Systematic clinical examination of early postpartum cows and treatment of puerperal metritis did not have any beneficial effect on subsequent reproductive performance

R. Dolezel, M. Vecera, T. Palenik, S. Cech, M. Vyskocil

University of Veterinary and Pharmaceutical Sciences, Brno, Czech Republic

ABSTRACT: The objective of this field trial was to evaluate the impact of a control program based on systematic clinical examination on Day 10 ± 3 *post partum* (*pp*) and treatment in the case of puerperal metritis on reproductive performance in dairy cows. Cows having serious dystocia as well as cows treated for retained placenta were not involved in the trial. The evaluation was performed by comparing reproductive performance between systematically examined cows (Group E, *n* = 83) and cows that were examined and treated occasionally on the basis of farmers' notifications of a pathological condition (Group C, *n* = 95). In Group E, reproductive performance was compared between cows with a mild form of metritis (Group E1, *n* = 18), cows with a severe form of metritis (Group E2, *n* = 14) and cows without puerperal metritis (Group E0, *n* = 51). Clinical examination consisted in rectal and vaginal palpation with inspection of the lochia manually withdrawn from the vagina. Cows with puerperal metritis were treated with an intramuscular administration of $PGF_{2\alpha}$ analogue – dinoprost. An intrauterine antibiotic (rifaximin foam) was added in cases of severe metritis. The examination and treatment (in cases of a pathological condition, *n* = 10) were repeated in Group E on Day 24 ± 3 *pp*. In addition, the incidence of puerperal metritis in the year seasons was evaluated. Occurrence of ovarian disorders (30.1 vs. 24.2%) and clinical endometritis (27.7 vs. 23.2%), calving to first service interval (83.2 vs. 85.4 days), pregnancy until Day 100 *pp* (30.8 vs. 35.3%) as well as until Day 150 *pp* (64.6 vs. 64.7%), services per conception (2.45 vs. 2.16), calving to conception interval (141.6 vs. 136.4 days), total culling rate (20.5 vs. 28.4%) and culling rate due to (sub)infertility (8.4 vs. 6.3) in Group E compared to Group C were not different. Only the first service pregnancy rate was lower in Group E (30.3 vs. 47.1%, $P < 0.05$). Even though no significant differences were found in the reproduction parameters between groups E1, E2 and E0, the worst parameters were in Group E2. The incidence of puerperal metritis in the year seasons was not different. The trial did not prove that there was a beneficial effect of systematic clinical examination on Day 10 ± 3 *pp* nor of treatment in cases of puerperal metritis, using $PGF_{2\alpha}$ and intrauterine antibiotic, on reproductive performance in dairy cows.

Keywords: cow; puerperium; metritis; diagnosis; therapy; reproduction parameters; season

Puerperal metritis and endometritis represent important causes of (sub)infertility in cows. The negative effect of these diseases on reproductive performance in dairy herds has been sufficiently evidenced (Nakao et al., 1992; Huszenicza et al., 1999; LeBlanc et al., 2002a; Kim and Kang, 2003; Maizon et al., 2004; Gilbert et al., 2005). The incidence of diseases is generally high (20–40%) and it can range between 10% and 80% depending on various internal or external factors as well as diag-

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nostic methods (Sagartz and Hardenbrook, 1971; Markusfeld, 1987; Stevenson and Call, 1988; Peeler et al., 1994; Gilbert et al., 2005; Foldi et al, 2006; Sheldon et al., 2006). The absence of external symptoms of these diseases and a low level of individual monitoring of cows in large herds cause many affected cows to remain undiagnosed. Thus, the low efficiency of routine inspection of postpartum cows and varying results of treatment make it harder to solve this problem. For this reason various management systems of uterine health were tested. But the effects of different diagnostic and therapeutic procedures on reproductive performance have not been unified. Data showed a positive effect (Montes and Pugh, 1993; Smith et al., 1998; Zhou et al., 2001) or no effect or in some cases negative effects (Paisley et al., 1986; Gilbert, 1992; Whitacre, 1992; Olson, 1996; Drillich et al., 2002).

The objective of our field trial was to evaluate the impact of a control system based on systematic clinical examination on Day 10 ± 3 *pp* and treatment in the case of puerperal metritis using prostaglandin $F_{2\alpha}$ and intrauterine antibiotic on reproductive performance in dairy cows. In addition, the occurrence of puerperal metritis in various year seasons was evaluated.

MATERIAL AND METHODS

Experimental animals, examination and treatment

The trial was performed on a dairy farm (600 Holstein cows, average milk yield 8 300 l) with high incidence of puerperal metritis as well as clinical endometritis and unsatisfactory reproductive performance. Cows calving in January, April, August and October 2005 were included in the trial with the exception of cows with serious dystocia as well as cows treated for retained placenta (n = 178). A clinical examination (vaginal palpation with manual withdrawal of the lochia and rectal palpation of the uterus) was performed within 10 ± 3 days *pp* at fortnight intervals. Thus, the cows underwent systematic clinical examination every second week (Group E, n = 83). These cows were split into subgroups according to clinical findings. The quality of lochia was considered as the most important parameter for diagnosis. The markedly purulent (Group E1, n = 18) or fetid (Group E2, n = 14) character of lochia was considered to be a symptom of puerperal metritis. Cows showing the normal lochia were included in Group E0 (n = 51). Cows in groups E1 and E2 were treated with a single administration of $PGF_{2\alpha}$ analogue – dinoprost (Dinolytic inj. ad us. vet., Pfizer, 25 mg *pro toto, i.m.*). In addition, the intrauterine administration of an antibiotic – rifaximin (Fatroximin endofoam ad us. vet., Fatro, 100 mg *pro toto*, *i.u.*) was performed on Day 3 or 4 after the initial treatment (administration of dinoprost) in Group E2. Clinical examination by rectal palpation and vaginal palpation with manual withdrawal of an exudate from the vagina were repeated in cows in groups E1 and E2 on Day 14 after the first clinical examination (Day 24 ± 3 *pp*). Ten cows showing symptoms of clinical endometritis at the second examination (retarded involution of the uterus and purulent or mucopurulent secretion in the vagina – content of pus > 50%) were treated again using the administration of dinoprost and intrauterine antimicrobial treatment with rifaximin (see above) or cephapirin (Metricure susp. ad us. vet., Intervet, 500 mg *pro toto*, *i.u.*). Cows without systematic clinical examination (Group C, n = 95) were examined occasionally on the basis of farmers' notifications of pathological discharge and were treated, in cases of puerperal metritis or clinical endometritis, similarly like Group E.

Evaluation and statistical analysis

The occurrence of ovarian disorders such as acyclicity (absence of the *corpus luteum* after Day 45 *pp*) and ovarian cysts (follicular structure > 25 mm in diameter and absence of the *corpus luteum* after Day 45 *pp*) as well as clinical endometritis (purulent or mucoporulent discharge after Day 40 *pp*), calving to first service interval, first service pregnancy rate, pregnancy rate by Day 100 *pp* and Day 150 *pp*, number of services per conception, calving to conception interval, total culling rate and culling rate in consequence of (sub)infertility were compared between Group E and Group C (during the evaluated period and various seasons) as well as between groups E1, E2 and E0. Absolute values were compared using Wilcoxon's test, while relative values were compared by Chi-square (χ^2) test. In addition, the occurrence of puerperal metritis in systematically examined cows (Group E) in winter (January), spring (April), summer (August) and autumn (October) was compared using χ^2-test.

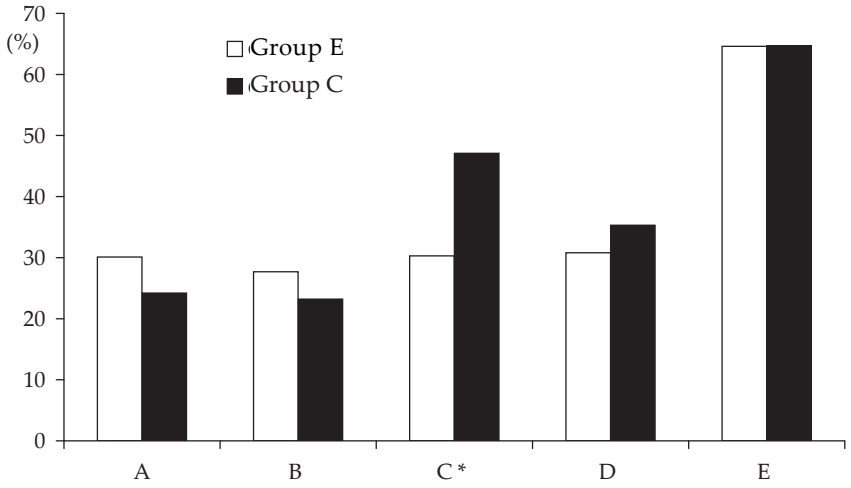

Figure 1. Incidence of ovarian disorders (A) and chronic endometritis (B), first service pregnancy rate (C*), pregnancy rate by Day 100 (D) and 150 (E) *pp* in cows with (Group E, $n = 83$) and without (Group C, $n = 95$) systematic postpartum examination

*$P < 0.05$

RESULTS

The reproduction parameters in cows in Group E compared to Group C were similar. The occurrence of ovarian disorders and clinical endometritis, first service pregnancy rate and pregnancy by Day 100 *pp* and Day 150 *pp* are shown in Figure 1. Only the first service pregnancy rate was lower in Group E (30.3 vs. 47.1%, $P < 0.05$). No differences were found in calving to first service interval, services per conception, calving to conception interval, total culling rate or in culling rate because of (sub)infertility between groups E and C (83.2 ± 41.87 vs. 85.4 ± 44.48 days, 2.45 vs. 2.16, 141.6 ± 70.77 vs. 136.4 ± 67.09 days, 20.5 vs. 28.4% and 8.4 vs. 6.3%, respectively). Likewise, similar values of the parameters were found in Group E compared to Group C in various year seasons. Only the total culling rate was higher ($P < 0.01$) in Group C during summer.

Even though no significant differences were found in the parameters between groups E1, E2 and E0, clearly higher values of the occurrence of ovarian disorders as well as clinical endometritis and calving to first service interval were observed in cows in Groups E1 and E2 compared to Group E0 (38.9 and 35.7 vs. 25.5%; 27.8 and 50.0 vs. 21.6%; 88.5 ± 51.77 and 90.3 ± 37.68 vs. 79.4 ± 39.99 days, respectively). In addition, the lowest value of the first service pregnancy rate and the highest values of the number of services per conception, calving to conception interval, and total culling rate were found in Group E2 compared with groups E0 and E1 (20.0 vs. 26.8 and 46.7%; 3.3 vs. 2.4 and 1.9; 169.8 ± 92.59 vs. 139.0 ± 70.12 and 131.5 ± 56.13 days; 28.6 vs. 19.6 and 16.7%). The occurrence of ovarian disorders and clinical endometritis, first service pregnancy rate and pregnancy until Day 100 *pp*, and until Day 150 *pp* in groups E0, E1 and E2 are shown in Figure 2.

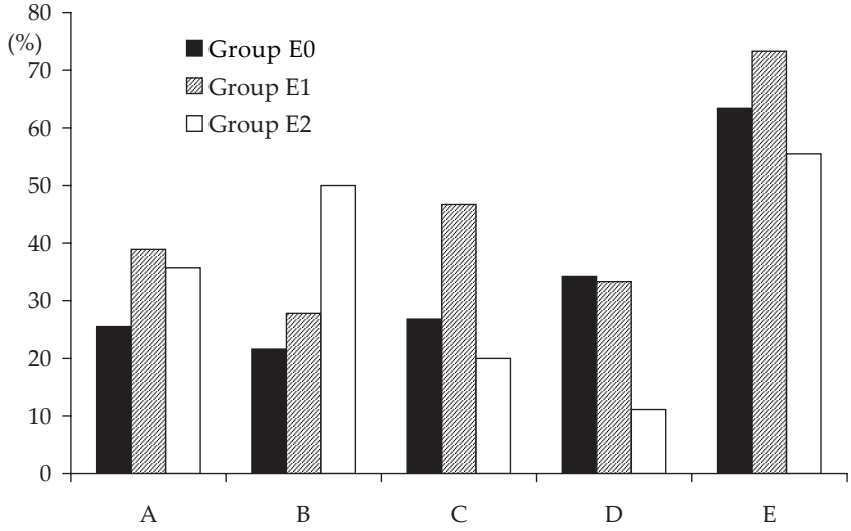

Figure 2. Incidence of ovarian disorders (A) and chronic endometritis (B), first service pregnancy rate (C), pregnancy by Day 100 (D) and 150 (E) *pp* in groups of cows without metritis (Group E0, $n = 51$), with purulent (Group E1, $n = 18$) or fetid (Group E2, $n = 14$) metritis

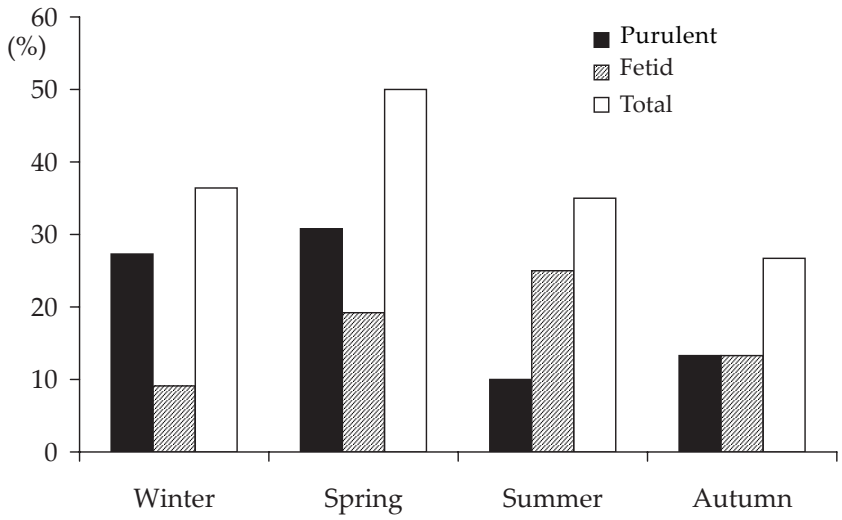

Figure 3. Incidence of puerperal metritis in systematically examined cows (n = 83) in the year seasons

The total incidence of puerperal metritis in systematically examined cows (Group E) was 38.6% throughout the four months of evaluation. The comparison of puerperal metritis occurrence in the particular year seasons did not show any statistical differences. Nevertheless, the highest occurrence of puerperal metritis was found in spring (Figure 3).

DISCUSSION

Puerperal metritis and endometritis have presented an important problem in bovine reproduction for many years. Although various preventive and control programs have been applied, the incidence of this disease has not changed in the last 30 years (Sheldon and Dobson, 2004). Diagnosis and treatment of uterine diseases are key components of fertility control programs. In our field trial we tested the importance of a systematic clinical examination on Day 10 ± 3 *pp* and of a treatment in cases of puerperal metritis using prostaglandin $F_{2\alpha}$ and intrauterine antibiotic for subsequent reproductive performance on a large-scale dairy farm. We hypothesised that this monitoring system would improve reproductive performance in comparison with cows that were examined and treated only occasionally on the basis of farmers' notifications of a pathological condition. But the results of this study did not support our hypothesis. Similar results were reported by Drillich et al. (2002), who did not find any significant differences in reproductive performance in cows systematically examined by rectal palpation between Day 20 and Day 26 *pp* for signs of endometritis (vaginal discharge, enlarged uterus) in comparison with cows examined only by external inspection for vaginal discharge. In their study the cows with endometritis were treated twice with $PGF_{2\alpha}$ in 14-day intervals. An ineffective monitoring system and/or method of treatment can explain these results rather than a missing relation between puerperal metritis and endometritis with reproductive performance in the herds.

The adverse effect of puerperal metritis, clinical endometritis as well as subclinical endometritis on reproductive performance has been described sufficiently (Nakao et al., 1992; Huszenicza et al., 1999; Kim and Kang, 2003; Gilbert, 2004; Sheldon and Dobson, 2004). For example, Maizon et al. (2004) described more days open *post partum* in cows with puerperal metritis as well as a longer interval from first breeding to conception. Garcia et al. (2003) found a significantly negative effect of puerperal metritis on the intervals partum-first insemination, partum-conception and on the number of artificial inseminations per gestation, which increased by 18.24 days, 46.16 days and 0.54, respectively. Gilbert et al. (2005) found days open 206 and 118, pregnancy until Day 300 *pp* 63% and 89% and first service pregnancy rate 11% and 36% in cows with and without endometritis, respectively. A higher risk factor for a low pregnancy rate to the first artificial insemination (OR = 1.46) was determined by Quintela et al. (2004). The connection of subclinical endometritis with a reduced relative pregnancy rate was proved by Kasimanickam et al. (2004). Even though no significant differences were found in reproduction parameters between cows with and without puerperal metritis in our trial, the evidently worse reproductive performance was found in

affected cows. Thus, the missing relation of these diseases with reproductive performance does not explain the failure of our hypothesis.

Although many methods of diagnosis of uterine inflammation have been described, very few of them are applicable in practice for puerperal metritis. Transrectal palpation is not an accurate method for the diagnosis of puerperal metritis because it does not enable to make a clear distinction between the normal and the affected uterus during 14 days *post partum*. Therefore, vaginal inspection or palpation and evaluation of lochia samples taken manually are the methods which are most often applied in diagnosing puerperal metritis. A purulent or fetid character of the lochia indicates the disease (Drillich et al., 2005; Williams et al., 2005; Drillich, 2006). Non-specific symptoms such as anorexia, drop in milk yield, dehydration and pyrexia can help to diagnose puerperal metritis. However, these symptoms are not sufficiently accurate because these are present only in some cases (Sheldon et al., 2006). Sheldon et al. (2004) stated that pyrexia is not consistently associated with puerperal metritis. Therefore, the monitoring of rectal temperature is less reliable than the examination for abnormal uterine discharge. The signs of systemic disease were found only sporadically and body temperature was not systematically measured in our trial. Cows with severe puerperal metritis caused by dystocia and/or retained placenta show the signs of systemic disease the most frequently. But these cows were not involved in our trial. Bacteriological examination does not increase the accuracy of diagnosis because findings are usually similar in pathological as well as physiological conditions during early puerperium (Zilaitis et al., 2004). Perhaps the quantity and spectrum of microbes could be helpful for diagnosis (Farin et al., 1989; Dohmen et al., 1995, 2000; Mateus et al., 2002; Williams et al., 2005). The evaluation of some parameters in peripheral blood, such as the number and activity of polymorphonuclear leucocytes (Zerbe et al., 2001), the occurrence of specific proteins such as haptoglobin or α_1 acid-glycoproteid (Skinner et al., 1991; Hirvonen et al., 1999), concentration of 13,14-dihydro,15-keto-$PGF_{2\alpha}$ (Youngquist and Bierschwal, 1985; Archbald et al., 1998; Mateus et al., 2003) or the level of interleukin-6 (Ishikawa et al., 2004) could be used for the diagnosis of puerperal metritis but the methods are neither specific nor practical. For this reason we considered vaginal examination and evaluation of the lochia on Day 10 ± 3 *pp* to be a sufficiently accurate diagnostic method for puerperal metritis in this field trial.

Several more methods are useful in diagnosing clinical endometritis. The progress of the uterus involution can be evaluated more accurately by transrectal palpation. The cervical diameter > 7.5 cm after Day 21 *pp* is considered to be a symptom of involution delay (LeBlanc et al., 2002a; LeBlanc, 2003). Nevertheless, transrectal palpation is not a sufficiently accurate diagnostic method because the uterine involution varies among cows due to the existing relation with various factors, except puerperal metritis or clinical endometritis. Moreover, the evaluation of uterine involution based on transrectal palpation is subjective (Sheldon et al., 2006). The evaluation of uterus size as well as uterine content in the framework of diagnosis of clinical endometritis can be improved by transrectal ultrasonography (Okano and Tomizuka, 1987; Kim-YongJun et al., 2006). Nevertheless, the examination of vaginal content for the presence of pus also represents an accurate and practical method for the diagnosis of clinical endometritis (Bretzlaff, 1987; Sheldon and Noakes, 1998; LeBlanc et al., 2002a). The second vaginal palpation aimed at the manual withdrawal of exudates was used for the diagnosis of clinical endometritis on Day 24 ± 3 *pp* in our trial.

Subclinical endometritis could not be diagnosed in our trial. It would be necessary to use either endometrial cytology (Kasimanickam et al., 2004; Zilaitis et al., 2004; Gilbert et al., 2005) or histological examination (Sagartz and Hardenbrook, 1971; Erices and Eulenberger, 1986; Rahman et al., 2002). But the latter method is invasive, expensive and time consuming. Furthermore, biopsy may be associated with delayed conception (Bonnet et al., 1993). Subclinical endometritis could influence our results because the high incidence and the negative effects of this disease on reproductive performance in cows have been described (Archbald et al., 1998; Gilbert, 2004; Kasimanickam et al., 2004, 2005).

Traditional methods of the therapy of puerperal metritis and clinical endometritis were used in our trial. The efficiency of $PGF_{2\alpha}$ in the therapy of these diseases and the beneficial effect on reproductive performance have been described and a single or repeated administration of prostaglandin either alone or in combination with another treatment for therapy or prevention of puerperal metritis or endometritis has been recommended for more than 25 years (Gustafsson, 1980; Stefan et al., 1984; Youngquist and Bierschwal, 1985; Benmrad and

Stevenson, 1986; Paisley et al., 1986; Pepper and Dobson, 1987; Wenzel et al., 1993; Sheldon and Noakes, 1998; Melendez et al., 2004). On the other hand, no effect of $PGF_{2\alpha}$ administration has been described either (Thomson et al., 1987; Drillich et al., 2005; Mejia and Lacau-Mengido, 2005; Hendricks et al., 2006). Knutti et al. (2000) found a positive effect of the intrauterine infusion of $PGF_{2\alpha}$ in cases of serious endometritis but a negative effect in cases of mild endometritis. In our trial $PGF_{2\alpha}$ was administered to cows with puerperal metritis on Day 10 ± 3 *pp* and the treatment was repeated in 10 cows that showed symptoms of clinical endometritis 14 days later.

The local antimicrobial treatment of puerperal metritis or endometritis usually includes an intrauterine administration of oxytetracycline, tetracycline, ampicillin with cloxacillin, gentamycin or cephapirin (Gustafsson, 1984; Olson et al., 1984a, 1986; Bretzlaff, 1987; Cairoli et al., 1993; Montes and Pugh, 1993; Smith et al., 1998; Ahlers et al., 2000; Konigsson et al., 2002; Zain, 2003). Although microbes in the postpartum bovine uterus are usually sensitive to penicillin, this antibiotic is not useful for local treatment during early puerperium because the microbes produce the enzyme penicillinase, which inhibits the effect of penicillin in the uterus (Olson et al., 1984b). In our trial we used rifaximin for the traditional local antimicrobial treatment of the uterus. This antibiotic was licensed and is applied very frequently in the Czech Republic in the intrauterine treatment of puerperal metritis as well as endometritis. The effectiveness of this antibiotic was described by Parmigiany and Truszkowska (1988), Marusi et al. (1991), Twardon et al. (2002) and Bar and Ezra (2005). But recently, doubtful spread and low efficacy of antibiotics in the uterus, detrimental effect on the endometrium and inhibition of local immunity have been considered disadvantages of the local treatment of puerperal metritis in comparison with systemic antimicrobial treatment.

At present systemic treatment using ceftiofur is preferable for the treatment of puerperal metritis (Drillich et al., 2001, 2003; Zhou et al., 2001; Risco and Hernandez, 2003; Chenault et al., 2004). Nevertheless, comparable cure rates and reproductive performances were found in cows with puerperal metritis treated with ceftiofur compared to affected cows treated by the intrauterine administration of ampicillin or ampicillin with oxacillin (Beetz, 2002). Accordingly, Smith et al. (1998) described a similar therapeutic effect of the intramuscular administration of procaine penicillin or ceftiofur sodium and of the intrauterine infusion of oxytetracycline in cows with puerperal metritis. Likewise, various methods of the antibiotic treatment of puerperal metritis (systemic, intrauterine or both) did not affect the frequency of subsequent development of endometritis (Butler et al., 2002). In addition, there were no significant differences in calving to first postpartum oestrus interval, calving to conception interval as well as services per conception after the endoarterial or intrauterine administration of novocaine or oxytetracycline in cows with puerperal metritis (Garcia et al., 2002). Ceftiofur was administered intramuscularly only to a few cows with severe puerperal metritis after placenta retention but no evaluation of these cases was performed. In the framework of evaluation of milk production as an indicator of health condition in postpartum cows affected by puerperal metritis, no differences were found between the methods of treatment (tetracycline vs. rifaximin, local antibiotics vs. local antibiotics with $PGF_{2\alpha}$, intervals between treatment 3–4 days vs. one week) in 6–12 days *pp* (Bar and Ezra, 2005). The treatment in their study was performed in an interval similar to our trial.

Generally, local antimicrobial treatment is preferred in cases of endometritis after Day 20 *pp*. Different effects of this treatment on reproductive performance in cows were also described. For example, Thurmond et al. (1993) did not find any beneficial effects of single intrauterine infusion with procaine penicillin or oxytetracycline. Recently, cephapirin has been recommended for the treatment of endometritis. A satisfactory therapeutic effect of cephapirin was described by Laven (2003), Ahmadi et al. (2005) and Kasimanickam et al. (2005). For this reason we used cephapirin in re-examined cows with symptoms of endometritis on Day 24 ± 3 *pp*.

Probably the date and frequency of the examination as well as treatment can influence the efficiency of control systems. The treatment of endometritis with $PGF_{2\alpha}$ or by intrauterine administration of cephapirin between Day 20 and Day 26 *pp* had no effect or in some cases negative (after $PGF_{2\alpha}$ in the absence of *corpus luteum*) effect on subsequent reproductive performance. But beneficial effects were found after cephapirin locally administered between Day 27 and Day 33 *pp* (LeBlanc et al., 2002b; LeBlanc, 2003). On the other hand,

Falkenberg and Heuwiser (2005) found that the administration of $PGF_{2\alpha}$ in a 14-day interval in cases of severe endometritis in the 4th and 6th week *post partum* was more effective than the same treatment two weeks later. Feldmann et al. (2005) described a higher efficacy of earlier local antimicrobial treatment (before Day 42 *pp*) as well as later (after Day 42 *pp*) $PGF_{2\alpha}$ treatment in cows with endometritis. Shams-Esfandabadi et al. (2004) performed the post-insemination intrauterine treatment of endometritis using oxytetracycline or penicillin. However, the treatment had no beneficial effect on the first service conception rate. We performed the initial examination and treatment on Day 10 ± 3 *pp* because we expected sufficiently visible clinical symptoms (pathological character of the lochia) of puerperal metritis at that time. Re-examination and re-treatment (in the cases of endometritis) were performed on Day 24 ± 3 *pp*. Some above-mentioned authors consider this time to be too early for efficient diagnosis and treatment of endometritis.

Even though no significant differences were found in the occurrence of puerperal metritis between the year seasons, the highest occurrence (50%) was found in the spring of our trial. Also, Markusfeld (1984) found a higher rate of uterine infection and a higher incidence of metritis in cows during winter and spring. But LeBlanc et al. (2002b) did not find any differences in the prevalence of endometritis in relation to the season.

The data show that various factors such as method, date and frequency of diagnosis as well as the treatment itself can influence the efficiency of fertility control programs. Eliminating from the study cows with the most severe puerperal metritis caused by dystocia and/or retained placenta could weaken the effect of systematic examination and treatment on subsequent reproductive performance in our trial because these cows usually have the strongest negative influence on reproductive performance. On the other hand, the inclusion of these cows in the study could also reduce differences between experimental (Group E) and control (Group C) cows because these cows usually show marked external symptoms of pathological conditions and the benefit of systematic examination during early puerperium is lower.

The results of our trial showed that the systematic clinical examination on Day 10 ± 3 *pp* and treatment in the case of puerperal metritis using $PGF_{2\alpha}$ and intrauterine antibiotic did not improve reproductive performance in dairy cows. Therefore, this control system of uterine diseases in cows is not sufficiently effective.

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Corresponding Author:

Prof. Assoc. MVDr. Radovan Dolezel, CSc., University of Veterinary and Pharmaceutical Sciences, Palackeho 1–3, 612 42 Brno, Czech Republic

Tel. +420 541 562 316, fax +420 541 562 332, e-mail: dolezelr@vfu.cz