

Concentration of Potentially Active Ceftiofur Residues in Plasma, Uterine Tissues and Uterine Secretions after Post-partum Administration of Ceftiofur Hydrochloride in Lactating Dairy Cows.

E.J. Schmitt¹, P.L.A.M. Vos², H. Okker², P. Scherpenisse², A.A. Bergwerff², and F.H. Jonker²

¹Pharmacia Animal Health, Coordination Center N.V., Rijksweg 12, 2870 Puurs, Belgium, and

²Department of the Science of Food of Animal Origin and Large Animal Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, Yalelaan 2, 3584 CM, Utrecht, The Netherlands;

Introduction

Cephalosporins have been recommended for the parenteral and local treatment of uterine infections in cattle (Chastant-Maillard & Aguer, 1998). Ceftiofur is a third generation cephalosporin with bactericidal activity. The third generation cephalosporins, typically containing an aminothiazole group, are active against Gram-negative bacteria, retain good activity for Gram-positive bacteria and are known to be resistant to β -lactamase enzymes (Prescott & Baggot, 1993). Relative high concentrations of ceftiofur have been found in utero after parental treatment of mares (Jonker, 1997).

Objectives

The objective of this study was to characterise the concentrations and decline of ceftiofur residues in plasma, uterine tissues (endometrium and caruncles) and uterine secretions of healthy Holstein-Friesian dairy cows following parturition. Samples were collected during the 24 hours after a single subcutaneous administration of ceftiofur hydrochloride at the dose of 1 mg/kg body weight in Holstein-Friesian dairy cows.

Materials and Methods

Four, multiparous adult Holstein Friesian dairy cows in their 9th month of gestation purchased at different Dutch dairy farms entered in this study. Cows weighed between 560 kg and 730 kg and calved spontaneously between February 18th and March 23rd of 2000.

Ceftiofur was administered in the form of the commercially available preparation of ceftiofur hydrochloride in a sterile oil suspension (Excenel[®] RTU Sterile Suspension; lot number 99G1624DDT, containing 50 mg ceftiofur equivalents/mL at the dose of 1 mg/kg body weight or 1 mL for 50 kg body weight. The treatment was administered subcutaneously.

For plasma, lochial fluid, caruncles and endometrium baseline samples were collected immediately before

ceftiofur hydrochloride administration (time point 0). Additional samples were collected 1, 2, 4, 8, 12 and 24 hours after treatment with ceftiofur hydrochloride.

Results

The concentration of ceftiofur residues in plasma reached a maximum of 2.85 ± 1.11 $\mu\text{g/mL}$ 2 hours after injection and decreased during the following 22 hours to reach 0.64 $\mu\text{g/mL} \pm 0.14$ $\mu\text{g/mL}$ at 24 h after treatment (Figure 1).

Mean concentrations of ceftiofur residues in lochial fluid of the four cows, increased to a peak concentration of 0.97 ± 0.25 $\mu\text{g/g}$ at 4 h and decreased to 0.22 ± 0.21 $\mu\text{g/g}$ at 24 h after treatment (Figure 1).

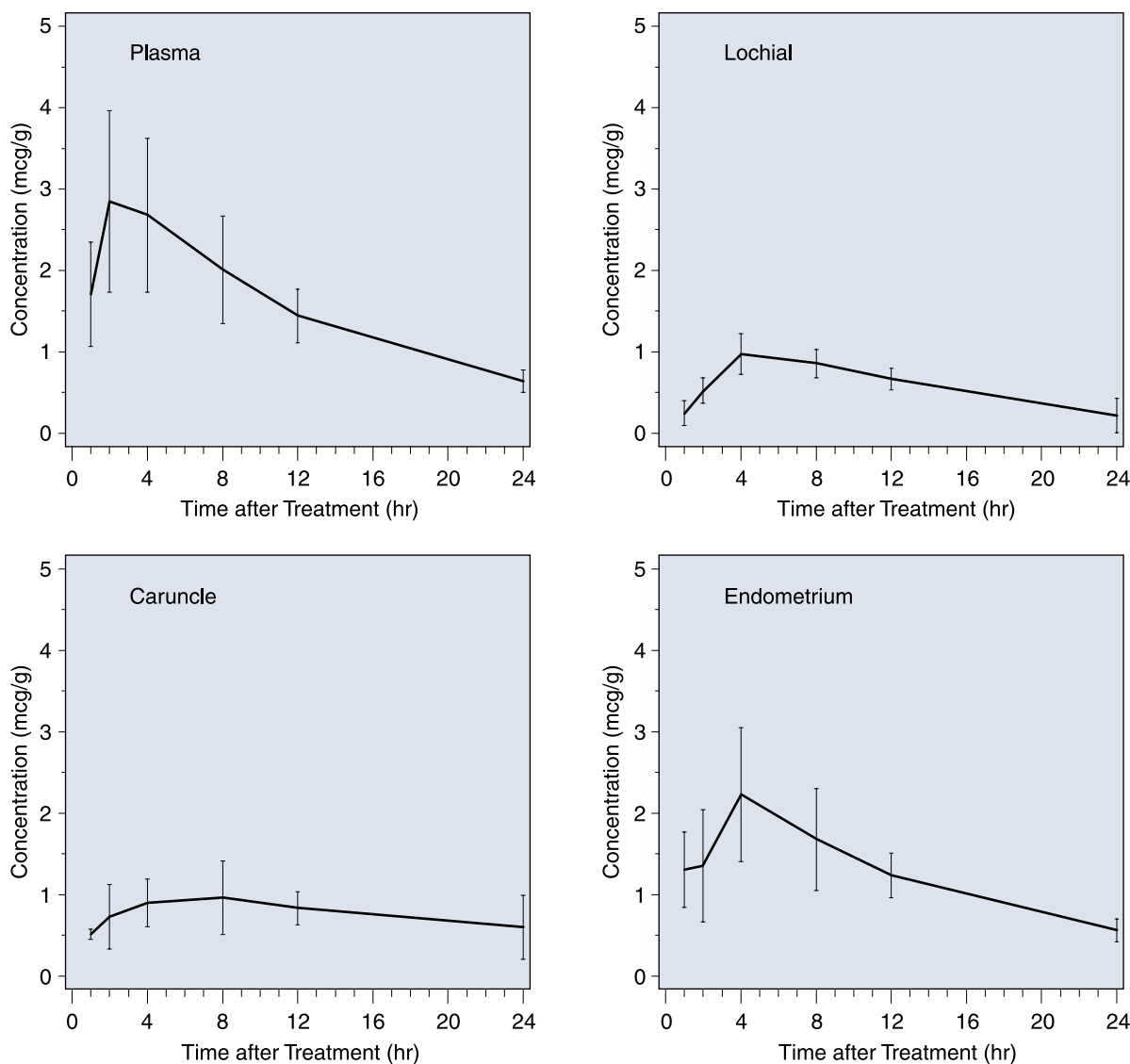
Mean concentrations for the cows reached a maximum of 0.96 ± 0.45 $\mu\text{g/g}$ at 8 h and decreased to 0.60 ± 0.39 $\mu\text{g/g}$ 24 h after administration (Figure 1).

The decline of ceftiofur residues concentrations in endometrium showed a pattern similar to what was observed with plasma. The highest level in endometrium was found at 4 h after treatment. Mean concentrations for the cows in the study varied between 2.23 ± 0.82 $\mu\text{g/g}$ at 4 h and 0.56 ± 0.14 $\mu\text{g/g}$ at 24 h after treatment (Figure 1).

Discussion

The ceftiofur residue concentrations reported in the present study were measured in healthy cows immediately after parturition. It can be hypothesised that the concentration of ceftiofur residues is higher at the uterine level in cows with acute puerperal metritis than that in healthy cows. Clarke and colleagues (1996), reported that the ceftiofur residues concentration were higher at bacterially induced inflammation sites. It is therefore likely that a similar phenomenon may increase the ceftiofur residues concentrations in the uterus during the inflammation process characteristic of acute puerperal metritis. The levels of ceftiofur residues would therefore be higher in diseased animals than those reported herein for uterine tissues of normal post-partum cows.

Figure 1. Concentration of ceftiofur and active metabolites in plasma ($\mu\text{g/mL}$), lochial fluid ($\mu\text{g/g}$), uterine tissues (endometrium (mg/g) and caruncle ($\mu\text{g/g}$)) after subcutaneous administration of ceftiofur hydrochloride at the dose of 1 mg/kg (mean \pm standard deviation (n=4 cows)).



In the current study, the concentrations of ceftiofur residues observed in plasma, in the uterine tissues and in lochial fluid are above the MIC of the major pathogens identified in acute puerperal metritis during the dosing interval at the dose used. This finding suggests that subcutaneous administration of ceftiofur hydrochloride should be effective for treatment of acute puerperal metritis if treatment duration is adequate.

References

Chastant-Maillard, S & Aguer D. (1998). Pharmacologie de l'utérus infecté: facteur de choix d'une thérapeutique.

In *Le Nouveau Peripartum*. Eds. Navetat, H. & Schelcher F. pp. 167-187. Société Française de Buiatrie.

Clarke, C.R. *et al.* (1996) Penetration of parenterally administered ceftiofur into sterile vs *Pasteurella haemolytica*-infected tissue chambers in cattle. *Journal of Veterinary Pharmacology and Therapeutics*, **19**, 376-381.

Jonker, F.H. (1997) Secretion of ceftiofur in equine endometrium after parenteral administration. *Journal of Veterinary Pharmacology and Therapeutics*, **20**(1), 37-38.

Prescott, J. & Baggot, D. (1993) Antimicrobial therapy in veterinary medicine. *Iowa University State Press*, 110-113.

PHARMACIA Animal Health

www.PharmaciaAH.com