Pharmacokinetics and pharmacodynamics of intravenous and transdermal flunixin meglumine in alpacas

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Introduction

Selection of drugs for use in South American Camelids (SAC) is difficult due to lack of approved products for use in these species. Drugs and drug dosages are selected from limited published data or extrapolated from other species. Administration of intravenous (IV) medications to SAC can be difficult due to challenges in restraint, limited venous access, and unique cervical anatomy. Pharmaceuticals administered routes other than IV are attractive for use in SAC.

Flunixin meglumine is a non-steroidal anti-inflammatory drug used in many species for its antipyretic, analgesic, and anti-inflammatory properties. In cattle, flunixin meglumine is specifically labeled for IV administration. A new transdermal (TD) formulation of flunixin has been developed and approved for use in cattle. The topical nature and longer duration of action compared to IV flunixin make this product ideal for use in SAC. The purpose of this study was to determine the pharmacokinetic and pharmacodynamic properties of IV and TD flunixin meglumine in alpacas.

Materials and Methods

This study was conducted using a randomized crossover design. Eight healthy female Huacaya alpacas were administered flunixin meglumine IV into a jugular vein at a dose of 1.0 mg/lb (2.2 mg/kg). Following a 10-day washout period, alpacas were administered flunixin meglumine TD at a dose of 1.5 mg/lb (3.3 mg/kg). Blood samples were collected at predetermined times from 0-48 h and 0-120 h following IV and TD dosing, respectively. Plasma drug concentrations were determined using liquid chromatography with mass spectroscopy. Pharmacokinetic analysis was completed using non-compartmental methods. The individual animal pharmacokinetic values were calculated and descriptive statistics (geometric mean, minimum, median, and maximum values) reported. Bioavailability was calculated for topical administration. At predetermined time points, 1 mL of whole blood was spiked with *E. coli* lipopolysaccharide to stimulate prostaglandin E2 (PGE2) production. Prostaglandin E2 concentrations were determined using a commercially available ELISA. The percent change in PGE2 production and 80% inhibitory concentration (IC80) were calculated.

Results

No adverse reactions were seen following IV or TD administration of flunixin meglumine. Mean elimination/terminal half-life (T½) after IV administration was 4.5 h (range 3.4 to 5.6 h) resulting from a mean apparent volume of distribution (Vz) of 570.6 ml/kg (range, 387.3 to 1142 ml/kg) and plasma clearance (CL) of 87.3 ml/kg/h (range, 55. 5-179.3 ml/kg/h). The mean Cmax, Tmax, and T½ for flunixin following TD administration were 106.4 ng/ml (range, 57.0 to 168.6 ng/ml), 13.6 h (range, 6.0 - 34.0 h), and 24.1 h (18.6 to 39.5 h), respectively. The mean bioavailability for TD flunixin was calculated as 25.05%. The mean 80% inhibitory concentration (IC80) of PGE2 by flunixin was 0.23 µg/ml (range, 0.01 to 1.38 µg/ml). Following IV administration, at 1 h, 2 h, and 4 h there was an over 80% decrease in PGE2 concentrations. Prostaglandin E2 concentrations were back to baseline levels by 12 h post-IV administration. Transdermal flunixin failed to inhibit PGE2 production at any time points.

Significance

All alpacas tolerated IV and TD administration of flunixin. Efficacy of IV and TD flunixin was measured by PGE2 suppression. Intravenous flunixin rapidly inhibited PGE2 for a short period of time. Transdermal flunixin had negligible effect on PGE2 inhibition at any timepoint. Poor bioavailability and suppression of PGE2 identified in this study indicates that TD flunixin administered at 1.5 mg/lb (3.3 mg/kg) is not recommended for use in alpacas.