RISK FACTORS, IMPACT, AND TREATMENT OF POSTPARTUM UTERINE DISEASES IN DAIRY COWS

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Introduction: Postpartum uterine disease is common in dairy cattle and is associated with substantial impairment of reproductive performance. The objectives of this study were to validate diagnostic criteria for clinical and subclinical endometritis, identify risk factors for postpartum uterine diseases, quantify their impact on reproduction, and determine the efficacy of prostaglandin F₂α (PGF) as treatment for endometritis.

Material & Methods: The study animals were 2178 Holstein cows in 6 commercial herds in Ontario, Canada and New York, USA. All cows were examined for endometritis at 35 (± 3; EXAM1) and 56 (± 3; EXAM2) days after parturition, using endometrial cytology (cytobrush technique), vaginal discharge scoring (Metricheck device), and cervical diameter measurement (transrectal palpation). Data from 1044 cows in 6 herds that were randomly assigned to the untreated control group (no PGF) in the clinical trial were used to derive diagnostic criteria for endometritis. Reproductive data were recorded until 200 days after parturition. Diagnostic criteria for cytological and clinical endometritis were determined based on detrimental impact on subsequent reproductive performance, using logistic regression and Cox proportional hazard models accounting for the effect of herd clustering. Comparison of diagnostic criteria was performed using endometrial cytology as the reference test or by quantifying the agreement between diagnostic approaches. At week 5 postpartum (Exam1), diagnostic criteria were ≥ 6 % polymorphonuclear cells (% PMN) and mucopurulent or purulent vaginal discharge for cytological and clinical endometritis, respectively. At week 8 postpartum (Exam2), diagnostic criteria were ≥ 4 % PMN and mucopurulent or purulent vaginal discharge for cytological and clinical endometritis, respectively. Prevalence at week 5 was 14 %, 9 %, and 6 % for cytological endometritis only (CYTO), clinical endometritis only, and both cytological and clinical endometritis, respectively. The precision of classification of endometritis by uterine cytology using the thresholds defined was high: intra-observer agreement (Kappa) was 0.82 (95 % confidence interval: 0.73-0.91; P < 0.01) and inter-observer agreement (Kappa) was 0.77 (95 % confidence interval: 0.69-0.85; P < 0.01). However, there was weak agreement between cytological and clinical endometritis (Kappa = 0.2 at week 5). Among cows with clinical endometritis, only 38 and 36 % had cytological endometritis at EXAM1 and EXAM2, respectively. Combination of diagnostic criteria did not improve the accuracy for predicting cytological endometritis or the agreement between cytological and clinical endometritis. Overall, these results suggested that cytological and clinical endometritis may represent different manifestations of reproductive tract disease. They also suggested that use of the terminology “clinical endometritis” may not be accurate in many cases, and that purulent vaginal discharge (PVD) may be more descriptive. A subset of 1363 cows in 3 herds that had weekly blood samples were used to investigate risk factors for reproductive tract inflammation. Calving history, periparturient disease incidence, and body condition score at calving and at 63 days after parturition were recorded. Serum non-esterified fatty acid concentration was measured during the week prior to expected calving. Serum NEFA, β-hydroxybutyric acid (BHBA), and haptoglobin concentrations were measured at 4 (± 3), 11 (± 3), and 18 (± 3) days after parturition. Serum progesterone concentration was measured at 21 (± 3), 35 (± 3), 49 (± 3), and 63 (± 3) days after parturition. Metritis was diagnosed by farm managers within the first 20 days after parturition as cows with temperature > 39.5 C and foul-smelling vaginal discharge. Cows were examined at 35 (± 3) days after parturition by a veterinarian for purulent vaginal discharge (Metricheck device) and cytological (≥ 6 % polymorphonuclear cells at endometrial cytology; cytobrush device) endometritis. Statistical analyses were performed using multivariable logistic regression models, accounting for the random effect of herd.

Results and Discussion: The incidence of RP, metritis, clinical endometritis, and cytological endometritis were 12 %, 18 %, 15 %, and 19 %, respectively. Among cows with RP, 33.2 % developed metritis. Among cows with metritis, 33 % and 32 % developed clinical and cytological endometritis, respectively. Among cows positive for endometritis, 22.8 % were positive for both clinical and cytological endometritis. Among cows with clinical endometritis, only 42 % had cytological endometritis at the same time. Among cows with cytological endometritis, only 32 % had clinical endometritis. Determination of optimal thresholds for dichotomization of values of NEFA, BHBA, and HAPTO for each week was based on highest sum of sensitivity and specificity for predicting each disease. Risk factors for metritis included increased NEFA (≥ 0.6 mmol/L) in the week before calving (odds ratio (OR) = 1.6; P = 0.02), dystocia (OR = 2.1, P < 0.01), retained placenta (OR = 6.3, P < 0.01), and increased HAPTO (≥ 0.8 g/L) in first week postpartum (OR = 2.1 P < 0.01). Risk factors for PVD included twinning OR = 2.2; P < 0.01, dystocia (OR = 2.1; P < 0.01), metritis (OR=2.3; P < 0.01), and increased haptoglobin (≥ 0.8 g/L; OR = 2.0; P < 0.01) in the first week postpartum. Risk factors for cytological endometritis included thin body condition score (≤ 2.75) at parturition (OR = 1.9; P = 0.03), hyperketonemia (≥ 1100 µmol BHBA/L; OR = 1.4; P = 0.03), and increased haptoglobin (≥ 0.8 g/L; OR = 1.5; P < 0.01) in the first week postpartum. These results suggest the hypothesis that PVD and cytological endometritis represent different conditions. The detrimental impacts of cytological and clinical endometritis on reproductive performance were significant and additive (table 1). Table 1. Effect of reproductive tract disease at week 5 postpartum on time to pregnancy. All cows were examined using the Metricheck device and cytobrush endometrial cytology at 32 to 38 days postpartum.
All 2178 cows were enrolled in a randomized clinical trial, where cows were randomly assigned to receive either PGF (25 mg dinoprost IM) at 35 and 49 days in milk (DIM), or to be untreated i.e., 2 injections of PGF, 2 weeks apart, or none. The design was to allow separation of the putative effect of PGF on endometritis from its effect of estrus synchronization for insemination. Therefore, cows were not eligible for insemination until at least 2 weeks, or enrollment in an ovulation synchronization program until 3 weeks after the second administration of PGF.

There was no effect of PGF treatment on probability of cure of CYTO or CLIN at 56 DIM (P > 0.20), or on time to first breeding or to pregnancy (P > 0.20). There was no effect of PGF treatment on the probability of cure of CYTO or PVD, irrespective of progesterone concentration at the time of treatment. Among cows affected by CYTO or PVD at EXAM1, 66 and 63 % had spontaneously cured at EXAM2, respectively. Cows persistently affected at EXAM2 had an increased time to pregnancy, and were more likely to have both CYTO and PVD at EXAM1. Administration of PGF at both 5 and 7 weeks postpartum did not mitigate the effects of CYTO or PVD on reproductive performance.

Statistical analyses were performed using linear mixed models, logistic regression models, and Cox proportional hazard models, accounting for the effects of experimental treatments and herd clustering. Milk production and culling were the outcomes. Primiparous and multiparous cows were modeled separately for milk production. Milk production of primiparous cows was unaffected by uterine diseases. The impact of metritis on milk production was variable over time in multiparous cows, reducing production per cow by 3.7 kg at first DHI test, but was not significantly different at later tests. Retained placenta reduced milk production by 2.6 kg/day in multiparous cows through the first four DHIA tests. The projected impacts of metritis and RP in multiparous cows were reductions of 259 kg and 753 kg over 305 days of lactation, respectively; these effects were additive. There was no effect of CYTO and PVD on milk production. Culling risks at 30 and 63 DIM were unaffected by RP and metritis. Culling hazard up to 300 DIM was unaffected by RP, metritis, CYTO or PVD, whether or not for pregnancy status, milk production, and displaced abomasum were accounted for. Uterine disease reduces pregnancy rate, which was a substantial risk factor for culling, but if affected cows become pregnant they were not at greater risk of culling.

Conclusions: These findings suggested that CYTO and CLIN may represent two different conditions. It is proposed that purulent vaginal discharge (PVD) terminology should be used instead of CLIN, because CLIN is not always reflective of endometrial inflammation. The source of vaginal discharge is unclear and requires further investigation. Approaches to treatment of postpartum uterine diseases require reassessment.

Key words: endometritis, metritis, prostaglandin, pregnancy.

<table>
<thead>
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<th>Uterine health classification</th>
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<th>Median time to pregnancy in days (survival analysis model)</th>
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<td>Unaffected by endometritis</td>
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<td>127 - 137</td>
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<td>Both cytological endometritis and PVD</td>
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<td>195</td>
<td>174 - 216</td>
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References:


