Theriogenology 85 (2016) 887–893

Contents lists available at ScienceDirect

Theriogenology

journal homepage: www.theriojournal.com

Effect of puerperal metritis on reproductive and productive performance in dairy cows in Argentina

M. Piccardi [a,*], G. Romero [b], G. Veneranda [b], E. Castello [b], D. Romero [c], M. Balzarini [a], G.A. Bó [d,e]

[a] Cátedra de Estadística y Biometría, Facultad de Ciencias Agropecuarias, Universidad Nacional de Córdoba, Córdoba, Argentina
[b] La Sibila (Grupo Los Lazos S.A.), Santa Fe, Argentina
[c] Zoetis Argentina, Buenos Aires, Argentina
[d] Instituto de Reproducción Animal Córdoba (IRAC), Córdoba, Argentina
[e] Medicina Veterinaria, Instituto de Ciencias Básicas y Aplicadas, Universidad Nacional de Villa María, Córdoba, Argentina

ARTICLE INFO

Article history:
Received 21 March 2015
Received in revised form 21 October 2015
Accepted 28 October 2015

Keywords:
Puerperium
Days open
Accumulated production
Hazard model

ABSTRACT

The objectives of this study were to evaluate the reproductive and productive performance of dairy cows with and without puerperal metritis and to evaluate the effectiveness of using a long-acting ceftiofur preparation. Dairy cows in one dairy farm, calving from July 2009 to January 2010, were examined between 3 and 14 days postpartum and classified on the basis of vaginal discharge into three groups: cows with normal discharge (control; C); cows with a bloody mucus purulent or pathologic nonfetid discharge (PnFD), and cows with bloody mucopurulent or purulent fetid discharge (PFD). Cows in C and PnFD groups were not treated, whereas those in the PFD group were randomly allocated to receive 2.2 mg/kg of ceftiofur subcutaneously behind the ear (PFD-T) or remain untreated (PFD-No T). From the 640 cows examined, 58.2% formed the C group, 13.4% formed the PnFD group, and 28.4% formed the PFD group. Survival curves differed between cows in the C group and PFD-No T group ($P = 0.0013$) and between PFD-No T versus PFD-T group ($P = 0.0006$). Survival curves of PnFD were intermediate and did not differ from those in the C group ($P = 0.2$) and PFD-T group ($P = 0.1$) but tended to be different from the PFD-No T group ($P = 0.056$). The postpartum interval to achieve a 25% pregnancy rate was 72 days for cows in the C group, 73 days for the PFD-T group, 83 days for PnFD group, and 95 days for the PFD-No T group. The chance of pregnancy in a cow in the C group was 1.98 times higher (95% confidence interval = 1.33, 3.08) and in cows in the PFD-T group was 2.16 times higher (95% confidence interval = 1.37, 3.50) than that in the PFD-No T group. Finally, the chance of pregnancy in cows in the PnFD group tended to be higher ($P = 0.08$) than that in the PFD-No T group but did not differ from the other two groups. Cumulative 305-day milk production was higher ($P < 0.0001$) in C group than those with vaginal discharge, regardless of fetidness and regardless of treatment. It is concluded that puerperal metritis affects the reproductive and productive performance of dairy cows and the treatment with ceftiofur was effective in reducing the adverse effects on reproductive performance but not on milk production.

1. Introduction

Puerperal metritis is an inflammation of all the layers of the uterus, which is characterized by the presence of a watery, reddish-brown vulvar discharge [1]. In some cases, puerperal metritis is classified as a disease complex

* Corresponding author. Tel.: 54-351-4334103/05/16/17/18.
E-mail address: monicapiccardi@gmail.com (M. Piccardi).

0093-691X/$ – see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.theriogenology.2015.10.038

without distinguishing the severity or clinical presentation, which hinders comparisons between studies [1]. Sheldon et al. [2] standardized the clinical definition of puerperal metritis to include clinical symptoms such as reduced milk production, dullness, or other clinical signs of toxemia with fever (>39.5 °C) within 21 days postpartum.

Several factors contribute to the etiology, severity, and duration of puerperal metritis. Several studies have suggested that risk factors for metritis include dystocia, twins, retained placenta, stillbirth, abortion, and prolapsed uterus [3–7]. Although metritis and endometritis are common postpartum uterine diseases that have a profound negative effect on reproduction in dairy cows [6,8–11], the reported results of their effects on milk production are conflicting [12–14]. Thus, Dubuc et al. [15] found that metritis decreased milk production only in multiparous cows.

Prevention and early treatment of puerperal metritis may result in an economic benefit because progress of the condition is avoided [16]. Treatment has historically involved intrauterine infusion of antibiotics [17,18] or injection with PGF2α [19,20]. Parenteral administration of ceftiofur sodium [21] or ceftiofur hydrochloride [22] has been shown to be effective for treatment of metritis. Ceftiofur reduced the incidence of metritis in cows with retained fetal membranes [10,23,24]. This effect was proposed to be linked with a decrease in the uterine pathogen load in the early postpartum period [25]. The information regarding its efficacy in the treatment of metritis in pasture-based production systems such as those in Argentina is limited. Previous studies performed in Argentina with dairy cows under total mixed ration formulated diets have shown that daily treatment with ceftiofur hydrochloride for three consecutive days did not affect the cure rate of metritis or peak milk production, but it increased the risk for pregnancy at timed artificial insemination (AI) and reduced the risk for reproductive culling [26]. However, one of the main problems regarding daily treatments in pasture-managed systems has been the failure to continue the treatments properly that significantly affect the cow's response to the therapy. Therefore, the objectives of this study were to evaluate the reproductive and productive performance of dairy cows with and without puerperal metritis and to reevaluate the effectiveness of using ceftiofur, a long-acting antibiotic treatment on those cows with metritis in pasture-based production systems.

2. Materials and methods

2.1. Data

The study was conducted from July 2009 to January 2010 in nine commercial dairy herds in the center of Santa Fe province (32°31′30.05″S; 61°16′40.87″W). The total population of the farm used for the study was 3300 milking cows with an average production of 7550 kg per lactation, and data from 690 animals calving during the period of the study were included. Animals were milked twice daily. Prepartum cows were housed in lots 30 days before parturition where they were fed daily and provided with water ad libitum. At least 35 m^2 was available to each cow. The diet consisted of corn silage, feed with anionic salts and alfalfa hay. This ration was composed of 14% protein, 1.6 Mcal net energy of lactation/kg of dry matter (DM). Lots were looked four times a day to observe periparturient cows.

All events occurring at calving were recorded by dairy staff. The type of calving was classified as: (1) normal calving (cows that had no difficulty in giving birth to a single calf without assistance); or (2) assisted calving (cows that needed assistance by herdsperson or veterinarian). Assisted calving was further rated as: assistance as a precaution, calf bad presentation, or a large-sized calf (forced extraction). Retained fetal membrane was considered if the placenta was not released within 24 hours of calving, for both normal and assisted calvings. The primiparous or multiparous state of the cow was considered as a second-level variable.

After calving, the cows were placed in a sanitary herd for 2 to 4 days and then transferred to a herd where all cows have calved recently (fresh cows). Diet consisted of alfalfa and graminoid grazing, corn silage, and balanced feed inside the milking parlor; diet was based on 16% protein, 1.5 to 1.7 Mcal net energy of lactation/kg DM, reaching a total of 18 to 20 kg DM intake in the first 21 days postpartum. Vaginal discharge of all cows was analyzed 3 to 14 days postpartum. The time window of the examination of vaginal discharge (3–14 days) was determined on the basis of the standard practice of the veterinarian health visit to the dairy farms, which is usually once every 2 weeks or even once every month for the commercial herds in Argentina. The type of discharge was determined by extraction with a clean palpation sleeve after vulva disinfection with water containing a quaternary ammonium solution (Bagodryl, Biogenesis-Bago, Buenos Aires, Argentina). The criteria to determine the presence of puerperal metritis was the presence of a fetid, watery, purulent, sometimes brown fluid discharge; depression, sunken eyes, and loss of appetite [2]. Thus, cows were classified as having three types of discharge: (1) normal discharge or control (C), with a similar appearance to egg whites; (2) pathologic nonfetid discharge (PnFD), with a mucopurulent or pathologic nonfetid discharge, and (3) pathologic fetid discharge (PFD), with bloody, mucopurulent or purulent, fetid discharge. Cows in C and PnFD groups were not treated with antibiotics, whereas those in the PFD group were subdivided into two subgroups; one was treated with 2.2 mg/kg of slow-release ceftiofur hydrochloride (Excede, Zoetis, Buenos Aires, Argentina) administered at the base of the ear (PFD-T), whereas the other subgroup was not treated with antibiotics (PFD- No T). The use of long-acting (slow release) ceftiofur is accepted in Argentina and other countries like the United States and Canada; it is not necessary to discard the produced milk from cows under treatment. However it could happen that such therapy may not be acceptable in other countries.

Afterward, between Days 21 and 30 postpartum, all cows were tested for possible clinical endometritis in cows that had normal discharge between 3 and 14 days postpartum and to check if those cows that had been treated were cured. The criterion used to diagnose clinical endometritis was the presence of a purulent or mucopurulent discharge, which was extracted with a clean sleeve after disinfection of the vulvar area, as described above. All cows which exhibited clinical endometritis at the time of checkup received a dose of PGF2α (25-mg dinoprost, Lutalyse; Zoetis, Argentina) intramuscularly.

Reproductive management started between Days 40 and 47 postpartum, when all cows were subjected to transrectal palpation to determine uterus condition and ovarian status and were given a dose of PGF2α. During the following 14 days, estrus was detected and those showing signs of estrus were inseminated following the AM-PM rule. Cows that were not in estrus received a second dose of PGF2α 14 days later and were inseminated 12 hours after estrus detection. Finally, cows that were not inseminated at 65 to 72 days postpartum were enrolled in a timed-AI protocol. The protocol consisted of inserting a device with 1.9-g progesterone (CIDR; Zoetis, Argentina) and an intramuscular application of 10-μg buserelin (GnRH, Receptal; MSD-Agvet, Argentina) on Day −10. On Day −3, the intravaginal device was removed and PGF2α was administered, followed by a second GnRH 56 hours later. All cows were timed artificially inseminated on Day 0, 72 hours after removal of the device. After insemination, all cows were painted at the base of the tail and estrus was observed between Days 18 and 24 after insemination. Pregnancy diagnosis was performed by transrectal palpation 50 days after insemination.

2.2. Statistical analyses

An exploratory analysis was initially performed to characterize the different animal groups according to the presence and type of discharge, number and type of calvings, and average days in milk to first service(D1S). A multiple logistic regression with odds ratio was obtained to evaluate assisted or normal calving and number of births as risk factors of metritis. A multiple logistic regression was adjusted using software version 9.0.1 JMP [27] to estimate the relative contribution of factors affecting the probability of conception at the first service and at the second service. The model included treatment, animal category, type of calving, and days in milk to service as independent variables. Model outputs included the regression coefficients and odds ratios, which indicate how the independent variables introduce changes in the probability of occurrence of an event, in this case, conception.

To evaluate the effect of number of days postpartum in which the cows were examined for vaginal discharge and treated for metritis on fertility, the 3 to 14 days postpartum window of examination was divided into two periods (3–8 days and 9–14 days). However, the statistical analysis did not reveal differences among time periods; thus, all the information was considered together as one data set. Survival curves were obtained to compare the proportion of pregnant animals across days in milk (DIM) depending on the types of discharge, and then, in relation to the type of calving (normal or assisted). The curves were calculated according to the Kaplan and Meier algorithm for each of the treatments (type of discharge), and the equality of two or more survival curves was compared with the log-rank test [28]. High log-rank values are associated with low P values (probability that the curves were different by chance). In this study, $P < 0.05$ was used to indicate statistically significant differences between survival curves. A Cox proportional hazard model [29] was also fitted using PROC PHREG of SAS [30] to estimate the risk of pregnancy in terms of treatment, animal category, type of calving (normal or assisted), and productive level. For the survival analysis and Cox regression, the animals cows entered the “at risk set” of pregnancy after the voluntary waiting period (45 days postpartum) to 150 days postpartum (last day of observation).

Finally, lactation curves for each animal category from each treatment were modeled considering the subject-specific effect given by the cow to estimate the accumulated 305-day yield and peak yield, using the PROC NLMIXED of SAS [30].

3. Results and discussion

The study evaluated 690 calvings; 50 of them were not included in the analysis due to cows being culled, lack of data on calving type, or any other incomplete information that may influence the results. Thus, 640 calvings were evaluated, with 372 (58.2%) being classified as C, 86 (13.4%) as PnFD, and 182 (28.4%) as PFD, the latter considered as exhibiting puerperal metritis. This group was randomly divided into two subgroups, one including 102 cows (15.90% of the total) that were treated (PFD-T) and the other group including the remaining 80 cows (12.50%) that were not treated (PFD- No T). The overall incidence of puerperal metritis was 28.4%. Of the 87 cows with assisted calving, 39.08% were classified as C, 13.79% as PFD, and 47.1% as PnFD. Dubuc et al. [10] reported that the incidence of metritis was 28% in cows with high risk of uterine disease (cows that experienced dystocia, twins, or retained placenta). Calving type turned out to be a risk factor ($P < 0.0001$) for metritis, with an odds ratio of 2.50 (95% confidence interval = 1.57, 3.99), suggesting that the chance of a cow that was assisted is 2.50 times more likely to present metritis than one with normal calving. It is expected that cows with dystocia would have higher incidences of metritis because this disease is associated with reproductive tract trauma and/or environmental infection produced by the farm personnel by using dirty forceps and chains to manipulate the cows and fetus [7,31].

This study comprised 240 calvings of primiparous and 400 of multiparous cows. In primiparous cows, 203 had normal calvings (84.58%), with 107 exhibiting normal discharge (52.7%) and 71 D1S, 34 (16.7%) PnFD and 79 D1S, 37 (18.2%) PFD-T and 75 D1S, and 25 (12.3%) PFD-No T and 64 D1S. Furthermore, 37 (15.5%) had assisted calvings, with 11 presenting normal discharge (29.7%) and 64 D1S, 6 (16.2%) PnFD and 77 D1S, 10 (27%) PFD-T and 74 D1S, and 10 (27%) PFD-No T and 65 D1S. In multiparous cows, 350 (87.5%) had normal calvings, of which 231 (66%) had normal discharge and 54 D1S, 40 (11.4%) were PnFD and 73 D1S, 40 (11.4%) PFD-T and 75 D1S, and 39 (11.1%) PFD-No T and 68 D1S. Fifty multiparous cows had assisted calving (12.5%), of which 23 had normal discharge (46%) and 65 D1S, 6 (12%) had PnFD and 81 D1S, 15 (30%) PFD-T and 92 D1S, and 6 (12%) PFD-No T and 86 D1S (Table 1). The number of calvings proved to be a risk factor ($P < 0.0112$) for metritis, with an odds ratio of 1.58 (95% CI = 1.11, 2.25), suggesting that the chance of a primiparous cow having metritis is 1.58 times higher than that of a multiparous cow.

Table 1
Number of cows evaluated (n) and average days in milk to first service (D1S) for each category considering type of calving and assigned treatment.[a]

Animal category	Type of calving	Treatments	D1S
Primiparous (n = 240)	Normal (n = 203; 84.5%)	Control (n = 107; 52.7%)	71
		PnFD (n = 34; 16.7%)	79
		PFD-T (n = 37; 18.2%)	75
		PFD-No T (n = 25; 12.3%)	64
	Assisted (n = 37; 15.5%)	Control (n = 11; 29.7%)	64
		PnFD (n = 6; 16.2%)	77
		PFD-T (n = 10; 27.0%)	74
		PFD-No T (n = 10; 27.0%)	65
Multiparous (n = 400)	Normal (n = 350; 87.5%)	Control (n = 231; 66.0%)	54
		PnFD (n = 40; 11.4%)	73
		PFD-T (n = 40; 11.4%)	75
		PFD-No T (n = 39, 11.2%)	68
	Assisted (n = 50; 12.5%)	Control (n = 23; 46.0%)	65
		PnFD (n = 6; 12.0%)	81
		PFD-T (n = 15; 30.0%)	92
		PFD-No T (n = 6; 12.0%)	86

PnFD = pathologic nonfetid discharge; PFD = pathologic fetid discharge; PFD-No T = untreated pathologic fetid discharge; PFD-T = treated pathologic fetid discharge.
[a] Treatments: control = normal discharge.

In the checkup held between 21 and 30 days postpartum, 29 (12.28%) primiparous and 49 (12.08%) multiparous cows exhibited clinical endometritis. They were distributed as follows, according to the type of discharge exhibited at first checkup: primiparous cows, 4 (3.38%) with normal discharge, 8 (20.0%) PnFD, 8 (17.02%) PFD-T and 9 (25.7%) PFD-No T, and multiparous cows, 15 (5.9%) with normal discharge, 7 (15.2%) PnFD, 14 (24.6%) PFD-T, and 13 (30.23%) PFD-No T. Considering the results from the first postpartum checkup, the percentage of cows diagnosed with clinical endometritis was lower ($P < 0.01$) in cows with normal discharge (19 of 371; 5.1%) than those with abnormal discharge on the first checkup (15 of 86, 17.4% of those with PnFD; 22 of 102, 21.5% of those with PFD-T; and 24 of 80, 30.0% of those with PFD-No T). Interestingly, no differences were detected between the later three groups. Hence, the percentage of cows in the PFD that were cured did not differ ($P > 0.05$) between the PDF-T (78%) and PDF-No T (70%) cows. Dubuc et al. [10] found that the proportion of cows that experienced spontaneous cure from first examination to the second examination was approximately 63 to 66%. Gautam et al. [32] reported 75% spontaneous cure in cows affected by purulent vaginal discharge; this proportion may be reflective of capacity of the cow to clear the infections using its own immune system.

3.1. First and second service conception rate

The only factor that resulted significant in the multiple logistic regression model adjusted for conception rate at first service was the type of discharge ($P = 0.0248$, Table 2). The conception rate at first service for cows with normal discharge (control group) was 34.5%, 30.2% for PnFD, 16.6% for PFD-No T, and 35.5% for PFD-T. Cows in group PFD-No T had lower conception rates than cows of the control group ($P = 0.0107$), whereas the other groups of cows did not differ significantly from the control group. Dubuc et al. [10] reported similar conception rates at first service, 35% for

Table 2
Likelihood ratio test (LRT) for each factor analyzed by multiple logistic regressions for conception rate at first and second service.

Factor	LRT	P value
TC1S[a]		
Treatment	9.3664	0.0248
Animal category	0.8810	0.3479
Type of calving	0.1521	0.6965
D1S[b]	0.0034	0.9538
CR2S[c]		
Treatment	4.1553	0.2452
Animal category	2.0952	0.1478
Type of calving	0.0640	0.8003
D2S[d]	0.3503	0.5540

[a] CR1S = first service conception rate.
[b] D1S = days to first service.
[c] TC2S = second service conception rate.
[d] D2S = days to second service.

unaffected group and 25% for purulent vaginal discharge group. The odds ratio (Table 3) showed significant differences between cows in PFD-No T and cows from PFD-T and control. Furthermore, conception rates tended to differ between groups PFD-No T and PnFD. However, there was no significant factor influencing conception rate at the second service. Conception rate at the second service was 29.8% for the control group, 26.7% for PnFD, 37.7% for PFD-T, and 23.6% for PFD-No T. Unfortunately, we did not inquire about the proportion of cows that experienced spontaneous cure between the two services.

3.2. Days open

Survival curves as a function of treatment were statistically different between the control and the PFD-No T groups ($P = 0.0013$) and between PFD-No T and PFD-T groups ($P = 0.0006$). The time to pregnancy (days open [DO]) of 25% of the control group was 72 days, 83 days for PnFD, 73 days for PFD-T, and 95 days for PFD-No T, indicating a 23-day delay to achieve the same percentage of pregnant animals in PFD-No T group compared to the control group (Fig. 1). These results are similar to the 34-day delay reported by LeBlanc et al. [6], the 24 and 25 days reported in two studies by Dubuc et al. [10,33].

Survival curves for DO according to treatments by type of calving: normal (A) and assisted (B) are shown (Fig. 2). In

Table 3
Odds ratio (OR) and 95% confidence intervals (LL: lower limit and UL: upper limit) for comparisons between treatments to determine their effect on conception rate first service.

Treatments[a]	OR	LL 95%	UL 95%	P value
Control vs. PnFD	1.2640	0.7482	2.1813	0.3851
Control vs. PFD-No T	2.4611	1.3187	4.9026	0.0040*
Control vs. PFD-T	0.9323	0.5763	1.5209	0.7770
PnFD vs. PFD-No T	1.9469	0.9077	4.3292	0.0874
PnFD vs. PFD-T	0.7375	0.3886	1.3857	0.3451
PFD-T vs. PFD-No T	2.6396	1.2859	5.6801	0.0077*

*P values <0.05 indicate statistically significant differences between the specified class and the reference class for the factor under study.
PnFD = pathologic nonfetid discharge; PFD = pathologic fetid discharge; PFD-No T = untreated pathologic fetid discharge; PFD-T = treated pathologic fetid discharge.
[a] Treatments: control = normal discharge.

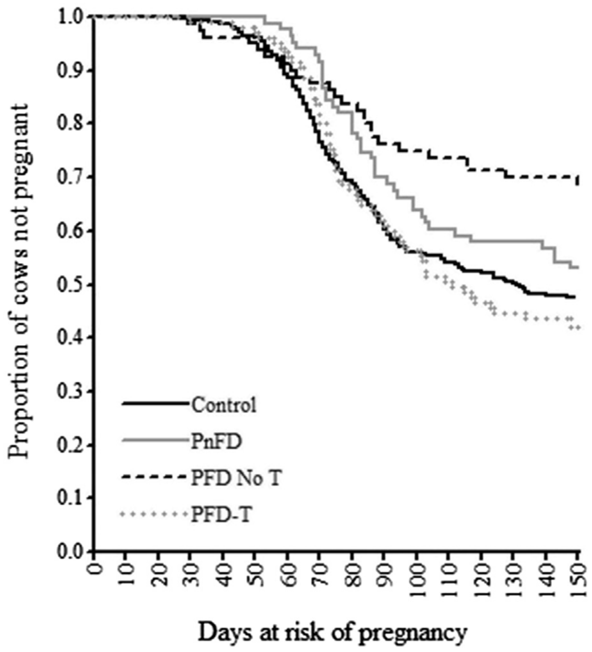

Fig. 1. Kaplan–Meier survival curves for time to pregnancy (days open) for lactations with different treatments (control = normal discharge; PnFD = pathologic nonfetid discharge; PFD-No T = untreated pathologic fetid discharge; PFD-T = treated pathologic fetid discharge).

normal calvings, the survival curves according to treatment were statistically different between the control group and the group PFD-No T (P = 0.002294), between PFD-No T and PFD-T group (P = 0.000920), and between PFD-No T and PnFD group (P = 0.055). The time to pregnancy (DO) of 25% of the control group was 72 days, 83 days for PnFD, 73 days for PFD-T, and 104 days for PFD-No T, indicating a 32-day delay for achieving the same percentage of pregnant animals between the control group and PFD-No T. Although assisted calvings were not statistically significantly different between treatments. The time to pregnancy (DO) of 25% of the animals was 65 days for control, 83 days for PnFD, 77 days for PFD-T, and 95 days for PFD-No T, suggesting a 35-day delay in achieving the same percentage of pregnant animals between the control group and PFD-No T.

Table 4 shows the estimated parameters for each explanatory variable of the proposed Cox proportional hazards regression model. The factors animal category, calving type, and production level showed no significant differences of pregnancy between levels except for the type of discharge, being the only explanatory variable that was statistically significant (P = 0.0016). The risk of pregnancy in a cow in the control group was 1.98 times higher than that in PFD-No T. The risk of pregnancy was also significantly higher (2.16) in cows belonging to PFD-T group than to PFD-No T.

In this study, 305-day yield estimated by the nonlinear model of primiparous cows was 6989 L for the control group, 6610 L for PnFD, 6749 L for PFD-No T, and 6819 L for PFD-T, with the control group showing the highest value (P = 0.0322). The 305-day yield estimated by the nonlinear model for multiparous cows was 7674 L for the control group, 7516 L for PnFD, 7562 L for PFD-No T, and 7410 L for PFD-T. Again, the control group showed the highest value, but the differences from the other groups were not significant (Table 5).

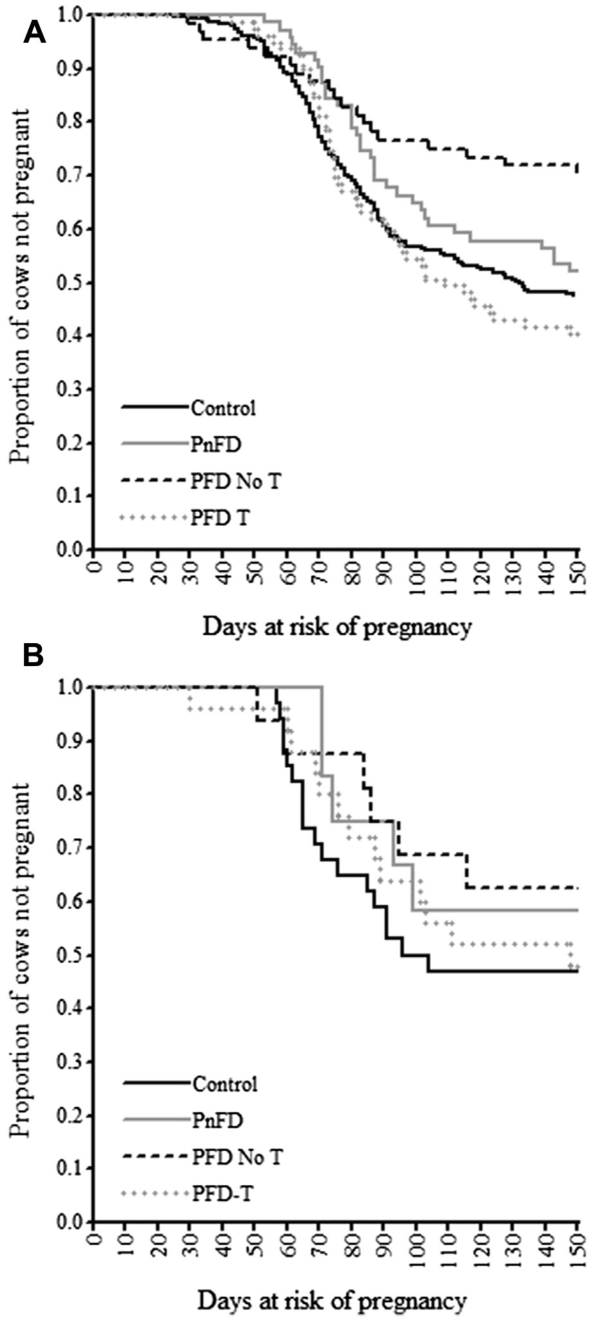

Fig. 2. Kaplan–Meier survival curves for time to pregnancy (days open) for cows with different treatments (control = normal discharge; PnFD = pathologic nonfetid discharge; PFD-No T = untreated pathologic fetid discharge; PFD-T = treated pathologic fetid discharge) by type of calving for normal calving (A) and assisted calving (B).

Peak yield estimated by the nonlinear model of primiparous cows was 27 L for the control group, 26 L for PnFD, 25 L for PFD-No T, and 26 L for PFD-T, with the lowest values being for PFD-No T group (P = 0.0035). Peak yield

Table 4
Parameters estimated for the explanatory variables in the Cox proportional hazards regression model of days open.

Explanatory variable	Coefficient	SE	LL 95%	UL 95%	LRT	P value
Treatment[a]						
PnFD	−0.0461	0.1354	−0.3210	0.2114	15.26	0.0016*
PFD-No T	−0.4697	0.1567	−0.8008	−0.1719		
PFD-T	0.3010	0.1185	0.0644	0.5302		
Animal category						
Heifer	0.0613	0.0592	−0.0555	0.1768	1.06	0.3021
Type of calving						
Normal	0.0172	0.0843	−0.1422	0.1891	0.04	0.8377
Production level						
High	−0.1119	0.0579	−0.2259	0.0014	3.74	0.0529

*P values <0.05 indicate statistically significant differences between the specified class and the class reference for the factor under study.
The missing class is considered as a reference for statistical comparisons, for the treatments: control; for animal category: cow; for type of calving: assisted, and for production level: low.
Abbreviations: LL, lower limit (for 95% confidence interval); LRT, likelihood ratio test; SE, standard error; UL, upper limit (for 95% confidence interval).
PnFD = pathologic nonfetid discharge; PFD = pathologic fetid discharge; PFD-No T = untreated pathologic fetid discharge treated; PFD-T = treated pathologic fetid discharge.
[a] Treatments: control = normal discharge.

estimated by the nonlinear model of multiparous cows was 34 L for the control group, 34 L for PnFD, 31 L for PFD-No T, and 32 L for PFD-T. Values of the PFD-No T group were lowest than those of control, PnFD, and PFD-T groups ($P = 0.0002$, Table 5).

Puerperal metritis affects reproductive and productive performance of lactating dairy cows. The treatment with ceftiofur was effective in reducing the adverse effects on reproduction. Giuliodori et al. [26] found that a 3-day therapy with ceftiofur was related to increased pregnancy rate at timed-AI. The most important risk factors for contracting puerperal metritis were cows with dystocia, twinning, retained fetal membranes, or a combination of these; these results agree with those of other research groups [3–5]. LeBlanc et al. [7] suggested that risk factors for metritis include dystocia, retained placenta, and other factors not included in this study. Giuliodori et al. [26] suggested that primiparous cows, cows with abnormal calving, and cows in poor energy balance during prepartum have increased risk for metritis. It was not the aim of this work to determine the individual effect of these factors on the incidence of puerperal metritis. We believe that cows with one or more of these disorders have a high risk for metritis. We found that the prevalence of puerperal metritis in cows that had assisted calvings (47.1%) was similar to that obtained by Markusfeld [34] and 28% found by Dubuc et al. [10].

Table 5
Production of 305-day yield in lactation and peak yield in cows with puerperal metritis that were treated or not with Excede (PFD-T and PFD-No T), cows with pathologic nonfetid discharge (PnFD) and cows with normal discharge (control).

Variables	305-day yield in lactation	Peak yield
Primiparous cows		
Control (n = 118)	6989 ± 67.7[b]	27.3 ± 0.2[b]
PnFD (n = 40)	6610 ± 119.3[a]	26.3 ± 0.4[b]
PFD-T (n = 47)	6819 ± 105.1[a]	26.5 ± 0.4[b]
PFD-No T (n = 35)	6749 ± 124.3[a]	25.3 ± 0.4[a]
Multiparous cows		
Control (n = 254)	7674 ± 69.4[a]	34.3 ± 0.3[b]
PnFD (n = 46)	7516 ± 164.7[a]	34.6 ± 0.7[b]
PFD-T (n = 55)	7410 ± 147.6[a]	32.4 ± 0.6[b]
PFD-No T (n = 45)	7562 ± 164.7[a]	31.3 ± 0.7[a]

[ab]averages with different letters are significantly different ($P < 0.05$).

Examination of cows after calving was implemented between Days 3 and 14, similarly to Upham [35]. In the present study, the intensity of the monitoring program of postpartum health may have led to early diagnosis and treatment of puerperal metritis. A study that analyzed the effect of this disease on reproduction [11] showed less effect of puerperal metritis in animals subjected to routine tests, compared to herds whose owner reported the disease. Furthermore, Harman et al. [36] found no effect of cows with dystocia, retained fetal membranes or early metritis during 56 to 120 days postpartum in terms of risk of conception. It is also noteworthy that although the percentage of cows cured at the second checkup was not different between the treated and untreated cows, those cows with metritis that were treated became pregnant earlier than untreated cows. Furthermore, the treated cows had a very similar reproductive performance to the control group. These contrasting results reported the effectiveness of the treatment on the reproductive performance of the cows with postpartum metritis and the limitations of the postpartum examinations performed to detect cows with endometritis. Evidently, more cows must have been cured after the antibiotic treatment than those not receiving any treatment to have a similar reproductive performance than those cows without postpartum metritis.

In a study by Benzaquen et al. [16] conducted in Florida, the incidence of puerperal metritis was 21%, whereas in our study it was 28.4%. The effect of puerperal metritis on pregnancy rate is exacerbated in the warmer months where cows at first service have an extensive period of nonpregnancy over the subsequent 150 days of the insemination period [16].

Regarding milk production, primiparous cows had a difference in production in both parameters, peak yield and 305-day yield, whereas multiparous cows had a significant difference in peak yield but only numeric differences in 305-day yield. Wittrock et al. [37] found differences in multiparous and no differences in primiparous cows and attributed the results to the lower dry matter intake. Wittrock et al. [37] also found that cows with puerperal metritis produced less milk until the seventh week after calving, at which point they recovered the production. The study from Dubuc et al. [15] is in agreement with the present study and reported that the effect of metritis on milk production depended on parity group. Giuliodori et al. [26] reported that clinical and puerperal metritis both have negative effects on lower milk yield in early lactation. The effect of metritis on milk production was variable over time in multiparous cows: it decreased milk production by 3.7 kg/cow at first test-day but was not different at the subsequent three tests. On the basis of projected 305-day production at the third test day, multiparous cows with metritis reduced 259 kg less milk per lactation than unaffected cows. Conversely, test-day milk reduction of primiparous cows was unaffected by metritis and 305-day projected production in primiparous cows was also unaffected by metritis. Another study using daily milk data from 500 cows in one herd reported a detrimental effect of metritis on milk production in all cows that was greater per day among cows culled lesser than 60 DIM but lasted up to 110 DIM among cows that were not culled [9]. Conversely, Fourichon et al. [14] reported that the presence of purulent vaginal discharge was not associated with an effect on milk production.

3.3. Conclusions

Puerperal metritis affects the reproductive and productive performance of dairy cows. Cows diagnosed with metritis that were untreated had a lower first service conception rate than those without metritis and those that were treated with ceftiofur. Although the percentage of cows cured at the second examination was not different between treated and untreated cows, there was a 22-day delay in achieving the same percentage of pregnant animals in cows with metritis that were nontreated compared to those treated. Finally, 305-day milk yield in both primiparous and multiparous cows was higher in those in the control group than in those with metritis that were treated or untreated, with differences of approximately 100 to 250 L, respectively. Thus, results can be interpreted to suggest that early treatment with ceftiofur hydrochloride in cows diagnosed with metritis is advantageous in relation to reproductive performance but not to reverse the negative effects of metritis on milk production.

References

[1] Lewis GS. Uterine health and disorders. J Dairy Sci 1997;80:984–94.
[2] Sheldon IM, Lewis GS, Leblanc S, Gilbert RO. Defining postpartum uterine disease in cattle. Theriogenology 2006;66:1516–30.
[3] Gröhn YT, Erb HN, McCulloch CE, Saloniemi HS. Epidemiology of reproductive disorders in dairy cattle: associations among host characteristics, disease and production. Prev Vet Med 1990;8:25–39.
[4] Correa MT, Erb H, Scarlett J. Path analysis for seven postpartum disorders of Holstein cows. J Dairy Sci 1993;76:1305–12.
[5] Kaneene JB, Miller R. Risk factors for metritis in Michigan dairy cattle using herd- and cow-based modelling approaches. Prev Vet Med 1995;23:183–200.
[6] LeBlanc SJ, Duffield TF, Leslie KE, Bateman KG, Keefe GP, Walton JS, et al. Defining and diagnosing postpartum clinical endometritis and its impact on reproductive performance in dairy cows. J Dairy Sci 2002;85:2223–36.
[7] Dubuc J, Duffield TF, Leslie KE, Walton JS, LeBlanc SJ. Risk factors for postpartum uterine diseases in dairy cows. J Dairy Sci 2010;93:5764–71.
[8] Gilbert RO, Shin ST, Guard CL, Erb HN, Frajblat M. Prevalence of endometritis and its effects on reproductive performance of dairy cows. Theriogenology 2005;64:1879–88.
[9] Overton M, Fetrow J. Economics of postpartum uterine health. In: Proceedings of Dairy Cattle Reproduction Council Convention Omaha, Nebraska. Hartland, WI: Dairy Cattle Reproductive Council; 2008. p. 39–43.
[10] Dubuc J, Duffield TF, Leslie KE, Walton JS, LeBlanc SJ. Randomized clinical trial of antibiotic and prostaglandin treatments for uterine health and reproductive performance in dairy cows. J Dairy Sci 2011;94:1325–38.
[11] Fourichon C, Seegers H, Malhe X. Effect of disease on reproduction in the dairy cows: a meta-analysis. Theriogenology 2000;53:1729–59.
[12] Bartlett PC, Kirk JH, Wilke MA, Kaneene JB, Mather EC. Metritis complex in Michigan Holstein-Friesian cattle: Incidence, descriptive epidemiology and estimated economic impact. Prev Vet Med 1986;4:235–48.
[13] Rajala PJ, Grohn YT. Effects of dystocia, RP, and metritis on milk yield in dairy cows. J Dairy Sci 1998;81:3172–81.
[14] Fourichon C, Seegers H, Bareille N, Beaudeau F. Effects of disease on milk production in the dairy cow: a review. Prev Vet Med 1999;41:1–35.
[15] Dubuc J, Duffield TF, Leslie KE, Walton JS, LeBlanc SJ. Effects of postpartum uterine diseases on milk production and culling in dairy cows. J Dairy Sci 2011;94:1339–46.
[16] Benzaquen ME, Risco CA, Archebald LF, Melendez P, Thatcher MJ, Thatcher WW. Rectal temperature, calving-related factors, and the incidence of puerperal metritis in postpartum dairy. J Dairy Sci 2007;90:2804–14.
[17] McDougall S. Effect of intrauterine antibiotic treatment on reproductive performance of dairy cows following periparturient disease. N Z Vet J 2001;49:150–8.
[18] Runciman DJ, Anderson GA, Malmo J, Davis GM. Effect of intrauterine treatment with cephapirin on the reproductive performance of seasonally calving dairy cows at risk of endometritis following periparturient disease. Aust Vet J 2008;86:250–8.
[19] LeBlanc SJ, Duffield TF, Leslie KE, Bateman KG, Keefe GP, Walton JS. The effect of treatment of clinical endometritis on reproductive performance in dairy cows. J Dairy Sci 2002;85:2237–49.
[20] Lefebvre RC, Stock AE. Therapeutic efficiency of antibiotics and prostaglandin F2 in postpartum dairy cows with clinical endometritis: an evidence-based evaluation. Vet Clin North Am Food Anim Pract 2012;28:79–96.
[21] Drillich M, Beetz O, Pfützner A, Sabin M, Sabin HJ, Kutzer P, et al. Evaluation of a systemic antibiotic treatment of toxic puerperal metritis in dairy cows. J Dairy Sci 2001;84:2010–7.
[22] Chenault JR, McAllister JF, Chester Jr ST, Dame KJ, Kausche FM, Robb EJ. Efficacy of ceftiofur hydrochloride sterile suspension administered parenterally for the treatment of acute postpartum metritis in dairy cows. J Am Vet Med Assoc 2004;224:1634–9.
[23] Drillich M, Pfützner A, Sabin HJ, Sabin M, Heuwieser W. Comparison of two protocols for the treatment of retained fetal membranes in dairy cattle. Theriogenology 2003;59:951–60.
[24] Drillich M, Reichert U, Mahlstedt M, Heuwieser W. Comparison of two strategies for systemic antibiotic treatment of dairy cows with retained fetal membranes: preventive vs. selective treatment. J Dairy Sci 2006;89:1502–8.
[25] Risco CA, Hernandez J. Comparison of ceftiofur hydrochloride and estradiol cypionate for metritis prevention and reproductive performance in dairy cows affected with retained fetal membranes. Theriogenology 2003;60:47–58.
[26] Giuliodori MJ, Magnasco RP, Becu-Villalobos D, Lacau-Mengido IM, Risco CA, De la Sota RL. Metritis in dairy cows: risk factors and reproductive performance. J Dairy Sci 2013;96:3621–31.
[27] JMP ® 9.0.1 Copyright©. SAS Institute Inc. Software for Windows. Cary, NC, USA 2010.
[28] Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–81.
[29] Cox DR. Regression models and life-tables. J Roy Stat Soc B 1972;34:187–220.
[30] SAS Institute. SAS/STAT Software for Windows 9.2. Cary, NC: SAS Institute Inc; 2008.
[31] Potter TJ, Guitan J, Fishwick J, Gordon PJ, Sheldon IM. Risk factors for clinical endometritis in postpartum dairy cattle. Theriogenology 2010;74:127–34.
[32] Gautam G, Nakao T, Koike K, Long ST, Yusuf M, Ranasinghe RM, et al. Spontaneous recovery or persistence of postpartum endometritis and risk factors for its persistence in Holstein cows. Theriogenology 2010;73:168–79.
[33] Dubuc J, Duffield TF, Leslie KE, Walton JS, LeBlanc SJ. Definitions and diagnosis of postpartum endometritis in dairy cows. J Dairy Sci 2010;93:5225–33.
[34] Markusfeld O. Factors responsible for post parturient metritis in dairy cattle. Vet Rec 1984;114:539–42.
[35] Upham GL. A Practitioner's approach to management of metritis endometritis: early detection and supportive treatment. In: Proceedings, 29th Annual Convention, American Association of Bovine Practitioners, San Diego, CA. Stillwater, OK: Frontier Printers Inc; 1996.
[36] Harman JL, Gröhn YT, Erb HN, Casella G. Event-time analysis of the effect of season of parturition, parity, and concurrent disease on parturition-to-conception interval in dairy cows. Am J Vet Res 1996;57:640–5.
[37] Wittrock JM, Proudfoot KL, Weary DM, Von Keyserlingk MA. Short communication: metritis affects milk production and cull rate of Holstein multiparous and primiparous dairy cows differently. J Dairy sci 2010;94:2408–12.