

DAIRY VETERINARY NEWSLETTER

May 2022

Bovine Metritis - Two Treatments Compared with No Treatment

Studies of treatments of diseases of dairy cattle are always of interest to me, and surveys as well as my experience show that comparisons of treatments are also important to many dairy veterinarians. Comparisons of multiple treatments for the same disease complex, such as evaluations of different antibiotics, electrolyte solutions, anti-inflammatory treatments, etc. are ideal, but today those are rare. Indeed, over the last 30 years, there are few refereed papers of any kind regarding treatment comparisons for most diseases of dairy cattle.

A paper by E. Oliveira et al. in J Dairy Sci, August 2020 reported on a study of bovine metritis treatment. Holstein cows from 3 Florida dairy farms were the potential study population. Within the herds of 4,400, 1,800, and 450 lactating cows, all cases of metritis with no concurrent disease diagnosed from May 2016 to June 2017 were studied. Metritis was diagnosed at either 5, 7 or 9 days in milk, based on a vaginal discharge scale (the entire scale was reported in the paper) from 1 = not fetid, normal lochia, viscous, clear, red, or brown, to 5 = fetid, thin, serous, or watery, may have been reddish-brownish, with or without pieces of necrotic tissue present; only cows with a vaginal discharge score of 5 were defined as having metritis, and were therefore enrolled if they had no other periparturient diseases or treatments. Exclusions were cows with concurrent: “calving within the withdrawal period for any antimicrobial agent, cows treated with any antimicrobial, steroidal or nonsteroidal anti-inflammatory, or antipyretic agents between calving and metritis diagnosis, cows submitted to caesarian section or fetotomy, cows that aborted (<260 d of gestation), cows that had uterine prolapse after delivery, and cows diagnosed with infectious (e.g., mastitis, gastroenteritis, pneumonia, peritonitis) or digestive (i.e., displaced abomasum) diseases at the time of metritis diagnosis.”



Vaginal discharge not definitive for metritis



Necropsy of uterus from toxic metritis death

Metritis treatment groups

Cows were blocked by parity (first calving [primiparous], second or more calving [multiparous]) and then randomly assigned to one of 3 treatment groups within each parity block using a random number generator. Treatments were chitosan microparticles (CM) 24 g dissolved in 40 ml of sterile distilled water, intrauterine infusion on day 0 (diagnosis), d 2 and d 4 (n = 276; 149 primiparous and 127 multiparous); ceftiofur crystalline-free acid (CEF) 6.6 mg/kg injected SQ in the base of the ear at day 0 and d 3 (n = 275; 147 primiparous and 128 multiparous), or control (CON) cows with no treatment at time metritis was diagnosed (n = 275; 139 primiparous and 136 multiparous).

Sample size calculation

The authors undertook an important step to avoid Type II error, where biologically significant differences in outcomes (such as cure rate %) are not found statistically significant only because the sample size is too small. In other words, the authors wanted a sufficiently large sample size so that differences they considered biologically significant would be detected as statistically significant if they were observed. Based on their expert opinions as well as two previous publications, the authors wanted to be able to detect a 75% cure rate for either CM or CEF as statistically higher than an expected 65% cure rate for CON untreated cows. They calculated that 259 cows per treatment group were needed to detect such cure rates as statistically significant if they were indeed found, and therefore aimed to enroll 275 cows per treatment group to “allow for up to 6% attrition”.

Additional treatments if required

If necessary, cows could receive “escape therapy”, a different treatment. Beginning on D 1, “Criteria for escape therapy were severe dehydration, anorexia, weakness, severe depression, systemic shock, or any other clinical signs that were attributable to metritis. - - The escape [antibiotic] therapy followed each herds’ standard treatment protocols. Cows that received escape therapy were considered a treatment failure.” The above criteria for one definition of treatment failure is reasonable in my opinion. However, in virtually all treatment comparison trials I have seen or conducted, *any additional therapy besides the proscribed treatment groups* is usually considered treatment failure or reason for exclusion from the trial. The authors did something interesting with additional *non-antibiotic* treatments: “Cows that did not receive antibiotics but received support therapy with hypertonic saline, oral electrolytes, dextrose, aspirin, meloxicam, or flunixin meglumine were not considered to have received escape therapy. The proportion of cows receiving support[ive] therapy - - was recorded.”

Metritis cure vs. failure case definitions

Cure for metritis was defined as cows with a vaginal discharge score <5 on d 6 or d 12 after enrollment. (Whether any cows had score < 5 on d 6 and then reverted to a score of 5 on d 12 was not stated.) I found this surprising, because the discharge score of 4 = “not fetid mucopurulent white, yellow or reddish-brownish discharge with $\geq 50\%$ pus”. That is certainly an improving case of metritis, but to me that does not describe what I would call a cure. There was no bacteriology on vaginal discharge or any specimens as part of the definition of cures vs. failures of treatment. Metritis treatment failure was defined as cows with a vaginal discharge score of 5 after 12 d, or that were sold or died < 13 d after enrollment.

Metritis related culling or death

All cows sold within 60 DIM were physically examined by a herd veterinarian, and all cows that died within 60 DIM were necropsied by a veterinarian. Reason for culling were classified as uterine related (metritis, pelvic inflammation, peritonitis, and mass in the pelvis), non-uterine-related (mastitis, injury, lung lesions, and several other categories of disease), or low milk yield.

Results

In addition to their complete description earlier, here is a brief review of the treatment group abbreviations: chitosan (CM), ceftiofur (CEF), untreated control (CON). The different treatments for metritis were associated with several important significant differences in outcomes: Cows receiving supportive treatment: CM 30% (P < 0.01 vs. both other treatments), CON 16%, CEF 9% (P = 0.04 vs. CON). Cows receiving additional antibiotic “escape therapy”: CM 26% (P < 0.01 vs. both other treatments), CON 12%, CEF 8% (not significantly different than CON, P = 0.21). Metritis cure on d 6: CM 37% (P ≤ 0.06 vs. both other treatments), CON 45%, CEF 52% (not significantly different than CON, P = 0.10). Metritis cure on d 12: CM 59%, CON 62% (not significantly different than CM, P = 0.44), CEF 78% (P < 0.01 vs. both other treatments).

It can be readily seen that CM was associated with more need for additional treatment and lower cure percentage for metritis than either CON or CEF, while CEF was associated with markedly higher cure rate than other treatments, especially 12 d after metritis was diagnosed and treatment was initiated. Also, the authors’ expertise based speculation that they wanted to be able to detect statistical significance if a 75% cure rate was observed vs. a 65% cure rate in untreated cows was quite accurate; those values were close to the actual cure rates in the study.

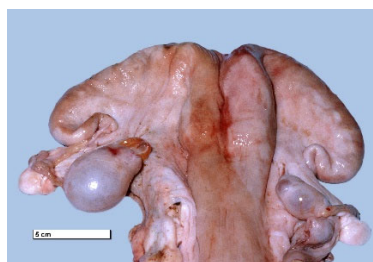
Cows that died within 60 DIM (no breakdown by causes of death was reported; presumably the deaths related to metritis were not significantly different among treatment groups but this was not stated): CM 12%, CEF 6%, CON 6%; there were no statistics presented. Certainly biologically it can be seen that CM cows were twice as likely to die within 60 DIM as either the untreated cows or the CEF treated cows.

Cows culled for uterine related conditions within 60 DIM: CM 8% (P < 0.01 vs. both other treatments), CEF 2%, CON 2% (not significantly different than CEF, P = 1.00). Culls for low milk yield within 60 DIM: CM 9%, CEF 5% (P = 0.05 vs. CM), CON 6% (not significantly different than other treatments). Metritis treatments did not affect culling within 60 DIM for non-uterine related conditions (P = 0.86), which was logical and helps validate the classification of non-uterine diseases.

Conclusions

It was interesting that neither deaths or uterine-related culls during the first 60 DIM differed between the untreated CON group or the CEF group, but CEF treatment was associated with higher metritis cure rate, and CM, the chitosan microparticles group was clearly associated with worse metritis outcomes than no treatment. In the paper’s conclusion, the authors made a good point about the above: “[Lack of culling differences from CON] may be a result of escape therapy because although [CON] cows were left untreated when first diagnosed with metritis, cows could receive support therapy and escape therapy if their condition worsened. Indeed, we observed that the proportion of cows receiving support therapy was greater in CON than CEF.”

Nearly all studies have limitations, and this study only included Holstein cows, and only compared two treatments, one of which was relatively new and clearly inferior, at least in the conditions of this study. Comparisons of more antibacterial treatments for bovine mastitis are indicated, but this study was well done overall and supported the use of ceftiofur crystalline-free acid as a treatment for bovine metritis.



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Utah State School of Veterinary Medicine 10th Anniversary Celebration, August 19 - 20, 2022

Utah State University is celebrating the 10th anniversary of the School of Veterinary Medicine, dating from when our first class of veterinary students began their freshman year in 2012.

There will be a celebration on August 19 and 20, 2022. Registration and information can be found at <https://vetmed.usu.edu/svm10>

The growth and success of the USU SVM program would of course never have been possible without the many veterinarians who have helped who did not attend our relatively new program, or did not graduate from Washington State University. We invite all veterinarians who have any connections with the SVM to attend the celebration.

If you know of other CE events or conferences of interest to dairy veterinarians, please let me know and I will publicize them.

Please let us know your comments and suggestions for future topics. I can be reached at (435) 760-3731 (Cell), or David.Wilson@usu.edu.

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