

Strategies for the treatment of dairy cows at high risk for postpartum metritis and for the treatment of clinical endometritis in Argentina

Julian A. Bartolome · Pablo Khalloub ·
Rodolfo Luzbel de la Sota · Marc Drillich ·
Pedro G. Melendez

Accepted: 5 July 2013

© Springer Science+Business Media Dordrecht 2013

Abstract The objectives of this study were to evaluate the efficacy of (1) administering ceftiofur hydrochloride in dairy cows with calving-related disorders to prevent metritis and (2) a combination of GnRH and PGF_{2α} for the treatment of clinical endometritis, under Argentinean dairy farming conditions. Cows at high risk (HRC) for metritis (dystocia, RFM >12 h postpartum, hypocalcaemia, twins, or stillbirth) were randomly assigned to receive either 1.1 mg/Kg of ceftiofur hydrochloride on three consecutive days (HRC treated group HRCT, *n*=110) or remained untreated (HRC control group HRCC, *n*=126). Cows with low risk (LRC, no calving-related disorders, *n*=868) did not receive any treatment (LRC group, *n*=868). All cows were examined for metritis between days 4 and 10 and for clinical endometritis between 24 and 30 days postpartum. The body condition score (BCS) was recorded at both examinations. Cows with endometritis at days 24 to 30 postpartum received either 1.5 mg of D-cloprostenol (PGF; *n*=129) or 100 μg of GnRH followed by

D-cloprostenol after 7 days (GnRH+PGF, *n*=119). There was no overall effect of treatment on the incidence of metritis or on time to pregnancy. Treatment, however, reduced the incidence of metritis in cows with high BCS (HRCT=24.0 %, HRCC=38.5 %) but had no effect in cows with low BCS (HRCT=38.7 %, HRCC=37.5 %). The proportion of pregnant cows by days in milk was greater (*P*<0.01) in LRC group compared with that of the HRCT and HRCC groups. No significant differences were found between groups PG and PG+GnRH. GnRH+PGF treatment, however, tended (*P*=0.06) to increase pregnancy rate in cows with a moderate loss of BCS (76.5 vs 65.2 %) but tended to reduce pregnancy rate (54.5 vs 76.0 %) in cows with a more pronounced loss in BCS (>0.75 points).

Keywords Calving-related disorder · Uterine infection · Treatment · Fertility · Dairy cows

J. A. Bartolome (✉)

Facultad de Ciencias Veterinarias, Universidad Nacional de La Pampa, Calles 5 y 116 S/N, General Pico 6360, La Pampa, Argentina

e-mail: bartolomejulian@yahoo.com.ar

P. Khalloub

Private Practice Martin Rodriguez 1585, Lincoln 6070, Buenos Aires, Argentina

R. L. de la Sota

Facultad de Ciencias Veterinarias, Universidad Nacional de La Plata, Calles 60 y 118 S/N, 1900 La Plata, Buenos Aires, Argentina

M. Drillich

Clinic for Ruminants, Section for Herd Health Management, Vetmeduni, Veterinärplatz 1, 1210 Vienna, Austria

P. G. Melendez

Facultad de Veterinarias, Universidad de Santo Tomas, Av. Ejército 146, Barrio Universitario, Santiago de Chile, Chile

Introduction

Calving-related disorders followed by metritis and endometritis have a negative impact on fertility and the economic situation of dairy farms worldwide. Related published research, however, mostly describes the efficacy of treatment protocols for dairy farms in western industrialized countries under intensive housing conditions. Thus, study results from North America or Europe cannot be generalized and adopted to other countries with different agricultural structures, climates, housing, and feeding conditions. Argentinean agriculture is represented by pasture-based extensive dairy farming on spacious grasslands, large dairy herds, and specific challenges, e.g., heat stress during summer.

Metritis as a result of postpartum (pp) uterine infection occurs within the first 3 weeks pp, most commonly within 10 days after calving (Lewis, 1997; Sheldon et al. 2006),

resulting in a reduction of fertility, milk production, and increasing costs for treatments and cow losses (Bartlett et al. 1986; Kelton et al. 1998). Metritis can be classified according to the degrees of severity in clinical and puerperal metritis. Clinical metritis (CM) is characterized by enlarged uterus and abnormal discharge. When cows in addition to these findings also show a rectal temperature >39.5 °C, dullness, and reduced milk production, this is defined (Lewis 1997; Sheldon et al. 2006) as puerperal metritis (PM). Other definitions, however, can be found in the literature (Smith et al. 1998; Chenault et al. 2004; Drillich et al. 2007; Sheldon et al. 2009). Cows experiencing calving-related disorders, i.e., dystocia, retained fetal membranes (RFM), acute hypocalcemia, twins, abortion, or stillbirths, are at higher risk of developing metritis (Markusfeld 1984; McDougall 2001; Sheldon and Dobson 2004; Potter et al. 2010). Other risk factors have been described, e.g., reduced feed intake before parturition (Huzzey et al. 2007), loss in body condition (Loeffler et al. 1999), parity (Urton et al. 2005), and season (Benzaquen et al. 2007).

Treatment of metritis is to some extent controversial including the use of local antibiotics, prostaglandins, and non-steroidal anti-inflammatory drugs, but there is general agreement that the systemic application of antibiotics is indicated in cases of metritis accompanied by fever (Smith et al. 1998; Chenault et al. 2004; Drillich et al. 2007). Since cows with calving-related disorders are at higher risk of developing metritis, an approach might be to monitor and/or treat affected cows immediately after calving. Studies on a therapeutic or preventive antibiotic treatment of cows with postpartum disorders found different results. A dosage of 2.2 mg/Kg of body weight of ceftiofur hydrochloride was effective for the prevention of metritis in cows experiencing calving-related disorders (Risco and Hernandez 2003). A lower dosage of ceftiofur hydrochloride (1.1 mg/Kg of body weight) was effective in reducing rectal temperature and clinical signs of illness in cows with elevated rectal temperature during the first 10 days pp (Zhou et al., 2001) but not in preventing cows with RFM from metritis (Drillich et al. 2006). The same dosage of ceftiofur hydrochloride was as effective to reduce fever in cows with RFM (Drillich et al. 2003).

Calving-related disorders result in higher prevalence of clinical endometritis at the end of the postpartum period (Sheldon and Noakes 1998; Sheldon et al. 2009; Potter et al. 2010). Clinical endometritis is characterized by mucopurulent vaginal discharge after 21 days pp (Sheldon and Noakes 1998) and can be categorized into different degrees according to the type of discharge (Williams et al. 2005; Sheldon et al. 2006). The diagnosis of endometritis is usually based on vaginal inspection with the use of a speculum or the Metricheck device (Pleticha et al. 2009) but can be complemented by collection of uterine samples for bacteriology or endometrial cytology (Kasimanickam et al.

2004; Westermann et al. 2010). Numerous treatments such as local or systemic antibiotics and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) have been evaluated (Leblanc et al. 2002; Kaufmann et al. 2010). The beneficial effect of $PGF_{2\alpha}$ is still under discussion (Lefebvre and Stock 2012). While some authors found the use of $PGF_{2\alpha}$ superior to other treatments (Heuwieser et al. 2000), other others did not (Hendricks et al. 2006; Dubuc et al. 2011). The administration of gonadotropin releasing hormone (GnRH) 7 to 10 days before a treatment with $PGF_{2\alpha}$ could help to ensure the presence of a CL (Janowski et al. 2001), which seems to improve the efficiency of $PGF_{2\alpha}$ (Sheldon and Dobson 2004). On the other hand, an increase in progesterone during the postpartum period might have a negative impact on uterine immune defenses and potentially aggravate uterine infections (Lewis 2004).

The objective of this study was to evaluate a strategy for postpartum dairy cows with calving-related disorders to reduce the risk for metritis and endometritis and to increase pregnancy rates. The strategy in cows with calving-related disorders included the treatment with 1.1 mg/Kg of ceftiofur hydrochloride in comparison to that in the untreated controls and for the treatment of clinical endometritis, the combination of GnRH and $PGF_{2\alpha}$ in comparison to $PGF_{2\alpha}$ alone.

Materials and methods

Study population

The study was conducted on a commercial dairy farm with 2,000 lactating Holstein cows on 1,250 ha located in the northeast of the province of Buenos Aires, Argentina. Cows were milked twice daily with an approximate 305-days rolling herd average of 8,050 Kg milk production. Cows were kept in extensive pasture system on grasslands, rotating for fresh pasture lots when grazed. Pasture was based on oat (*Avena sativa*) during winter and alfalfa (*Medicago sativa*) during summer. Feeding was supplemented in dry lots before milking with corn silage (*Zea maiz*), alfalfa hay, and concentrate to meet or exceed the requirements of lactating dairy cows (NRC, 2001). All dry cows were moved to a common calving pen 20 to 30 days before expected parturition. Reproductive management included a breeding season from 1 May 1 to 15 March to avoid calving during summer, a voluntary waiting period of 45 days, and artificial insemination at detected estrus by visual observation. A veterinarian visited the farm routinely every week. This service included diagnosis of pregnancy and the examination of nonpregnant cows by transrectal palpation. Nonpregnant cows with a corpus luteum detected at the ovaries received a luteolytic dose of $PGF_{2\alpha}$ for induction of estrus.

The study has been conducted in accordance with the national animal welfare legislation and according to the standards of good veterinary practice. All persons involved gave their informed consent prior to their inclusion in the study.

Study design

From March to December 2008, parturitions from 1,104 cows were recorded and included in the study. Cows with fetotomy or C-section were not included in the study. After calving, cows were classified into two groups, high risk cows (HRC) group and low risk cows (LRC) group. Cows that experienced calving-related disorders as dystocia, RFM >12 h pp, hypocalcaemia, twins or stillbirth, were regarded as HRC group ($n=236$). Cows in the HRC group were randomly assigned by flipping a coin to receive either 1.1 mg/Kg of ceftiofur hydrochloride on three consecutive days (IM, Microflud Ceft LPU[®], Vetanco, Buenos Aires, Argentina; HRCT group, $n=110$), or remained untreated as controls (HRCC group, $n=126$). The LRC group included cows with normal parturition and with no calving-related disorders ($n=868$). Cows in the LR group did not receive any treatment within the first 4 days after calving, i.e., when the first gynecological examination was done.

First vaginal examination was performed for all cows (LRC, HRCT, HRCC) between 4 and 10 days pp using the Metricheck[®] device (SimcroTech, Hamilton, New Zealand). Diagnosis of CM was based on the presence of brownish or reddish odorous discharge without general symptoms, i.e., depressed attitude, reduced feed intake, and PM if in addition to the discharge rectal temperature was ≥ 39.5 °C and/or general symptoms occurred. Parity and body condition score (BCS, scale 1.0 to 5.0 with 0.25 intermediary steps; Ferguson et al. 1994) were recorded at the time of diagnosis of metritis. Cows with PM were treated systemically with either penicillin or ceftiofur according to the criteria of the local veterinarian.

Between 24 and 30 days pp, all cows were reexamined using the Metricheck. The cervicovaginal mucus was evaluated and classified into endometritis categories according to Williams et al. (2005): Score 0–1, clear to transparent mucus; 2, mucopurulent with 50 % mucus and 50 % pus; 3, white to yellow purulent discharge sometimes bloody. Cows with score 2 and 3 ($n=248$) were regarded as clinical endometritis and randomly assigned by flipping a coin to receive 1.5 mg of D-cloprostenol (2 mL, IM, Vetazina[®], Vetanco; PGF, $n=129$) or 100 µg of gonadoreline diacetate tetrahydrate (2 mL, IM, Ovarelin[®], Vetanco) followed by D-cloprostenol 7 days later (GnRH+PGF, $n=119$). Body condition score was recorded at the time of diagnosis of endometritis, and the difference in BCS to first scoring was calculated.

After 30 days pp, cows were moved randomly to different areas of the farm with separate milking parlors and subjected to the routine reproductive management which included artificial insemination at detected estrus. Pregnancy diagnosis was performed by transrectal palpation of the genital tract at 40 to 46 days post-insemination by the veterinarian. On 31 July 2009, the study was terminated, and the status of each cow (pregnant, open, culled or dead) and the interval from parturition to conception were determined using the farm's records (DC305; Valley Agricultural Software, Tulare, USA). Culled or dead cows were considered pregnant or open according to their last diagnoses before the event.

Statistical analyses

The effect of group (LRC, HRCT, HRCC), parity (primiparous or multiparous), BCS at 4 to 10 days pp (low, ≤ 2.75 ; high, > 2.75), and interactions on the proportion of cows with metritis (CM, PM, or no metritis), as well as the effect of group, parity, BCS score at 24 to 30 days pp, change of BCS (loss or no change; cutoff=0.75 points of lost between both evaluations), and interactions on clinical endometritis (score 0–1, 2, and 3) was evaluated using ordinal logistic regression models. The proportion of pregnant cows was analyzed in another ordinal logistic regression model with group, parity, metritis, clinical endometritis, treatment PGF or GnRH+PGF, and change of BCS as variables. For logistic regression, we used the backward elimination procedure and variables remained in the final model if $P < 0.15$ (Agresti 1996). The proportion of culled and dead cows in each group was compared using chi-squared test. The interval from parturition to first service and parturition to conception (IPC) was evaluated by analysis of variance and IPC also using survival analysis (Cox's proportional hazards model including group, parity, and interaction group \times parity). Level of significance was set at $\alpha = 0.05$.

Results

Overall, 236 cows out of 1,104 calving events (21.4 %) experienced some type of calving-related disorders. The proportion of primiparous cows was 33.3 % for HRCC, 30.9 % for HRCT, and 34.9 % for LRC ($P=0.24$). The proportion of cows with high body condition score was 61.9 % for HRCC, 71.8 % for HRCT, and 72.9 % for LRC ($P=0.05$). The incidence of CM and PM was 4.5 % and 11.2 % for cows in LR group ($n=868$), 9.1 % and 28.2 % in HRCT ($n=110$) and 8.7 % and 38.1 % in HRCC ($n=126$). The final logistic regression model (Table 1) revealed an interaction ($P < 0.01$) between BCS (at 4 to 10 days pp) and group and an effect of parity ($P < 0.01$) on the proportion of cows with CM, PM, or no metritis at 4 to 10 days pp.

Table 1 The effect of the interaction between group and BCS at 4 to 10 days pp adjusted by parity on the proportion of cows with no metritis, clinical, or puerperal metritis determined between 4 and 10 days pp

	Categories of metritis at 4 to 10 days pp			AOR	95 % CI	P value
	No metritis % (n)	CM % (n)	PM % (n)			
BCS at 4–10 days pp group						
<i>P</i> <0.01						
High BCS (> 2.75)						
HRCC (n=78)	53.8 % (42)	7.7 % (6)	38.5 % (30)	2.0	1.5–2.7	
HRCT (n=79)	68.4 % (54)	7.6 % (6)	24.0 % (19)	1.3	0.9–1.9	
LRC (n=633)	87.2 % (552)	4.1 % (26)	8.7 % (55)	0.5	0.4–0.6	
Low BCS (≤2.75)						
HRCC (n=48)	52.1 % (25)	10.4 % (5)	37.5 % (18)	2.0	1.4–2.9	
HRCT (n=31)	48.4 % (15)	12.9 % (4)	38.7 % (12)	2.2	1.5–3.4	
LRC (n=234)	76.5 % (179)	5.6 % (13)	17.9 % (42)	Ref	–	
Parity						
<i>P</i> <0.01						
Multiparous (n=725)	81.4 % (590)	12.7 % (92)	5.9 % (43)	0.6	0.5–0.7	
Primiparous (n=379)	73.4 % (278)	22.2 % (84)	4.5 % (17)	Ref.	–	

CM clinical metritis, PM puerperal metritis, AOR adjusted odds ratio, CI confidence interval, days pp days postpartum, HRCC high risk cows control, HRCT high risk cows treated, LRC low risk cows, Ref referent

The incidence of CM or PM in the three groups was different depending on the body condition score at the time of examination. In addition, the incidence of metritis was greater in primiparous than multiparous cows (Table 1).

Out of the total of 1,104 cows examined at 4 to 10 days pp, 896 were examined for the presence of clinical endometritis between 24 and 30 days pp. Twenty-one cows (16.7 %) in HRCC, 22 cows (20.0 %) in HRCT, and 165 cows (19.0 %) in the LRC group were not examined because they were culled or not presented to the veterinarian. There was a tendency for an effect of the group ($P=0.06$) and an effect of diagnosis at 4 to 10 days pp ($P<0.01$) on the proportion of cows with clinical endometritis between 24 and 30 days pp. Incidence of clinical endometritis tended to be greater in

HRC compared to LRC ($P=0.06$), and there was no difference ($P=0.79$) between HRCC and HRCT groups. Cows experiencing metritis between 4 and 10 days pp had a greater prevalence of clinical endometritis compared to cows with no metritis (Table 2). No significant effect was found for parity, BCS, or change in BCS on the proportion of cows with clinical endometritis.

The logistic regression model for the risk of pregnancy revealed an effect of group ($P<0.01$) and parity ($P<0.001$) and a tendency ($P=0.06$) for interaction between treatment of endometritis and change in BCS on the proportion of pregnant cows. The proportion of pregnant cows was greater in cows with normal parturition (LRC) compared to those cows with calving-related disorders (HRCT, HRCC) and was greater for primiparous than multiparous cows (Table 3). In

Table 2 The effect of group adjusted by categories of metritis diagnosed between 4 to 10 days pp on the proportion of cows with different categories of clinical endometritis diagnosed by Metrichheck between 24 and 30 days pp

	Metricheck score			AOR	95 % CI	P value
	0–1 % (n)	2 % (n)	3 % (n)			
Group						
<i>P</i> =0.06						
HRCC (n=105)	65.7 % (69)	12.4 % (13)	21.9 % (23)	0.7	0.5–1.0	
HRCT (n=88)	55.7 % (49)	22.7 % (20)	21.6 % (19)	0.6	0.4–0.9	
LRC (n=703)	79.1 % (556)	11.8 % (83)	9.1 % (64)	Ref	–	
Metritis						
<i>P</i> <0.01						
No metritis (n=717)	80.7 % (579)	11.8 % (85)	7.4 % (53)	1.6	1.2–2.3	
CM (n=37)	37.8 % (14)	10.8 % (4)	51.4 % (19)	1.5	0.8–2.6	
PM (n=142)	57.0 % (81)	19.0 % (27)	23.9 % (34)	Ref	–	

CM clinical metritis, PM puerperal metritis, AOR adjusted odd ratios, CI confidence interval, Ref referent, HRCC high risk cows control, HRCT high risk cows treated, LRC low risk cows

Table 3 The effect of groups adjusted by parity and the interaction between treatment for endometritis (PGF or GnRH+PGF) and change in body condition score on the proportion of pregnant cows and risk of nonpregnancy

Group	Pregnancy risk		AOR	95 % CI	P value
	%	n			
Group					
HRCC	60.3	76/126	2.7	1.2–6.1	<i>P</i> <0.01
HRCT	60.0	66/110	1.8	0.8–3.9	
LRC	73.9	642/868	Ref.	–	
Parity					
Multiparous	65.8	477/725	3.6	1.8–7.1	<i>P</i> <0.001
Primiparous	81.0	307/379	Ref.	–	
Treatment BCS change					
<i>P</i> =0.06					
Loss in BCS ≤0.75					
PGF	65.2	58/89	0.6	0.2–1.6	
GnRH+PGF	76.5	65/85	0.4	0.1–1.0	
Loss in BCS >0.75					
PGF	76.0	19/25	0.4	0.1–1.3	
GnRH+PGF	54.5	12/22	Ref.	–	

AOR adjusted odd ratios, CI confidence interval, Ref referent, HRCC high risk cows control, HRCT high risk cows treated, LRC low risk cows

cows with a moderate loss of BCS (<0.75 points), there was a tendency (*P*=0.06) towards greater proportion of pregnant cows for GnRH+PGF compared to PGF (76.5 vs 65.2 %), but this tendency was vice versa for cows with greater losses of BCS (54.5 vs 76.0 %; Table 3). No significant effects were found for diagnosis at 4 to 10 days pp, different categories of clinical endometritis, and BCS on the proportion of pregnant cows.

There was no significant difference in the number of dead or culled cows between HRCC and HRCT from the initiation of the study on March 2008 until July 2009. The proportion of dead cows was 6.3 % (8/126) for HRCC, 5.4 % (6/110) for HRCT, and 4.4 % (38/868) for the LRC group (*P*=0.57). The number of culled cows was 18.2 % (23/126) for HRCC, 17.3 % (19/110) for HRCT, and 13.9 % (121/868) for the LRC group (*P*=0.32). The interval from calving to first service was not different between groups (92.6 days for HRCC, 88.4 days for HRCT, and 88.1 days for the LRC group; *P*=0.58). The interval from calving to conception was 212.0 days for HRCC, 238.6 days for HRCT, and 181.6 days for the LRC group. Survival analysis of time to pregnancy (ICP) found cows in LRC group pregnant earlier than cows experiencing calving-related disorders (*P*<0.01) and that there was no difference between HRCC and HRCT (Fig. 1). In contrast to the analysis of proportion of pregnant cows, the Cox's proportional hazards model found no significant effects for group (HR=1.27, CI95=0.77–2.08, *P*=0.35), parity (HR=0.89, CI95=0.38–2.07, *P*=0.79) and interaction group × parity (HR=0.92, CI95=0.68–1.25, *P*=0.60) on the time to pregnancy.

Discussion

This study, conducted under pasture-based extensive housing conditions in Argentina, showed the limited effects of a preventive systemic antibiotic treatment of cows experiencing calving-related disorders to reduce the prevalence of metritis or to increase the proportion of pregnant cows. This study conducted on one commercial dairy farm cannot

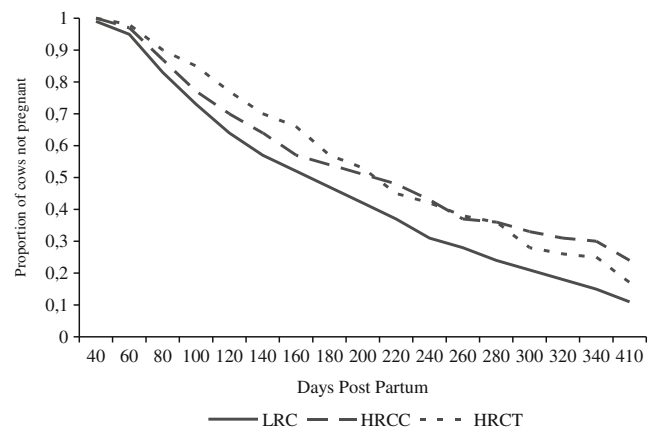


Fig. 1 Survival distribution function for days to pregnancy in cows of different groups (low risk cows LRC=868, high risk cows control HRCC=126, and high risk cows treated HRCT=110; *P*<0.05). Kaplan–Meier curves were developed, and significant effects were checked by log–rank test, Wilcoxon test, and $-2\log$ (LR) test. The three tests were significant. A test for proportionality was conducted, and nonsignificant effects were found between control group and the other two curves (*P*=0.73). So there was not enough evidence to reject proportionality, and it was assumed the proportionality for the model

be regarded as representative but confirms findings of other reports on the preventive use of antibiotics in postpartum dairy cows (Drillich et al. 2006). In general, the preventive use of antibiotics is questionable as this inevitably means that animals that might stay healthy will be treated, which will increase the unnecessary exposure of bacteria to antibiotics, thereby increasing the risk of antibiotic resistance. However, some paper suggest a preventive antibiotic treatment of cows with calving-related disorders (Risco and Hernandez 2003), and for many farmers, other aspects, e.g., improved pregnancy rates, are also essential. Thus, this study was conducted to elucidate if this treatment strategy might be beneficial or should be rejected.

The treatment with ceftiofur hydrochloride overall did not reduce the incidence of clinical or puerperal metritis determined between 4 and 10 days pp. While in this study, we used a dosage of 1.1 mg/Kg of cetiofur for 3 days; Risco and Hernandez (2003) used 2.2 mg/Kg of ceftiofur for 5 days right after parturition in cows with retained placenta and reduced the incidence of metritis in these cows. Chenault et al. (2004) reported a higher efficacy of 2.2 mg/Kg than 1.1 mg/Kg of ceftiofur for the treatment of puerperal metritis. It can be speculated if a higher dosage of ceftiofur or a prolonged treatment would have decreased the occurrence of CM, PM, or endometritis. For practitioners, however, it should be noted that the approved dosage of ceftiofur hydrochloride differs between countries.

The effect of treatment on the incidence of puerperal metritis in cows with calving-related disorders, however, seems to be affected by BCS at the time of examination. The interaction between BCS and treatment, indicating that the ceftiofur treatment could have been efficacious in cows with high BCS, requires further investigation since the number of cows in this condition was limited. The relationship between BCS, feed intake, and the occurrence of metritis has been described in the literature and can be explained by the detrimental effects of a negative energy balance on the immune system (Huzzey et al. 2007). Other studies, however, did not find any effect of BCS or interaction between BCS and treatment on the incidence of metritis (Overton et al. 2003).

The occurrence of endometritis and the proportion of pregnant cows were additional criteria for the evaluation of the different treatment strategies. Treatment with ceftiofur did not significantly affect the occurrence of clinical endometritis and the proportion of pregnant cows, culled or dead at the end of the study. Studies using various treatment regimens for postpartum uterine disorders have not reported differences in cows culled during postpartum (Drillich et al. 2003), in reproductive performance (Risco and Hernandez 2003; Goshen and Shpigel 2006), or milk production (Hendricks et al. 2006; Drillich et al. 2007). As PM cows were treated according to the protocol at the time of diagnosis, however, it remains unclear if cows in this group were

negatively affected by disease or benefited from treatment at 4 to 10 days pp.

The prevalence of clinical endometritis in Argentinean dairy herds has been reported recently by Plöntzke et al. (2011) as 35 % at 18 to 32 days pp and is within the range of our findings. The prevalence of clinical endometritis was greater in cows experiencing calving-related disorders (risk groups) than in cows with normal parturition. The treatment GnRH+PGF tended to increase the proportion of pregnant cows compared with group PGF, only when the loss of BCS was moderate (≤ 0.75 BCS points), but was detrimental in cows with a more severe loss of BCS. Because no findings of ovarian activity have been recorded, it remains unclear if cows with higher or lower BCS have reacted differently to GnRH. However, we need to acknowledge that the number of cows with metritis could have been assigned unbalanced in the groups of cows with clinical endometritis, and similarly, treatment for endometritis could have potentially affected the metaphylactic treatment for metritis. Therefore, since the test for interactions between metaphylactic treatment of metritis and treatment of clinical endometritis and body condition score end up with a limited number of cows in each condition, further studies are necessary to confirm these findings. The main aspect of this study, however, was to compare management strategies, not single cow treatments.

In conclusion, this study did not find a beneficial effect of a preventive treatment with 1.1 mg/Kg of ceftiofur hydrochloride on three consecutive days on the prevalence of uterine infections and reproductive performance. However, the treatment seems to reduce the prevalence of puerperal metritis in cows with high body condition score. In addition, a treatment with GnRH (24 to 30 days pp) followed by prostaglandin 7 days later seems to be beneficial for fertility only in cows with a moderate loss of BCS but detrimental for cows with a more severe loss in BCS (> 0.75 points). Further research is required to confirm these findings.

Acknowledgments The authors thank “Pedro Lacau e Hijos” Dairy Farms for the herd used, their staff for assistance during the study, and Vetanco Argentina SA for the partial funding.

References

- Agresti, A. (Ed.), 1996. An introduction to categorical data analysis. 1st ed., John Wiley & Sons, Inc., New York.
- Bartlett, P.C., Kirk, J.H., Wilke, M.A., Kaneene, J.B., 1986. Metritis complex in Michigan Holstein-Friesian cattle: incidence, descriptive epidemiology and estimated economic impact. *Preventive Veterinary Medicine*, 4, 235–248.
- Benzaquen, M.E., Risco, C.A., Archbald, L.F., Melendez, P., Thatcher, M.J., Thatcher, W.W., 2007. Rectal temperature, calving-related factors, and the incidence of puerperal metritis in postpartum dairy cows. *Journal of Dairy Science*, 90, 2804–2814.

- Chenault, J.R., McAllister, J.F., Chester, S.T., Dame, K.J., Kausche, F.M., Robb, E.J., 2004. Efficacy of ceftiofur hydrochloride sterile suspension administered parenterally for the treatment of acute postpartum metritis in dairy cows. *Journal of the American Veterinary Medical Association*, 224, 1634–1639.
- Drillich, M., Pfützner, A., Sabin, H.-J., Sabin, M., Heuwieser, W., 2003. Comparison of two protocols for the treatment of retained fetal membranes in dairy cattle. *Theriogenology* 59, 951–960.
- Drillich, M., Reichert, U., Mahlstedt, M., Heuwieser, W., 2006. Comparison of two strategies for systemic antibiotic treatment of dairy cows with retained fetal membranes: preventive vs. selective treatment. *Journal of Dairy Science* 89, 1502–1508.
- Drillich, M., Voigt, D., Forderung, D., Heuwieser, W., 2007. Treatment of acute puerperal metritis with flunixin meglumine in addition to antibiotic treatment. *Journal of Dairy Science*, 90, 3758–3763.
- Dubuc, J., Duffield, T.F., Leslie, K.E., Walton, J.S., LeBlanc, S.J., 2011. Randomized clinical trial of antibiotic and prostaglandin treatments for uterine health and reproductive performance in dairy cows. *Journal of Dairy Science*, 94, 1325–1338.
- Ferguson, J.M., Galligan, D.T., Thomsen, N., 1994. Principal descriptors of body condition score in Holstein cows. *Journal of Dairy Science*, 77, 2695–2703.
- Goshen, T., Shpigel, N.H., 2006. Evaluation of intrauterine antibiotic treatment of clinical metritis and retained fetal membranes in dairy cows. *Theriogenology*, 66, 2210–2218.
- Hendricks, K.E.M., Bartolome, J.A., Melendez, P., Risco, C., Archbald, L.F., 2006. Effect of repeated administration of PGF_{2α} in the early post partum period on the prevalence of clinical endometritis and probability of pregnancy at first insemination in lactating dairy cows. *Theriogenology*, 65, 1454–1464.
- Heuwieser, W., Tenhagen, B.A., Tischer, M., Lühr, J., Blum, H., 2000. Effect of three programmes for the treatment of endometritis on the reproductive performance of a dairy herd. *The Veterinary Record*, 146, 338–341.
- Huzzey, J.M., Veira, D.M., Weary, D.M., von Keyserlingk, M.A., 2007. Prepartum behavior and dry matter intake identify dairy cows at risk for metritis. *Journal of Dairy Science*, 90, 3220–3233.
- Janowski, T., Zduńczyk, S., Mwaanga, E.S., 2001. Combined GnRH and PGF_{2α} application in cows with endometritis puerperalis treated with antibiotics. *Reproduction in Domestic Animals*, 36, 244–246.
- Kasimanickam, R., Duffield, T.F., Foster, R.A., Gartley, C.J., Leslie, K.E., Walton, J.S., Johnson, W.H., 2004. Endometrial cytology and ultrasonography for the detection of subclinical endometritis in postpartum dairy cows. *Theriogenology*, 62, 9–23.
- Kaufmann, T.B., Westermann, S., Drillich, M., Plöntzke, J., Heuwieser, W., 2010. Systemic antibiotic treatment of clinical endometritis in dairy cows with ceftiofur or two doses of cloprostenol in a 14-d interval. *Animal Reproduction Science*, 121, 55–62.
- Kelton, D.F.K., Lissemore, D., Martin, R.E., 1998. Recommendations for recording and calculating the incidence of selected clinical diseases of dairy cattle. *Journal of Dairy Science*, 81, 2502–2509.
- LeBlanc, S.J., Duffield, T.F., Leslie, K.E., Bateman, K.G., Keefe, G.P., Walton, J.S., Johnson, W.H., 2002. The effect of treatment of clinical endometritis on reproductive performance in dairy cows. *Journal of Dairy Science*, 85, 2237–2249.
- Lefebvre, R.C., Stock, A.E., 2012. Therapeutic efficiency of antibiotics and prostaglandin F_{2α} in postpartum dairy cows with clinical endometritis: an evidence-based evaluation. *Veterinary Clinician of North American Food Animal Practitioners*, 28, 79–96.
- Lewis, G.S., 1997. Uterine health and disorders. *Journal of Dairy Science*, 80, 984–994.
- Lewis, G.S., 2004. Steroidal regulation of uterine immune defenses. *Animal Reproduction Science*, 82/83, 281–294.
- Loeffler, S.H., de Vries, M.J., Schukken, Y.H., 1999. The effects of time of disease occurrence, milk yield, and body condition on fertility of dairy cows. *Journal of Dairy Science*, 82, 2589–2604.
- McDougall, S., 2001. Effect of intrauterine antibiotic treatment on reproductive performance of dairy cows following periparturient disease. *New Zealand Veterinary Journal*, 49, 150–158.
- Markusfeld, O., 1984. Factors responsible for post parturient metritis in dairy cattle. *The Veterinary Record* 114, 539–542.
- NRC., 2001. *Nutrient Requirements of Dairy Cattle*, 7th revised edition, National Academy of Sciences, Washington, DC.
- Overton, M.W., Sischo, W.M., Reynolds, J.P., 2003. Evaluation of effect of estradiol cypionate administered prophylactically to postparturient dairy cows at high risk for metritis. *Journal of the American Veterinary Medical Association*, 223, 846–851.
- Pleticha, S., Drillich, M., Heuwieser, W., 2009. Evaluation of the Metricheck device and the gloved hand for the diagnosis of clinical endometritis in dairy cows. *Journal of Dairy Science*, 92, 5429–5435.
- Plöntzke, J., Madoz, L.V., De la Sota, R.L., Heuwieser, W., Drillich, M., 2011. Prevalence of clinical endometritis and its impact on reproductive performance in grazing dairy cattle in Argentina. *Reproduction of Domestic Animals*, 46, 520–526.
- Potter, T.J., Guitian, J., Fishwick, J., Gordon, P.J., Sheldon, I.M., 2010. Risk factors for clinical endometritis in postpartum dairy cattle. *Theriogenology*, 74, 127–134.
- Risco, C.A., Hernandez, J., 2003. Comparison of ceftiofur hydrochloride and estradiol cypionate for metritis prevention and reproductive performance in dairy cows affected with retained fetal membranes. *Theriogenology*, 60, 47–58.
- Sheldon, I.M., Noakes, D.E., 1998. Comparison of three treatments for bovine endometritis. *The Veterinary Record*, 142, 575–579.
- Sheldon, I.M., Dobson, H., 2004. Postpartum uterine health in cattle. *Animal Reproduction Science*, 82/83, 295–306.
- Sheldon, I.M., Lewis, G.S., LeBlanc, S., Gilbert, R.G., 2006. Defining postpartum uterine disease in cattle. *Theriogenology* 65, 1516–1530.
- Sheldon, I.M., Cronin, J., Goetze, L., Donofrio, G., Schubert, H.-J., 2009. Defining postpartum uterine disease and the mechanisms of infection and immunity in the female reproductive tract in cattle. *Biology of Reproduction*, 81, 1025–1032.
- Smith, B.I., Donovan, G.A., Risco, C., Little, R., Young, C., Stanker, L.H., Elliott, J., 1998. Comparison of various antibiotic treatments for cows diagnosed with toxic puerperal metritis. *Journal of Dairy Science*, 81, 1555–1562.
- Urton, G., von Keyserlingk, M.A., Weary, D.M., 2005. Feeding behavior identifies dairy cows at risk for metritis. *Journal of Dairy Science*, 88, 2843–2849.
- Westermann, S., Drillich, M., Kaufmann, T.B., Madoz, L.V., Heuwieser, W., 2010. A clinical approach to determine false positive findings of clinical endometritis by vaginoscopy by the use of uterine bacteriology and cytology in dairy cows. *Theriogenology*, 74, 1248–1255.
- Williams, E.J., Fischer, D.P., England, G.C.W., Dobson, H., Pfeiffer, D.U., Sheldon, I.M., 2005. Clinical evaluation of postpartum vaginal mucus reflects uterine bacterial infection and the inflammatory response to endometritis in cattle. *Theriogenology*, 63, 102–117.
- Zhou, C., Boucher, J.F., Dame, K.J., Moreira, M., Graham, R., Nantel, J., Zuidhof, S., Arfi, L., Flores, R., Neubauer, G., Olson, J., 2001. Multilocation trial of ceftiofur for treatment of postpartum cows with fever. *Journal of the American Veterinary Medical Association*, 219, 805–808.