

# Disposition of ampicillin trihydrate in plasma, uterine tissue, and lochial fluid of post-partum dairy cattle

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## Introduction

Dairy cattle are susceptible to numerous infectious and metabolic disorders in the immediate post-parturient period. Acute puerperal metritis (APM) is one of the most common clinical conditions seen in modern dairy cattle, affecting 18-33% of all cattle that calve. Antimicrobials are a mainstay of therapy for cattle with APM. Currently, three antimicrobials are labeled for systemic therapy in cattle with APM. Of these, products containing ceftiofur as the active compound are used most frequently. The United States Food and Drug Administration recently passed an order prohibiting the extra-label use of cephalosporins in major food-producing species because of concerns over the development of resistance to similar 3rd generation cephalosporin compounds used in critically ill human patients. Thus, it is prudent to consider and investigate the use of other antimicrobials for cattle with this important clinical disease. While emerging evidence would suggest that ampicillin trihydrate would have value as a therapeutic agent in dairy cattle with APM, the disposition of the drug in plasma, uterine tissue, and lochial fluid has not been investigated.

## Materials and Methods

Ampicillin trihydrate was administered intramuscularly (IM) at a dose of 11 mg/kg of body weight every 24 h (n = 6, total of 3 doses) or every 12 h (n = 6, total of 5 doses) for 3 days. Concentrations of ampicillin were measured in plasma, uterine tissue, lochial fluid, and milk using High Performance Liquid Chromatography (HPLC) with ultraviolet absorption. A two-way ANOVA with one factor repetition was used to assess the effect of sample type (plasma, milk, lochial fluid, endometrial

tissue), dosing interval (12 h vs 24 h) and interactions between sample type and dosing interval each on measured and calculated pharmacokinetic variable. When applicable, multiple pairwise comparisons were made using the Holm-Sidak method. Differences were considered significant at  $P < 0.05$ .

## Results

Quantifiable ampicillin concentrations were found in plasma, milk, and lochial fluid of all cattle within 30 min, 4 h, and 4 h of administration of ampicillin trihydrate, respectively. There was no significant effect of dosing interval (every 12 versus every 24 h) and no significant interactions between dosing interval and sampling site on the pharmacokinetic variables measured or calculated. Median peak ampicillin concentration at steady state was significantly higher in lochial fluid after 24 h dosing (5.27  $\mu\text{g/mL}$ ) than in other sample types and significantly higher in plasma than in milk or endometrial tissue at 3.11  $\mu\text{g/mL}$ , 0.49  $\mu\text{g/mL}$  and 1.55  $\mu\text{g/mL}$ , respectively.

## Significance

Ampicillin trihydrate administered once daily by the IM route at the label dose of 11 mg/kg of body weight achieves therapeutic concentrations in milk, lochial fluid, and endometrial tissue of healthy post-partum dairy cattle. Twice daily administration does not provide any advantages over once daily dosing. While the use of ampicillin trihydrate to treat cattle with acute puerperal metritis is currently extra-label, this drug may serve as an alternative to currently available antimicrobials should they become unavailable or ineffective.