

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 ± 0.32 vs 3.08 ± 0.92 L/kg, $P=0.0011$) and drug clearance rates (0.466 ± 0.099 vs 0.850 ± 0.194 mL/min/kg, $P=0.0006$). The disease group also had a lower area under the curve/dosing interval (81.2 ± 18.3 vs 44.7 ± 8.5 h \times $\mu\text{g/mL}$, $P=0.0006$), steady state concentration maximum (5.56 ± 1.51 vs 3.29 ± 0.43 $\mu\text{g/mL}$, $P=0.0006$), and dose-adjusted peak steady state concentrations (2.45 ± 0.66 vs 1.44 ± 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.

Materials and Methods

Eighty-four percent (84%; 325 of 387) of Wisconsin dairy farms producing in excess of 25,000 lb (11,340 kg) of milk daily participated in a survey consisting of 60 scripted questions. Milk quality results were obtained for a 2-year period, and results were analyzed for farms that used the same bedding type in all pens during the entire study period. Bedding types consisted of inorganic bedding (IB – primarily sand), manure solids (MB – primarily from digesters), and other organic bedding (OB – primarily wood products). Associations among bedding type, bedding management, other farm management practices, and Rolling Herd Average, were modeled for 227 herds. The relationships between bulk-milk somatic cell score (BMSCS), bedding type, and selected management practices were analyzed in repeated measures mixed models for each bedding type using PROC MIXED (SAS 9.4).

Results

Inorganic bedding was used most commonly (68%) followed by OB (22%) and MB (10%). Farms on which MB was used contained more cows and withheld more milk from sale ($2.4 \pm 0.30\%$ of lactating cows) than farms bedding with IB ($1.6 \pm 0.08\%$; $P=0.005$). Farms using MB had more cows milking on <4 quarters as compared to herds using other bedding types (6.3%, 4.8%, and 4.5% for MB, OB, and IB, respectively, $P=0.055$). Producers using IB had lesser BMSCS than producers using either MB or OB ($P<0.001$). BMSCS was greater in the summer. For farms using IB, increased BMSCS was associated with adding bedding more than once weekly ($P=0.039$), presence of a written milking protocol ($P<0.001$), not drying teats ($P=0.002$), and use of deep bedded stalls ($P=0.065$). For farms using OB, increased BMSCS

was associated with presence of a manager during all milking shifts ($P=0.001$) and failure to completely replace bedding from the back of the stalls ($P<0.001$). BMSCS in herds using OB increased by 0.019 log units for each 1% increase in cows milking on <4 quarters ($P=0.057$). For farms using MB, increased BMSCS was associated with presence of a written milking protocol ($P<0.001$). BMSCS for herds using MB increased 0.14 log units for each 1 point increase in the percent of cows with milk discarded ($P=0.014$). Rolling herd average was 2,537 lb (1,153 kg) greater on farms using IB as compared to farms using MB, and 1,674 lb (761 kg) greater for farms using with IB as compared to farms using OB ($P<0.001$). Rolling herd average was 799 lb (353 kg) greater for farms where the farmer understood the definition of subclinical mastitis ($P=0.017$). RHA was 2,143 lb (974 kg) greater for farms milking 3 times daily than those milking twice daily ($P<0.001$). Rolling herd average decreased by 125 lb (56.7 kg) for each 1 point increase in the percent of cows milking on <4 quarters ($P=0.001$).

Significance

As compared to IB, use of MB resulted in considerable decreases in milk yield and reduced milk quality. Herds using MB or OB appeared to have higher mastitis as measured by BMSCC, a greater proportion of cows with milk discarded, and a higher proportion of cows milking on <4 quarters. Rolling herd average was greatest for farms that used IB, milked 3 times per day, were managed by farmers who could define subclinical mastitis, and for herds that had fewer cows milking on <4 quarters. When considering the use of manure bedding, farmers should be aware of the economic consequences of reduced milk yield and poorer milk quality.