Effect of dehorning pain on the pharmacokinetics of transdermal flunixin in Holstein calves

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Introduction

Dehorning is a common husbandry practice performed on calves in the United States. Calves undergoing the dehorning process have been documented to be under significant pain and distress. Flunixin meglumine has been shown to mitigate the pain associated with dehorning. Furthermore, transdermal flunixin is the only medication in the United States with a label for pain control in cattle. This study was conducted to determine if pain influences the pharmacokinetics and anti-inflammatory properties of flunixin meglumine when administered by the transdermal route.

Materials and Methods

Sixteen weaned male Holstein calves, ages 6 to 8 weeks of age, were enrolled. Prior to dehorning, all calves received flunixin meglumine intravenous to determine bioavailability of topically applied flunixin. A cross-over block design was used for this study with 8 calves in each treatment group. Calves were randomly assigned to either a topical flunixin and dehorn (PAIN) group or a topical flunixin and sham dehorn (NO PAIN) group in the first replicate. Calves were then assigned to the opposite treatment in the second replicate. Calves were administered flunixin meglumine topically (1.5 mg/lb; 3.33 mg/kg) as a pour-on concurrently with hot iron dehorning or sham dehorning. Plasma drug concentrations were determined using LC/MS-MS. Pharmacokinetic parameters were determined using non-compartmental analysis. Prostaglandin E2 (PGE2) concentrations was determined using a commercial ELISA assay. The 80% inhibition concentration (IC80) of flunixin on PGE2 was determined for each calf in all phases of the study. Pharmacokinetic data were statistically analyzed using paired T-tests and Wilcoxon rank sums for nonparametric data. PGE2 concentrations were log transformed and analyzed using repeated measures.

Results

Pain significantly increased the plasma half-life of flunixin (10.1 h vs 7.2 h; P=0.02). There were differences in pain vs no pain on the bioavailability, maximum concentration, and volume of distribution, but these differences were not significant. There was no effect of pain on PGE2 concentrations (P=0.20). However, there was a treatment (pain vs no pain) by time interaction (P=0.04). PGE2 concentrations were significantly lower in the pain group at 48 and 72 hours (P=0.01 and P=0.03, respectively). The IC80 of flunixin on PGE2 was determined to be 0.039 μg ml-1 for the NO PAIN phases and 0.026 μg ml-1 in the PAIN phases (P=0.88).

Significance

The pain associated with dehorning alters the pharmacokinetics and anti-inflammatory properties of transdermal of flunixin when administered topically.