Randomized clinical trial of ceftiofur hydrochloride treatment to prevent acute puerperal metritis in dairy cows having *Escherichia coli* in their uterus at day 1 postpartum

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Introduction

Ceftiofur is a class 1 antibiotic (World Health Organization classification) and there is an increasing pressure from the veterinary and medical bodies to revisit its use for treating and preventing diseases in dairy cows such as acute puerperal metritis (APM). The presence of *Escherichia coli* (*E. coli*) in the uterus of dairy cows at day 1 postpartum was shown to increase by 3 the risk of subsequently developing APM. Unfortunately, there are no data describing the efficacy of ceftiofur treatment to prevent APM in the subset of cows with *E. coli* in their uterus at day 1 postpartum. Therefore, the objective of the study was to quantify the efficacy of ceftiofur treatment in dairy cows with *E. coli* in their uterus at day 1 postpartum to prevent APM.

Materials and Methods

A total of 300 cows from a commercial dairy herd were enrolled at parturition during a 1-year period in this randomized clinical trial. Participating cows were examined by an animal health technician 24 hours after parturition. At that time, 2 bacteriological samples were collected from the body of the uterus of the cow using guarded mare swabs. The first sample was sent to the diagnostic laboratory service of the Faculté de médecine vétérinaire of the Université de Montréal (St-Hyacinthe, QC, Canada) for bacterial culturing and identifying the presence of *E. coli* (reference test). The second sample was cultured on the farm using a Triplate system to identify the presence of uterine coliforms (including *E. coli*). Both test results were provided after 48 hours (day 3 postpartum). If cows were positive for *E. coli* using the reference standard test, they were randomly assigned to 1 of 2 groups: 1-control group (no treatment), 2-ceftiofur group (1.0 mg/lb [2.2 mg] of ceftiofur hydrochloride per lb/kg of body weight IM SID for 5 days). All cows were observed daily during the first 20 days-in-milk (DIM) for diagnosing APM based on the following criteria: temperature ≥103°F (39.5°C), brown-red fetid vaginal discharge and systemic signs of illness (drop in milk, dullness, drop in feed intake, etc.). The person in charge of APM diagnosis was blinded to culture results and treatment allocation. Statistical analyses were calculated considering the cow as the unit of interest. In a first step, prevalence of APM was computed for all groups of cows and the dependent variable was the occurrence of APM. Logistic regression and Kaplan-Meier survival models were used to assess the efficacy of ceftiofur. In a second step, sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were computed from 2x2 tables comparing the reference standard test to the Triplate results.

Results

A total of 300 Holstein cows had their uterus cultured in this study and 121 cows of these cows (40.3%) had *E. coli* in their uterus at day 1 postpartum. From the cow population enrolled in the clinical trial, 62 cows were in the control group and 59 cows were in the ceftiofur group. The prevalence of APM was 6.7% (12/179) in the cows without uterine *E. coli*. For cows enrolled in the clinical trial, the prevalence of APM was 29.0% (18/62) in the control group and 8.5% (5/59) in the ceftiofur group ($P=0.02$). The median time to APM diagnosis was 7 DIM in cows without *E. coli* in their uterus, 7 DIM in cows from the control group, and 10 DIM in cows from the ceftiofur group ($P<0.01$). The Se, Sp, PPV, and NPV of Triplate results were 95.0, 97.8, 96.6, and 96.7%, respectively.

Significance

Overall, these results show the efficacy of ceftiofur treatment for preventing APM in cows having *E. coli* in their uterus at day 1 postpartum, and that APM occurs later in cows treated with ceftiofur compared with other cows. They also show that on-farm identification of *E. coli* using the Triplate system is an accurate method. Future research should validate these results in a larger number of cows/herds and investigate the reasons for the delay of APM occurrence in cows treated with ceftiofur.