Efficacy of ceftiofur hydrochloride sterile suspension administered parenterally for the treatment of acute postpartum metritis in dairy cows

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Objective—To evaluate the efficacy of ceftiofur hydrochloride sterile suspension administered parenterally for treatment of acute postpartum metritis (APM) in dairy cows.

Design—Multilocation, randomized block, field trial.

Animals—406 cows in the first 14 days postpartum.

Procedure—Cows with rectal temperatures $\geq 39.5^\circ$C (103.1 $^\circ$F) without clinical signs of respiratory or gastrointestinal tract disease and with a fetid vaginal discharge were allocated randomly in blocks of 3 to 3 treatment groups: sterile saline (0.9% NaCl) solution administered at a dosage of 2 mL/45.4 kg (2 mL/100 lb), SC or IM, once daily for 5 days (control); or ceftiofur hydrochloride administered at a dosage of 1.1 or 2.2 mg of ceftiofur equivalents (CE)/kg (0.5 or 1 mg/lb, respectively), SC or IM, once daily for 5 days. Cows were evaluated on days 6, 10, and 14, and clinical cure or failure to cure was determined. Clinical cure was defined as no additional antimicrobial treatment administered, rectal temperature $< 39.5^\circ$C, and absence of a fetid vaginal discharge.

Results—On day 14, clinical cure rates were 77%, 65%, and 62% for the 2.2 mg of CE/kg, 1.1 mg of CE/kg, and control groups, respectively. No significant differences were detected in clinical cure rates between control and treatment groups on day 10 or 6.

Conclusions and Clinical Relevance—Ceftiofur hydrochloride administered at a dosage of 2.2 mg of CE/kg, SC or IM, once daily for 5 days was efficacious for treatment of APM in dairy cows. (J Am Vet Med Assoc 2004;224:1634–1639)

Acute postpartum or puerperal metritis (APM) is common after parturition in dairy cows, with a reported incidence rate ranging from 3% to 36%. The condition is characterized by clinical signs accompanied by a copious fetid vaginal discharge, with or without retention of fetal membranes. Clinical signs include fever, anorexia, depression, and reduced milk production. The uterus is often swollen and friable, and manipulation by rectal palpation may cause perimetritis. If treated with antimicrobials, APM generally is not life-threatening; however, certain cases are difficult to resolve and may evolve into toxic or septic sequelae. Left untreated, APM can lead to death.

Escherichia coli, Arcanobacterium pyogenes, and gram-negative anaerobes are commonly isolated from the uteri of cows with APM within 14 days of calving. Results of 1 study indicate that coliform flora, especially E coli, were present in 91% of the samples collected from affected cows in the week after parturition. Pathogenic flora in the uterus changes with time after parturition and with the severity of the disease. Obligatory anaerobes grow in the uteri of severely affected cows, and a synergetic action of A pyogenes, Bacteroides species, and Fusobacterium necrophorum has been suggested. Antimicrobial treatment of APM is not expected to eliminate these pathogens but rather to control the bacterial infection and clinical progression, permitting the host’s defense system to effect a cure.

Treatment of APM has been subject to debate. Antimicrobial, anti-inflammatory, and estrogenic agents often are used and administered systemically, by intrauterine infusion, or both. There is general agreement for treatment with antimicrobials systemically when systemic clinical signs are observed. Little has been published on the efficacy of parenteral antimicrobials administered alone for the treatment of APM in cows. A similar condition in postpartum women has been studied extensively and has been treated with cephalosporins. Therefore, several authors have hypothesized that targeted-spectrum cephalosporins such as ceftiofur administered systemically may be similarly efficacious for APM in cattle and should be evaluated. Ceftiofur hydrochloride sterile suspension is approved for treatment of respiratory disease and interdigital necrobacillosis (footrot) in lactating cows in many countries, with a short to no milk withdrawal time. Alternative antimicrobial regimens used for treatment of APM often require a milk withdrawal time or an extended pre-slaughter tissue withdrawal time. These characteristics led us to further evaluate use of ceftiofur hydrochloride for treatment of APM.

This study was designed on the basis of findings of another study in which ceftiofur sodium was evaluated for the treatment of toxic puerperal metritis in lactating cows. Results of that study, which did not include a negative control, indicated that ceftiofur was as effective as other antimicrobial regimens for the treatment of toxic puerperal metritis in cows. The purpose of the study...
reported here was to assess ceftiofur hydrochloride sterile suspension for treatment of APM in dairy cows, compared with a negative-control treatment group.

Materials and Methods

This study was performed in 8 commercial dairy farms: California (n = 3), New York (2), and 1 dairy farm each in Florida, Michigan, and Texas. Herd sizes ranged from 1,100 to 3,600 cows in lactation at the time the study was performed. The owner of each dairy signed an informed consent agreement before initiation of the study. Cows were housed in open-sided barns that were curtained in the northern locations. Each barn had a central feed alley equipped with headlocks to restrain cows. The study was performed from May to October 2000.

Lactating, commercial grade, Holstein dairy cows in the early postpartum period were eligible for inclusion in the study. Cows were excluded from study if they had been treated since calving with systemic antimicrobial, steroid or nonsteroidal anti-inflammatory, estrogen, antipyrine, oxytocin, or prostaglandin agents. In addition, cows with periparturient complications (defined as caesarian section, leeto my, or uterine prolapse) were excluded.

At each location, the study investigator was a licensed veterinarian that was unaware of the allocation of individual cows to treatment groups. This was accomplished by the assignment of a treatment assistant (TA) at each location, who allocated cows to respective treatment groups and administered all experimental treatments.

Farm personnel monitored rectal temperatures of all cows each morning for the first 14 days postpartum when cows were confined by feed bunk headlocks. The study investigator was notified of all cows with rectal temperatures ≥ 39.5°C (103.1°F). Those cows were examined by the study investigator. During this examination, vaginal discharge was scored: 0, no discharge observed; 1, not fetid, normal lochia (viscous; red, brown, or clear); 2, not fetid; thick mucus; cloudy, clearing, or clear; 3, not fetid; may be purulent, mucopurulent, or chocolate brown; or 4, fetid; may be red or pink to chocolate brown; thin, serous, and watery; with or without pieces of necrotic tissue. In addition, during the examination the study investigator determined and recorded a dehydration score (0, normal; 1, mild; or 2, severe), extent of scleral injection (0, normal; 1, some; or 2, moderate or severe), heart rate (beats/min), and rumen contractions (number of contractions/min). The study investigator conducted a physical examination on each cow, and cows determined to have traumatic gastritis, gastroenteritis, displaced abomasum, hemorrhagic sepsis, complicated pneumonia, laminitis, or mastitis were excluded from enrollment. Therefore, the following criteria were required for cows to be enrolled in the study: ≤ 14 days postpartum, rectal temperature ≥ 39.5°C, vaginal discharge score of 4, and absence of exclusion criteria.

The TA randomly allocated cows in blocks of 3 to each of the 3 treatment groups: sterile saline (0.9% NaCl) solution for injection administered at a dose of 2 mL/45.4 kg (2 mL/100 lb; negative control); ceftiofur hydrochloride administered at a dose of 1.1 mg of ceftiofur equivalents (CE)/kg (0.5 mg of CE/lb; 1.0 mL/45.4 kg [1.0 mL/100 lb]), hereafter referred to as the 1.1 mg of CE/kg treatment group; or ceftiofur hydrochloride administered at a dose of 2.2 mg of CE/kg (1.0 mg of CE/lb; 2.0 mL/45.4 kg [2.0 mL/100 lb]), hereafter referred to as the 2.2 mg of CE/kg treatment group. The TA administered the appropriate treatment once daily for 5 consecutive days (study days 1 to 5) by either SC or IM injection (only 1 route of administration within each dairy) and recorded rectal temperature each day.

The study investigator evaluated each cow on study days 6 or 7, 10 ± 1, and 14 ± 1 (hereafter referred to as study days 6, 10, and 14, respectively; 1, 5, and 9 days after the last treatment), and a response of clinical cure or failure to cure was determined. Clinical cure was defined as no additional or alternative antimicrobial treatment administered during the observation period, rectal temperature < 39.5°C, and absence of a fetid vaginal discharge (vaginal discharge score ≤ 3). If any of these criteria were not met, the cow was considered as a failure to cure. During these examinations, rectal temperature, vaginal discharge score, number of rumen contractions per minute, heart rate, dehydration score, and scleral injection score were evaluated by the study investigator and recorded.

Study investigators were permitted to administer supportive fluid therapy at any time after cows were enrolled in the study. Cows that required additional antimicrobial treatment, as determined by the study investigator, were removed from the study at that point in time and considered as failure to cure for statistical analyses.

Statistical analyses—For purposes of analyses, the study was a randomized, complete block design with order-of-entry of groups of 3 cows within a herd as the blocking factor. Clinical cure, the primary end point, was analyzed sequentially; beginning on study day 14, then study day 10, and then study day 6. A ceftiofur hydrochloride dose group was defined to be significantly efficacious if it had a significantly higher clinical cure rate than that of the control group on any of the 3 days of evaluation with values of P ≤ 0.05 considered significant.

Clinical cure rates for the 2 ceftiofur hydrochloride treatment groups were compared with the control group by use of a generalized linear mixed model with binomial error and logit link by use of computer software. In this model, the fixed effect was treatment and the random effects were investigator, blocks within herd, and investigator-by-treatment interaction. Penalized quasi-likelihood equations were used for parameters estimation. The variance components were computed by use of the restricted maximum likelihood algorithm. The denominator degrees of freedom for the statistical tests were computed by use of the Satterthwaite option.

Rectal temperatures during study days 1 to 6, 10, and 14 were analyzed as a general linear mixed model with repeated measures by use of computer software. Fixed effects were treatment, days, and treatment-by-day interaction. Random effects were investigator (ie, location) and blocks (order-of-entry triples). For the repeated option, the subject was cow-within-investigator-and-treatment, and the variance-covariance matrix was best modeled by the spatial power structure.

By use of the definition of clinical cure rate, the 1.1 mg of CE/kg treatment group did not have a significant effect on clinical cure rate on study days 6, 10, or 14, compared with the control group. However, in this treatment group, a significantly lower rectal temperature was detected on study days 1 to 5 and on study day 6, compared with the reduction of rectal temperature in the control group. To evaluate this observation further, additional retrospective statistical analyses were performed. For these analyses, the definition of clinical cure was expanded to include all of the following conditions: no additional or alternative antimicrobial treatment administered during the observation period; rectal temperature < 39°C (102.2°F; which was more stringent than < 39.5°C used in the initial definition of clinical cure rate); absence of a fetid vaginal discharge; rumen contractions ≥ 2/min (defined as normal); scleral injection score of 0 (normal); and dehydration score of 0 (normal). Clinical cure rates on study day 14 for all treatment groups were statistically analyzed as described.

Results

Of the 406 cows enrolled in the study, 60.6% were primiparous, 18.3% were in the second lactation, 12.3%
RUMINANTS were in the third lactation, and the remaining 8.6% were in the fourth or greater lactation. The exact parity mix of each herd was not documented; however, the higher percentage of primiparous cows than multiparous cows enrolled in the study was consistent with the premise that primiparous cows require more assistance during parturition and experience more damage to the reproductive tract during parturition than multiparous cows. Both conditions are predisposing factors for APM.

Of the cows included in the study, 25% were included by day 3 postpartum, 50% by day 5 postpartum, 75% by day 7 postpartum, and (by protocol design) 100% by day 14 postpartum. Five of the 8 dairy farms did not include any cows in the study after day 12 postpartum. These observations provide support for surveillance of rectal temperatures of all cows for at least 10 to 12 days postpartum for early detection of APM.

Of the 406 cows enrolled, 376 were included in the statistical analyses. The 30 cows not included in the analyses were removed because of documented protocol deviations. At the end of the study (study day 14), clinical cure rates were 77%, 65%, and 62% for the 2.2 mg of CE/kg, the 1.1 mg of CE/kg, and the control group, respectively, with 77% significantly (P = 0.01) greater than 62% (Table 1). No significant difference was detected between the control group and the 1.1 mg of CE/kg treatment group (P = 0.295) on study day 14. No significant differences were detected in clinical cure rates between the control group and either of the ceftiofur hydrochloride treatment groups on study day 6 or 10.

A significant (P = 0.023) treatment-by-day interaction was detected for daily mean rectal temperatures among treatment groups. This observation warranted comparisons at additional time points, and 4 time points were chosen: during the 5 days of treatment, and study days 6, 10, and 14, independently (Fig 1). During the 5 days of treatment, cows in the ceftiofur hydrochloride treatment groups had similar reductions in rectal temperature that were significantly (P ≤ 0.012) larger than the reduction in rectal temperature observed in cows in the control group. On study day 6, ceftiofur hydrochloride administered at a dose of 1.1 mg of CE/kg resulted in a significantly (P = 0.037) lower rectal temperature than that in the control group, and ceftiofur hydrochloride administered at a dose of 2.2 mg of CE/kg resulted in a marginally lower rectal temperature than that in the control group (P = 0.075). On study days 10 and 14, there were no significant differences detected in rectal temperatures among the 3 treatment groups (P > 0.3).

Mean vaginal discharge score was 4 for all treatment groups on study day 1, consistent with the inclusion criteria. Vaginal discharge scores decreased, nearly linearly, to a mean of 2.5 in all treatment groups by study day 14 (Fig 2). Percentage of cows with abnormal scleral injec-

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**Table 1—Clinical cure rates (%) for cows with acute postpartum metritis treated with saline (0.9% NaCl) solution (control) or ceftiofur hydrochloride administered at a dosage of 1.1 or 2.2 mg of ceftiofur equivalents/kg (0.5 or 1 mg/lb, respectively), SC or IM, once daily for 5 days**

<table>
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<td>118 23</td>
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*Significantly (P = 0.01) different from value for control group.

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**Figure 1**—Mean rectal temperatures of cows with acute postpartum metritis (APM) during and after treatment with saline (0.9% NaCl) solution (control; circles, dashed line) or ceftiofur hydrochloride administered at a dosage of 1.1 mg of ceftiofur equivalents (CE/kg) (0.5 mg/lb; diamonds, solid line) or 2.2 mg of CE/kg (1 mg/lb; squares, dotted line), SC or IM, once daily for 5 days. Conversion from Fahrenheit to Celsius, °C = (°F - 32) × 5/9.

**Figure 2**—Mean vaginal discharge score of cows with APM before, during, and after treatment with saline solution (control) or ceftiofur hydrochloride administered at a dosage of 1.1 or 2.2 mg of CE/kg, SC or IM, once daily for 5 days. Vaginal discharge was scored as 0, no discharge observed; 1, not fetid, normal lochia (viscous; red, brown, or clear); 2, not fetid; thick mucus, cloudy, clearing, or clear; 3, not fetid; may be purulent, mucopurulent, or chocolate; 4, fetid; may be red or pink to chocolate brown; thin, serous, and watery; with or without pieces of necrotic tissue. See Figure 1 for key.
tion scores, abnormal dehydration scores, and abnormally low number of rumen contractions (< 2/ min) declined in all groups during the study (Fig 3–5, respectively). Clinical observations tended to return towards normal during the course of the study.

By use of the revised definition, clinical cure rates were significantly greater for both the 2.2 mg of CE/kg (41%; \( P = 0.004 \)) and the 1.1 mg of CE/kg (37%; \( P = 0.021 \)) treatment groups, compared with clinical cure rates of the control group (29%).

**Discussion**

To the knowledge of the authors, this is the first report of a multilocation, blinded study with antimicrobial treatment alone, administered IM or SC and compared with a negative control, for the treatment of APM in lactating dairy cows. Results of this study indicated that use of antimicrobial treatment alone, administered parenterally, affects a positive clinical outcome. In addition, results of this study indicate the efficacy of ceftiofur hydrochloride for treatment of APM when administered at a dose of 2.2 mg of CE/kg.

The reduction in rectal temperature observed during study days 1 to 6 in the 1.1 mg of CE/kg treatment group indicated that this dose had a beneficial effect in cows with APM. This observation stimulated additional retrospective statistical analyses conducted on a modified definition of clinical cure rate. These analyses revealed that cows in the 1.1 mg of CE/kg treatment group had a significantly higher clinical cure rate than those in the control group. These observations identified the clinical benefit of the administration of ceftiofur hydrochloride at a dose as low as 1.1 mg of CE/kg for the treatment of APM.

Results of this study are consistent with the present knowledge of the use of ceftiofur hydrochloride for treatment of APM. Okker et al\(^1\) reported that at 24 hours after administration of ceftiofur hydrochloride (1 mg of CE/kg, SC) on day 1 postpartum in healthy dairy cows, the concentrations of ceftiofur and active metabolites were 0.64 µg/mL in

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**Figure 3**—Percentage of cows with APM and abnormal scleral injection scores treated with saline solution (control) or ceftiofur hydrochloride administered at a dosage of 1.1 or 2.2 mg of CE/kg, SC or IM, once daily for 5 days. Abnormal scleral injection was scored as 1, some; or 2, moderate or severe.

**Figure 4**—Percentage of cows with APM and abnormal dehydration scores treated with saline solution (control) or ceftiofur hydrochloride administered at a dosage of 1.1 or 2.2 mg of CE/kg, SC or IM, once daily for 5 days. Abnormal dehydration was scored as 1, mild; or 2, severe.

**Figure 5**—Percentage of cows with APM and an abnormal number of rumen contractions (<2 contractions/min) treated with saline solution (control) or ceftiofur hydrochloride administered at a dosage of 1.1 or 2.2 mg of CE/kg, SC or IM, once daily for 5 days.
plasma, 0.56 µg/mg in endometrium, 0.60 µg/mg in caruncles, and 0.22 µg/ml in lochial fluid. These concentrations exceed the reported minimal inhibitory concentrations for E coli, A pyogenes, and F necrophorum, pathogens associated with APM.

Results of additional clinical studies evaluating the effectiveness of ceftiofur for treatment of either APM or toxic postpartum metritis have been published, all of which used positive controls and did not include negative controls. Schmitt et al compared ceftiofur hydrochloride administered at a dose of 1.0 mg of CE/kg (0.45 mg/lb), SC, once daily for 5 days (n = 87 cows) with oxytetracycline hydrochloride administered at a dosage of 10 mg/kg (4.5 mg/lb), IM, once daily for 5 days (88) for treatment of APM. Oxytetracycline was chosen as a positive control (4.5 mg/lb), IM, once daily for 5 days (88) for treatment of APM. Oxytetracycline was chosen as a positive control because it is registered for treatment of metritis in some European Union countries at this dose. Inclusion criteria were rectal temperature ≥ 39.5°C and a fetid vaginal discharge. Clinical cure on day 7 after the first treatment was defined as rectal temperature < 39°C and no clinical signs of depression. Clinical cure on day 15 was defined the same as on day 7 with the additional requirement of no fetid vaginal discharge. Significant differences were not detected for clinical cure rates for ceftiofur hydrochloride and oxytetracycline treatment groups on day 7 (64.8% and 58.1%, respectively) or day 15 (70.5% and 71.2%, respectively). During treatment on days 2 to 5, cows treated with ceftiofur hydrochloride had significantly lower rectal temperatures than cows treated with oxytetracycline. The authors of that study concluded that SC administration of ceftiofur hydrochloride at a dosage of 1.0 mg of CE/kg for 5 consecutive days was effective in treating APM in dairy cows.

Drillich et al enrolled cows with toxic postpartum metritis, which was defined as rectal temperature ≥ 39.5°C and a fetid reddish brown vaginal discharge. Cows were allocated to each of 3 treatment groups: group 1 received ceftiofur (600 mg, IM) daily for 3 consecutive days (n = 70); group 2 received ampicillin (2,500 mg) and cloxacillin (2,500 mg) administered intrauterine plus ampicillin (600 mg, IM), all administered once daily for 3 consecutive days (79); and group 3 received the same intrauterine treatment as group 2 plus ceftiofur (600 mg, IM) daily for 3 days (78). Clinical cure was defined as rectal temperature < 39.5°C on the sixth day after the first treatment was administered, regardless of other clinical signs. On the basis of rectal temperature alone, clinical cure rates were high (82.9%, 84.8%, and 84.6% for treatment groups 1, 2, and 3, respectively). However, of those cows defined as cured on day 6, 63.2%, 44.8%, and 43.1% in groups 1, 2, and 3, respectively, had a fetid vaginal discharge on day 6. By use of this information, redefining cure rate as rectal temperature < 39.5°C, and absence of fetid vaginal discharge, cure rates on day 6 of approximately 30%, 47%, and 42.8% can be calculated for treatment groups 1, 2, and 3, respectively. These cure rates are similar to those reported here by use of this same definition of cure on day 6 after initial treatment (23%, 27%, and 26% for the cows receiving 0, 1.1, or 2.2 mg of CE/kg for 5 days, respectively). Use of rectal temperature alone as a determination of cure may provide an overestimate of cure.

Smith et al enrolled cows with toxic postpartum metritis, which was defined as rectal temperature > 39.2°C (102.6°F), a flaccid uterus, and a fetid vaginal discharge. Cows were allocated to 3 presently used treatment regimens: procaine penicillin G (22,000 U/kg [10,000 U/lb], IM) administered once daily for 5 days; procaine penicillin G (22,000 U/kg, IM) administered once daily for 5 days plus intrauterine infusion of oxytetracycline (6 g dissolved in sterile water) on days 1, 3, and 5; or ceftiofur sodium (2.2 mg of CE/kg, IM) administered once daily for 5 days. Clinical cure rate was not evaluated; however, differences were not detected in subsequent milk yield, rectal temperature, or serum haptoglobin concentrations between the 3 treatment groups. Results of the study suggest that there were no differences in treatment efficacy among the antimicrobial treatment regimens administered. The studies of Drillich et al, Schmitt et al, and Smith et al used similar inclusion criteria (rectal temperature and a fetid vaginal discharge) and used these identical clinical signs to classify the underlying disease state as either APM or toxic postpartum metritis. For future clinical studies, the authors suggest that toxic postpartum metritis be defined on the basis of clinical signs of toxemia, potentially including clinical signs of depression, reduced milk production, or anorexia, in addition to increased rectal temperature and a fetid vaginal discharge, whereas cows with increased rectal temperature and fetid vaginal discharge without additional clinical signs should be defined as having APM.

Drillich et al, Schmitt et al, and Smith et al used a study design that included a positive control consisting of an antimicrobial treatment regimen commonly used for treatment of APM. However, a true test of effectiveness cannot be concluded from studies by the use of a positive control. The only conclusion that can be made is that the experimental treatment tested was inferior to, not inferior to, or superior to the positive control, with the assumption that the antimicrobial treatment regimen used for the positive control was efficacious. Therefore, results from these 3 studies can be interpreted to indicate that ceftiofur administered at a point dose of at least 1.0 mg of CE/kg was as effective as other antimicrobial treatment regimens that are typically used in the treatment of APM. Furthermore, results of these studies indicate that the intrauterine administration of antimicrobials provided no additional benefit to that which was obtained by use of systemic administration of antimicrobials alone.

Zhou et al evaluated the effect of administration of ceftiofur at a dosage of 1.0 mg of CE/kg either IM or SC daily for 3 days to cows (n = 169) with rectal temperatures ≥ 39.5°C, compared with a control group (161) that received no antimicrobial treatment. Additional clinical signs were not required for cows to be included in the study; however, the presence of other clinical signs of disease was recorded. Clinical cure on day 10 after the first treatment was defined as no additional antimicrobial treatment administered, rectal temperature < 39.5°C, and absence of clinical signs of any disease. No significant difference was detected in cure rates between treatment groups for cows without vagi-
nal discharge at study initiation (66.5% for control and 69.1% for the ceftiofur treatment group). In contrast, in cows with a vaginal discharge at study initiation, significant differences in cure rates were detected between ceftiofur (n = 52 [56%]) and control (41 [28.9%]) groups. However, the authors of that study indicated that a limitation of the study was a lack of uniform evaluation criteria for vaginal discharge. Results of the study indicate that ceftiofur administered at a dose of 1 mg of CE/kg to cows with increased rectal temperatures, without additional clinical signs of disease, had no effect on subsequent observations. However, in cows with vaginal discharge at study initiation, this dose provided a significantly greater cure rate than that observed in untreated controls.

A limitation of the study reported here was the absence in the literature of recognized objective diagnostic criteria for either APM or clinical cure. A description of the evolution of APM in untreated cows is also absent in the literature. Therefore, the inclusion criteria and definition of clinical cure used for this study evolved through discussions with clinical experts. Increased rectal temperature usually accompanies APM; however, the choice of ≥ 39.5°C was arbitrary. Fetal vaginal discharge was chosen because it is an early clinical sign of APM and provided documentation that the increased temperature was a consequence of APM and not in response to other diseases of bacterial origin. Since this study was initiated, similar inclusion criteria and definitions for clinical cure have been reported for other studies evaluating the use of antimicrobials for treatment of APM. Other clinical signs including dehydration, scleral injection, and number of rumen contractions per minute were recorded during the study but were not considered in the definitions of clinical cure. In the retrospective statistical analyses, which incorporated these clinical observations into the definition of clinical cure, both doses of ceftiofur hydrochloride caused significantly greater cure rates on study day 14, compared with the negative control group. These results are consistent with the findings of Schmitt et al, who included depression scores in the definition of clinical cure or failure to cure. These clinical signs are well-documented sequelae of APM and are used by veterinary practitioners in the diagnosis of APM and in evaluating response to treatments. Therefore, incorporation of clinical signs, such as depression, dehydration, or rumen contractions, into the definition of clinical cure is supportable.

Of the studies summarized herein, only Smith et al reported an end point of economic importance (subsequent milk production) following administration of various antimicrobial regimens for treatment of APM. Additional studies are needed to evaluate the effect of the administration of ceftiofur hydrochloride alone for the treatment of APM on end points of economic interest, such as subsequent milk production and reproductive performance, or an estimate of sustainability (productivity and cull rate) of cows in the herd.

References

*Excenel RTU sterile suspension, Pfizer Animal Health, New York, NY.

**GLIMMIX, version 6.1, SAS Institute Inc, Cary, NC.

**PROC MIXED, version 6.1, SAS Institute Inc, Cary, NC.