

# Altered plasma pharmacokinetics of ceftiofur hydrochloride in cows affected with severe clinical mastitis

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## Introduction

Mastitis is a frequent problem among dairy cows that reduces milk yield and increases cull rates. Therapy with the cephalosporin antibiotic ceftiofur hydrochloride (CEF) can reduce the need for culling, but the incidence of CEF violative residues has increased annually since 2011. This pattern indicates that disease status may affect the pharmacokinetics (PK) of CEF. The objective of this study was to compare the plasma PK of CEF between healthy dairy cattle and those afflicted with severe clinical mastitis. Our hypothesis is that cows affected with severe infectious disease will have altered CEF PK relative to healthy cows, necessitating variance in dose regimens and withdrawal periods.

## Materials and Methods

Eight cows with naturally occurring, severe mastitis and 8 clinically healthy cows were treated with CEF at 1 mg/lb (2.2 mg/kg) CEF of body weight (2 mL/100 lb) once daily for 5 days via the intramuscular route. Blood was collected for plasma harvest at 0, 8, 16, and 24 hours after the first CEF administration, and every 8 hours thereafter until 120 hours after the final dose. Plasma samples were analyzed for CEF concentrations using liquid chromatography coupled with mass spectrometry.

## Results

With the exception of time 0, CEF was detected at all time points. Compared to control cows, the disease group had higher volume of distribution ( $1.44 \pm 0.32$  vs  $3.08 \pm 0.92$  L/kg,  $P=0.0011$ ) and drug clearance rates ( $0.466 \pm 0.099$  vs  $0.850 \pm 0.194$  mL/min/kg,  $P=0.0006$ ). The disease group also had a lower area under the curve/dosing interval ( $81.2 \pm 18.3$  vs  $44.7 \pm 8.5$  h  $\times$   $\mu\text{g/mL}$ ,  $P=0.0006$ ), steady state concentration maximum ( $5.56 \pm 1.51$  vs  $3.29 \pm 0.43$   $\mu\text{g/mL}$ ,  $P=0.0006$ ), and dose-adjusted peak steady state concentrations ( $2.45 \pm 0.66$  vs  $1.44 \pm 0.19$   $\mu\text{g/mL}$ ,  $P=0.0006$ ). All other PK parameters were not different between the two groups.

## Significance

Altered PK, as suggested by this trial, may contribute to decreased efficacy of CEF in the treatment of severe disease and result in an increased risk for the development of a violative residue in meat. Further research is needed to more completely characterize drug distribution in diseased cattle and to study the effect of co-administration of other drugs on drug distribution. This study suggests that diseased cattle should be included in drug approval trials to accurately determine dosage regimens and withdrawal periods.

# Association of bedding type with production and milk quality on larger Wisconsin dairy farms

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## Introduction

On modern dairy farms bulk milk SCC is associated with the prevalence of intramammary infection. Bacterial exposure at the teat-end is a primary source of exposure to potential mastitis pathogens, and reducing this exposure is a fundamental aspect of controlling environmental mastitis.

As farm size has increased, an increasing diversity of bedding types is used. Teats may be in direct contact with bedding materials for 12 to 14 hours/day, making bedding a primary reservoir for mastitis pathogens. The objective of this study was to determine bedding and milking management practices associated with milk production and bulk-milk quality on large Wisconsin dairy farms.