

Use of an ultrafiltration device in gland cistern for continuous sampling in healthy and mastitic quarters of lactating cattle

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Introduction

Pharmacokinetic studies of the drugs in the milk are often limited due to infrequent sampling associated with milking. Alternatively, frequent sample collection with repeated milking may increase drug elimination. The objective of this study was to determine the feasibility of continuously sampling the udder using ultrafiltration.

Materials and Methods

An ultrafiltration probe was placed into the gland cisterns of normal quarter and mastitic quarters of 4 mature mid-lactation Jersey cows with naturally occurring mastitis. An ultrafiltration probe was secured to the caudal or lateral aspect of the udder depending on the quarter being sampled. The timed interval samples were collected at 0, 2, 4, 6, 8, 12, 18, 24, 28, 32, 36, 48, 60, 72, 84, and 96 hours post-drug administration. Plasma samples were collected at the same time points. Whole milk samples from each quarter were also taken every 12 hours at milking. Each cow received 1 mg/lb (2.2 mg/kg) of flunixin intravenously prior to milking at time 0 and was milked by machine every 12 hours. Flunixin concentrations in the plasma, milk, and milk ultrafiltrates were analyzed by use of ultra-high-performance liquid chromatography with mass spectrometry. Pharmacokinetic parameters for plasma and milk ultrafiltrate were determined using noncompartmental analysis.

Results

There were no significant impacts on the appearance of the milk or the ability to milk the cows after implantation of the ultrafiltration probes. Mean flunixin plasma terminal elimination half-life was 3.38 ± 1.33 hr. Flunixin was at or below the level of detection ($0.001 \mu\text{g}/\text{mL}$) in the plasma of all of the cows 48 h after intravenous administration. The concentration of flunixin collected from the ultrafiltration probes in the mastitic quarters were higher than that of the healthy quarter. The mean area under the curve was higher in mastitis quarters than healthy quarters ($1.24 \pm 0.91 \text{ hr} \cdot \mu\text{g}/\text{mL}$ and $0.28 \pm 0.24 \text{ hr} \cdot \mu\text{g}/\text{mL}$, respectively). Samples of milk ultrafiltrate demonstrated peaks in flunixin concentrations between 30 to 36 hours in milk that were not observed in total milk or plasma samples.

Significance

Collection of ultrafiltration samples from the mammary gland of cows provides a viable means to continuously assess drug concentrations in the milk while continuing to milk the cow normally. This allows for optimal pharmacokinetic modeling of active drug concentrations over time. These studies demonstrate the utility of continuous sampling of milk via ultrafiltration for future pharmacokinetic/pharmacodynamics studies in cattle.