

Comparison of flunixin pharmacokinetics and milk elimination in healthy cows and cows with mastitis

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Introduction

Flunixin meglumine (FLU) is a non-steroidal anti-inflammatory drug that is labeled for use in dairy cattle for regulation of inflammation in endotoxemia and for the control of pyrexia associated with bovine respiratory disease and acute bovine mastitis at a dose of 1.0 mg/lb (2.2 mg/kg), IV every 24 hours or 0.5 mg/lb (1.1 mg/kg), IV, every 12 hours. The milk withdrawal time for FLU is 36 hours. Currently, FLU is the second most common violative drug residue found in the dairy industry. The reason for the numerous illegal FLU drug residues remains unclear; however, prolonged clearance in cows with mastitis, compared with that in healthy cows is one possible explanation. Cows with mastitis may have prolonged elimination of 5-hydroxy flunixin (5OH), the marker residue for FLU in milk, which results in milk FLU residues greater than the tolerance limit of 2 ppb after 36 hours. The objective of this study was to determine if the pharmacokinetics and milk elimination of FLU and 5OH differed between healthy cows and cows with mastitis.

Materials and Methods

Twenty lactating Holstein cows were enrolled in a case-control study. Ten cows had naturally occurring mastitis and 10 healthy cows served as controls. All cows received 1.0 of FLU/lb (2.2 mg/kg), IV, 1.0 of ceftiofur/lb (2.2 mg/kg), IM, and an intramammary antimicrobial (cephapirin or ceftiofur) administered in accordance with the label instructions. Blood samples were collected at 0, 0.25, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours after FLU administration. Composite milk samples were collected at 0, 2, 12, 24, 36, 48, 60, 72, 84, and 96 hours after FLU administration. Plasma and milk samples were analyzed

by ultra-high-pressure liquid chromatography with mass spectrometric detection.

Results

For FLU in plasma samples, differences in area under the curve, mean residence time and clearance of were observed between groups. Mean clearance of FLU was 120.2 and 67.0 mL/hour/kg for healthy cows and cows with mastitis, respectively. For 5OH in milk samples at the 36-hour milk withdrawal time, 8 cows with mastitis had 5OH residues in their milk greater than the tolerance limit of 2 ppb. Flunixin residues were found in the milk from cows with mastitis up to 60 hours after FLU administration, whereas in control cows, FLU residues were only detected up to 24 hours after FLU administration.

Significance

Flunixin residues identified in tissue and milk from dairy cows may be related to mastitis-induced alterations in FLU plasma pharmacokinetics and milk elimination. Milk elimination of 5OH is prolonged in cows with mastitis, compared with that in healthy cows, which can result in violative FLU milk residues past the 36-hour labeled withdrawal time. The ratio of FLU to 5OH in the milk is altered in cows with mastitis, compared with that in healthy cows; thus, further research needs to be conducted to determine whether 5OH is the appropriate milk marker residue in cows with mastitis. Findings of this study suggested that withdrawal times determined in healthy cattle may not always be accurate in diseased cattle.