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Post-calving administration of uterine stimulants does not improve reproductive performance in dairy cows

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ABSTRACT: The aim of this study was to evaluate the effects of administration of oxytocin, in combination with dinoprost or ergometrin, after parturition on the occurrence of clinical endometritis and subsequent reproductive performance in dairy cows. The cows, without retained foetal membranes, were assigned to one of three groups. No treatment was performed in the control group (Group C, *n* = 229). However, intramuscular administrations of oxytocin (30 IU) on Days 1 and 2 *post partum*, in combination with dinoprost (25 mg, Group D, *n* = 123) or ergometrin (15 mg, Group E, *n* = 130) administered on Day 7 *post partum*, were performed in experimental groups. Vaginal discharge score (VDS, 1–5), uterine content score (UCS, 1–3) on Day14 to 21 *post partum*, number of treatment interventions (TI), proportion of non-treated cows (NT) because of endometritis, calving to first insemination interval (CI), first insemination conception rate (CR), and proportion of pregnant cows by Day 150 *post partum* (PC), were compared among groups. There was no significant difference among groups for any parameter. Average values were 2.08, 2.24 and 2.06 (VDS); 1.49, 1.51 and 1.45 (UCS); 0.86, 0.93 and 0.74 (TI); 59.4, 54.2 and 54.7% (NT); 73.9 ± 15.2, 75.4 ± 17 and 74.2 ± 17 days (CI); 41.4, 38.9 and 44.3% (CR); and 75.4, 77.7 and 80.5% (PC) for Groups C, D and E, respectively. There was no significant benefit of preventive administration of oxytocin, in combination with dinoprost or ergometrin, after parturition on reproductive performance in dairy cows.

Keywords: cow; endometritis; oxytocin; dinoprost; ergometrin; reproductive parameters

Abbreviations

CI = calving to the first insemination interval, **CR** = first insemination conception rate, **NT** = non-treated cows, **PC** = proportion of pregnant cows by day 150 *post partum*, **TI** = treatment interventions, **TMR** = total mixed ration, **UCS** = uterine content score, **VDS** = vaginal discharge score

Uterine disorders, classified as clinical metritis, clinical and subclinical endometritis and pyometra, are an important cause of impaired fertility in dairy cows (Sheldon et al. 2008). They cause prolonged calving to first insemination interval, lower conception rate, lower proportion of pregnant cows and higher culling rates (Borsberry and Dobson 1989; Fourichon et al. 2000; Tsousis et al. 2010). The incidence of uterine disorders varies between 10% and 80%, depending on various internal or external factors, as well as the diagnostic methods used (Sheldon et al. 2006). Early treatment of clinical metritis is recommended, because untreated clinical metritis may continue as clinical or subclinical endometritis (Williams 2013). However, many affected cows remain undiagnosed, due to the absence of clinical symptoms and an insufficient level of individual inspection of postpartum cows (Dolezel et al. 2008). Therefore, preventive systematic treatments of uterine diseases without individual investigation of cows, including uterine stimulants or antibiotics (Mollo et al. 1997; Palomares et al. 2010; Dubuc et al. 2011; Kaya et al. 2012; McLaughlin et al. 2013), have been described, although results have been conflicting. Nevertheless, direct uterotonic effects of oxytocin or dinoprost on the myometrium have been reported (Gajewski et al. 1999; Bajcsy et al. 2006) with

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possible implications for reproductive programs in dairy herds. The effect of ergometrin on the myometrium was inconsistent (Gajewski et al. 1999); however, this drug was traditionally used in the Czech Republic and many articles concerning its effects have been published. Because of contradictory results in studies with one-time use of uterotonics in postpartum cattle, the objective of this study was to evaluate the effects of repeated administration of oxytocin, in combination with a single administration of ergometrin or dinoprost, on the occurrence of clinical endometritis and subsequent reproductive performance in dairy cows. The hypothesis was that preventive, repeated uterotonic treatment during early puerperium promotes uterine involution and lowers the incidence of uterine diseases without antibiotic treatment.

MATERIAL AND METHODS

Cattle and treatment. Cattle used in the study were kept at a commercial dairy farm (700 cows) under usual farm conditions. Average milk yield was 9000 kg per year, cows were fed a total mixed ration (TMR) containing corn silage, alfalfa haylage, cut straw and concentrates. Four types of TMR were fed, according to the lactation phase. Cows that calved from June 2013 to March 2014 were included in the study. Cows without retained foetal membranes (n = 482) were randomly allocated into three groups. Intramuscular administrations of oxytocin (Oxytocin inj., Bioveta, 30 IU *pro toto*) on Days 1 and 2 *post partum*, in combination with dinoprost (Dinolytic inj., Pfizer, 25 mg *pro toto*) on Day 7 *post partum* were performed in Group D (n = 123). Intramuscular administrations of oxytocin (Oxytocin inj., Bioveta, 30 IU *pro toto*) on Days 1 and 2, in combination with ergometrin (Ergometrin, Bioveta, 15 mg *pro toto*) on Day 7 *post partum* were performed in Group E (n = 130). No treatment was performed in the control group (Group C, n = 229).

Examination and evaluation. Vaginal contents were obtained using a Metricheck device on Day 14 to 21 *post partum*. A previously described vaginal discharge score (VDS) (McDougall et al. 2007) was used for evaluation of the content. The VDS scores were defined as follows: 0 (no material retrieved), 1 (clear mucus), 2 (a few flecks of pus), 3 (mucopurulent discharge with < 50% pus), 4 (purulent discharge with >50% pus) or 5 (purulent discharge with > 50% pus and foul-smelling). Uterine content score (UCS) was evaluated at the same time by rectal palpation. Score 1 was assigned when the uterus was empty without fluctuation. Score 2 was assigned when fluctuation was present but the maximum diameter of the uterine horns did not exceed the width of three fingers. Score 3 was assigned when the diameter of the horns was larger than 3 fingers and fluctuation was present, or the uterus was located deep in the abdominal cavity and palpation of the entire uterus was impossible. The average VDS and UCS were calculated.

The number of interventions necessary for clinical endometritis treatment (TI) in Groups C, D and E was evaluated. The algorithm described below has been used for treatment of clinical endometritis: UCS 1 and VDS ≤ 2: without treatment, UCS 1 and VDS ≥ 3: intrauterine treatment (0.1 g of rifaximin, Fatroximin endofoam, Fatro, Italy), followed by re-checking two weeks later. UCS ≥ 2: treatment with dinoprost or ergometrin (intramuscular), irrespective of VDS, with subsequent re-check one week later. At the time of re-check, the same algorithm was used. In the case of unsuccessful rifaximin treatment (VDS ≥ 3), intrauterine infusion of 0.5 g of cephapirin (Metricure, MSD Animal Health, the Netherlands) was performed. If the cephapirine treatment was unsuccessful (VDS ≥ 3) at the time of the next re-check (two weeks later), an iodine infusion (Jodofoam, Duna-coop, Hungary) was performed. Experimental cows were given one point for each intervention, irrespective of type (intramuscular or intrauterine) of the treatment. Also, the proportion of non-treated cows because of endometritis (NT) was evaluated.

In addition, calving to first insemination interval (CI), first insemination conception rate (CR) and the proportion of cows pregnant by Day 150 *post partum* (PC), were evaluated. Data necessary for evaluation of reproductive performance were retrieved from farm records (Alpro Windows PC program).

Moreover, the proportions of cows with VDS 1, VDS 1+2, UCS 1 and UCS 3 at the time of the first examination as well as proportions of cows with less or equal to one treatment and more than or equal to four treatments because of endometritis were calculated.

Cows developing concurrent pathological conditions (mastitis, lameness, digestive problems) were not excluded from the study.

This experiment was approved by the Institutional Animal Care Committee (No. 3, 2013).

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Statistical analysis. Vaginal discharge score, uterine content score, number of treatment interventions and calving to first insemination interval were reported as mean plus standard deviation. The statistical evaluation of the differences among groups was performed using Student's *t*-test and the Kruskal-Wallis non-parametric test. The proportion of non-treated cows, first insemination conception rate and proportion of pregnant cows by Day 150 *post partum* were evaluated using the Chi^2 test. Statistical analyses were carried out using Excel software.

RESULTS

Average values of the main evaluated parameters are shown in Table 1. No significant differences among the groups were found for any of the parameters.

The additional parameters were observed as follows: The proportions of cows with vaginal discharge score 1 were 48, 39.8 and 42.3% and proportions of cows with a VDS 1+2 were 65.5, 63.4 and 67.7% in Groups C, D and E, respectively. Furthermore, in these groups, proportions of cows with UCS 1 were 62.9, 61.5 and 67.7%, while proportions of cows with UCS 3 were 12.3, 10.1 and 10.0% in Groups C, D and E, respectively. Proportions of cows without treatment because of endometritis or with less or equal to one treatment were 53.9, 52.5 and 53.1% or 72.4, 71.3 and 82.8%, and proportions of cows with four treatments were 3.5, 5.7 and 2.3% in Groups C, D and E, respectively. None of the differences in proportions among groups were significant.

DISCUSSION

Uterotonic effects of oxytocin and carbetocin were described during measurement of the intrauterine pressure using an intracervically introduced open tip catheter system (Bajcsy et al. 2006); therefore, similar beneficial clinical effects of those drugs on uterine involution were expected. In addition, the direct uterotonic effect of dinoprost, expressed by increased electrical activity in the myometrium, was demonstrated (Gajewski et al. 1999), even if it was not fully in agreement with another study in which different methods of evaluation of uterine motility were used (Hirsbrunner et al. 1998). In contrast, the effects of ergometrin on uterine contractility were inconsistent, when recorded using electrodes surgically implanted into the myometrium before parturition (Gajewski et al. 1999). Either an increase or no change in the total duration of electrical activity was reported. The same was observed during ultrasound investigation (Gajewski et al. 1999).

Oxytocin has been used for preventive treatment against retained foetal membranes (RFM), however, with contradictory results. No positive effects were reported (Hickey et al. 1984; Palomares et al. 2010) in a herd of Zebu cattle that had optimal reproductive health, with a very low incidence of RFM (Palomares et al. 2010). On the contrary, in a herd with a high incidence of RFM (over 20%), there was a positive effect of oxytocin treatment (Mollo et al. 1997). Early postpartum dairy cows treated with carbetocin had a lower occurrence of RFM (Kudlac and Zamecnik 1984). However, Barrett et al. (2009) concluded that routine administration of a single injection of either oxytocin or carbetocin after calving had no significant benefit.

Table 1. Vaginal discharge score (VDS 1–5), uterine content score (UCS 1–3) on Day 14 to 21 *post partum*, number of treatment interventions (TI), proportion of non-treated cows (NT), calving to first insemination interval (CI), first insemination conception rate (CR) and proportion of pregnant cows until Day 150 *post partum* (PC) in control cows (Group C) and cows treated with oxytocin 30 IU *i.m.* on Day 1 and Day 2 + dinoprost 25 mg *i.m.* on Day 7 (Group D) or ergometrin 15 mg *i.m.* on Day 7 (Group E)

Parameters	Group C	Group D	Group E
VDS ($\bar{x}$ ± SD)	2.08 ± 1.23	2.24 ± 1.27	2.06 ± 1.11
UCS ($\bar{x}$ ± SD)	1.49 ± 0.7	1.51 ± 0.71	1.45 ± 0.71
TI ($\bar{x}$ ± SD)	0.86 ± 1.11	0.93 ± 1.2	0.74 ± 1.0
NT (%)	59.4	54.2	54.7
CI (days, $\bar{x}$± SD)	73.9 ± 15.2	75.4 ± 17	74.2 ± 17
CR (%)	41.4	38.9	44.3
PC (%)	75.4	77.7	80.5

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Young and Anderson (1986) and McClary et al. (1989) reported the positive effects of $PGF_{2\alpha}$ on selected reproductive parameters in cattle. The authors concluded that it was mediated through a direct effect on the uterus. Improvement of the uterine environment by stimulation of uterine tone and removal of postpartum uterine debris was described by McClary et al. (1989). Nevertheless, in a recent large study, $PGF_{2\alpha}$ did not improve reproductive performance (Dubuc et al. 2011). Furthermore, a critical meta-analysis did not reveal an improvement of reproductive performance in cows with endometritis after treatment with $PGF_{2\alpha}$ (Haimerl et al. 2013). However, in those studies, $PGF_{2\alpha}$ was given later after parturition.

As a result of non-uniform or, up to now, controversial results, the objective of this study was to evaluate the effect of repeated administration of oxytocin on Days 1 and 2 *post partum*, followed by a single administration of ergometrin or dinoprost on Day 7 *post partum*, on the occurrence of clinical endometritis and subsequent reproductive performance in dairy cows. The early uterotonic effect of oxytocin should be followed by subsequent treatment with dinoprost or ergometrin on Day 7 after parturition, when the cervix is usually open and discharge of the remaining uterine content is possible. Similar combined preventive treatment with oxytocin and $PGF_{2\alpha}$ was determined to be beneficial, especially after dystocia. However, ceftiofur was also included in the treatment protocol (Kaya et al. 2012).

Our hypothesis was that preventive, repeated uterotonic treatment during early puerperium hastens uterine involution and thereby lowers the incidence of uterine diseases without antibiotic treatment.

In our study, the diagnosis of uterine disease was based on clinical examination, including evaluation of vaginal discharge using a Metricheck device and evaluation of uterine content by rectal palpation. Vaginal discharge score is sufficient for evaluation of the severity of uterine infections (Williams et al. 2005). Rectal examination was not described in recent studies for evaluation of treatment outcomes; however, it is the traditional and standard method for evaluation of the uterus in clinical practice.

Also, the system of endometritis treatment used in our study could be open to discussion, because many studies have been published in this field (Kaufmann et al. 2010; Dubuc et al. 2011; Haimerl et al. 2013; McDougall et al. 2013). Nevertheless, this system was used for all cows in the same way and therefore it should not have influenced the final evaluation in this study.

The evaluated variables should reflect all aspects of expected effects of uterotonic treatment. Clinical findings between Day 14 to 21 and the number of interventions necessary for clinical endometritis treatment should have detected direct effects of preventive treatment on uterine health. In addition, reproductive parameters should measure the subsequent effects of preventive uterine treatment.

However, in the present study, there were no significant differences between treated and non-treated cows. It is difficult to explain this outcome, because this study consisted only of clinical observation, without direct measurement of the uterine response to the treatment. Also, examination of metabolic status (subclinical ketosis, acid base balance disturbances) of cows was not performed, so possible local factors causing low myometrium activity on this farm were not identified. Regardless, the length of the study and the large number of animals involved should have diminished the effects of possible metabolic disorders. Furthermore, observed Groups (D, E, C) were analysed concurrently during the whole period of observation. Nevertheless, even an effect on the uterine content score, expected as early as one week after the last treatment, was not observed. Doses of oxytocin (30 IU) and ergometrin (15 mg) were within the usual recommended range; however, administration of higher doses (50 IU oxytocin and 20 mg of ergometrin) could have had stronger effects on uterine contractility. A further study using higher doses of uterine stimulants, perhaps on several farms to overcome possible local farm effects, might be informative in this regard.

We conclude that repeated treatment of postpartum cows using uterine stimulants, with the aim of prevention of endometritis and improvement of reproductive performance in dairy cows, was not effective. Therefore, it remains necessary to find more effective methods for this purpose.

REFERENCES

Bajcsy AC, Szenci O, van der Weijden GC, Doornenbal A, Maassen F, Bartyik J, Taverne MAM (2006): The effect of a single oxytocin or carbetocin treatment on uterine contractility in early postpartum dairy cows. Theriogenology 65, 400–414.

doi: 10.17221/8492-VETMED

Barrett AJ, Murray RD, Christley RM, Dobson H, Smith RF (2009): Effects of the administration of oxytocin or carbetocin to dairy cows at parturition on their subsequent fertility. Veterinary Record 165, 623–626.

Borsberry S, Dobson H (1989): Periparturient diseases and their effect on reproductive performance in five dairy herds. Veterinary Record 124, 217–219.

Dolezel R, Vecera M, Palenik T, Cech S, Vyskocil M (2008): Systematic clinical examination of early postpartum cows and treatment of puerperal metritis did not have any beneficial effect on subsequent reproductive performance. Veterinarni Medicina 53, 59–69.

Dubuc J, Duffield TF, Leslie KE, Walton JS, LeBlanc SJ (2011): Randomized clinical trial of antibiotic treatments for uterine health and reproductive performance in dairy cows. Journal of Dairy Science 94, 1325–1338.

Fourichon C, Seegers H, Malher X (2000): Effect of disease on reproduction of the dairy cow: a meta-analysis. Theriogenology 53, 1729–1759.

Gajewski Z, Thun R, Faundez R, Boryczko Z (1999): Uterine motility in the cow during puerperium. Reproduction in Domestic Animals 34, 185–191.

Haimerl P, Heuwieser W, Arlt S (2013): Therapy of bovine endometritis with prostaglandin $F_{2\alpha}$: A meta-analysis. Journal of Dairy Science 96, 2973–2987.

Hickey GJ, White ME, Wickenden RP, Armstrong DA (1984): Effects of oxytocin on placental retention following dystocia. Veterinary Record 25, 189–190.

Hirsbrunner G, Kűpfer U, Burkhardt H, Steiner A (1998): Effect of different prostaglandins on intrauterine pressure and uterine motility during diestrus in experimental cows. Theriogenology 50, 445–455.

Kaufmann TB, Westermann S, Drillich M, Plontzke J, Heuwieser (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.

Kaya D, Ay SS, Kucukaslan I, Beceriklisoy HB, Agaoglu AR, Findik M, Ozyurtlu N, Aslan S (2012): The effectiveness of combined preventive treatment with ceftiofur, oxytocin and $PGF_{2\alpha}$ on fertility parameters in cows. Revue de Medecine Veterinaire 163, 302–308.

Kudlac E, Zamecnik B (1984): Effects of carbetocin (Depotocin inj. Spofa) on prevention of retained placenta in postpartum cows (in Czech). Biologizace a chemizace zivocisne vyroby – veterinaria 20, 131–140.

McClary DG, Putnam MR, Wright JC, Sartin Jr JL (1989): Effect of early postpartum treatment with prostaglandin $F_{2\alpha}$ on subsequent fertility in the dairy cow. Theriogenology 31, 565–570.

McDougall S, Macaulay R, Compton C (2007): Association between endometritis diagnosis using a novel intravaginal device and reproductive performance in dairy cattle. Animal Reproduction Science 98, 9–23.

McDougall S, de Boer M, Compton C, LeBlanc S (2013): Clinical trial of treatment programs for purulent vaginal discharge in lactating dairy cattle in New Zealand. Theriogenology 79, 1139–1145.

McLaughlin CL, Stanisiewski EP, Risco CA, Santos JE, Dahl GE, Chebel RC, LaGrow C, Daugherty C, Bryson L, Weigel D, Hallberg J, Lucas MJ (2013): Evaluation of ceftiofur crystalline free acid sterile suspension for control of metritis in high-risk lactating dairy cows. Theriogenology 97, 725–734.

Mollo A, Veronesi MC, Cairoli F, Soldano F (1997): The use of oxytocin for the reduction of cow placental retention and subsequent endometritis. Animal Reproduction Science 48, 47–51.

Palomares RA, Gutierrez JC, Portillo G, Boscan JC, Montero M, Lopez Y, Maxwell HS, Carson RL, Soto E (2010): Oxytocin treatment immediately after calving does not reduce the incidence of retained fetal membranes or improve reproductive performance in crossbred Zebu cows. Theriogenology 74, 1414–1419.

Sheldon IM, Lewis GS, LeBlanc S, Gilbert RO (2006): Defining post-partum uterine disease in cattle. Theriogenology 65, 1516–1530.

Sheldon IM, Williams EJ, Miller ANA, Nash DM, Herath S (2008): Uterine diseases in cattle after parturition. Veterinary Journal 176, 115–121.

Tsousis G, Sharifi AR, Hoedemaker M (2010): Increased risk of conception failure in German Holstein Friesian cows with chronic endometritis. Reproduction in Domestic Animals 45, 1114–1117.

Williams EJ (2013): Drivers of post-partum uterine disease in dairy cattle. Reproduction in Domestic Animals 48, 53–58.

Williams EJ, Fischer DP, Pfeiffer DU, England GCW, Noakes DE, Dobson H, Sheldon IM (2005): Clinical evaluation of postpartum vaginal mucus reflects uterine bacterial infection and the immune response in cattle. Theriogenology 63, 102–117.

Young IM, Anderson DB (1986): Improved reproductive performance of dairy cows treated with dinoprost tromethamine soon after calving. Theriogenology 26, 199–208.

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