 72, 96, and 120 hours following intravenous administration or 0, 4, 8, 12, 16, 20, 24, 48, 72, 96, 120, and 144 hours following oral administration of meloxicam. Meloxicam was extracted from plasma and quantified using LCMS-MS. In phase two, 48 healthy, postpartum lactating Holstein cows were randomly allocated within 24 hours of freshening to treatment groups based on days in milk (DIM). Groups included 0, 3, 7, 10, 14, and 21 DIM. Cows were orally administered meloxicam (0.45 mg/lb; 1.0 mg/kg) and milk was sampled at 0, 8, 16, 24, 48, 72, 96, and 120 hours. Meloxicam was extracted from milk and quantified using LCMS-MS to determine DIM transition point for withdrawal time based on FDA criteria.

Results

Results of phase one indicated a decreased clearance in postpartum cows, which results in a longer half-life and increased bioavailability. This result was most evident after intravenous administration. Clearance corrected relative bioavailability of postpartum versus mid-lactation cows was 130%. Results of phase two indicate a milk withdrawal of at least 120 hours for postpartum cows up to 21 DIM after oral administration of meloxicam. Cows > 21 DIM through mid-lactation require a milk withdrawal time of 96 hours after oral administration of meloxicam.

Significance

Due to decreased clearance and increased bioavailability, orally administered meloxicam remains in the milk longer in postpartum than mid-lactation dairy cattle, necessitating longer withdrawal times based on DIM.

References

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