

Pharmacokinetics of intravenous and oral firocoxib in preweaned calves and evaluation of perioperative analgesia following cautery dehorning

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Introduction

The pharmacokinetics of firocoxib after IV and PO administration to preweaned calves and perioperative analgesic effects following cautery dehorning were investigated.

Materials and Methods

Ten Holstein calves (mean \pm SD, 98.6 \pm 11.7 lb [44.8 \pm 5.3 kg]) approximately 30 days old were administered firocoxib (0.5 mg/kg, IV or PO) in a randomized cohort design with a 14-day washout period. Blood samples were collected at predetermined times immediately before and for 96 hours after firocoxib administration, and the plasma firocoxib concentration was determined by liquid chromatography-tandem mass spectrometry. Pain biomarkers including ocular temperature as determined by infrared thermography, mechanical nociception threshold as determined by pressure algometry, heart rate, and serum cortisol and substance P concentrations were evaluated following cautery dehorning. Computer software was used to estimate pharmacokinetic parameters for firocoxib with a 1-compartment model for IV administration and a 2-compartment model for PO administration.

Results

Following IV administration, the geometric mean elimination half-life was 6.7 hours (range, 4.6 to 9.7 hours), volume of distribution in a steady state was 1410.7 mL/lb (range, 956.6 to 3282.4 mL/lb) (3,103.5 mL/kg [range, 2,104.5 to 7,221.4 mL/kg]), and clearance was 55.3 mL/h/lb (range, 45.7 to 71.23 mL/h/lb) (121.6 mL/h/kg [range, 100.06 to 156.7 mL/h/kg]). Following oral administration, maximum plasma concentration was 127.9 ng/mL (range, 102.5 to 151.3 ng/mL), time to maximum plasma concentration was 4.0 hours (range, 2.6 to 5.6 hours), and elimination half-life was 18.8 hours (range, 14.2 to 25.5 hours). Bioavailability of oral firocoxib was calculated as 98.4% (range, 87.1% to 117.6%). Ocular temperature was changed from baseline for 24 hours after firocoxib administration.

Significance

The pharmacokinetic findings from this study suggested that firocoxib has excellent bioavailability and slow elimination kinetics and may be clinically applicable for use in preweaned calves; however, perioperative analgesia in preweaned calves requires further study.