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Effectiveness of intrauterine treatment with cephapirin in dairy cows with purulent vaginal discharge

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ABSTRACT

The objective of this study was to assess the efficacy of cephapirin intrauterine treatment preceding a timed artificial insemination protocol in lactating dairy cows with purulent vaginal discharges (PVDs). Holstein dairy cows (n = 1247) from 18 herds were enrolled in a controlled randomized clinical trial. At 34 days in milk (DIM; ±7 days), cows had a genital examination (transrectal palpation, vaginoscopy, and uterine bacteriology). They were randomly assigned to either the control group (CONT, no treatment) or the treatment group (CEPH) consisting of 1 intrauterine infusion of 500-mg cephapirin benzathine (RCL) (Metricure, Merck Animal Health, Montreal, Canada) regardless of the uterine health status. All cows were systematically enrolled in a presynch-ovsynch protocol for the first insemination. A second genital examination was made 2 weeks later. Cows that received any systemic or local antibiotics 10 days prior sampling to the end of the synchronization protocol were excluded from the study. Reproductive data of cows were collected for at least 300 DIM, entered in a databank, and validated (health record management software, DSAHR). Pregnancy diagnosis was done by transrectal palpation at the routinely scheduled veterinarian visits. On the basis of the highest sum of sensibility and specificity for pregnancy status at 120 DIM, the optimal cutoff for vaginal discharge score was determined as the presence of cloudy discharge with or without purulent material (PVD+, score 2). With a prevalence of 21.6% at 34 DIM, PVD+ was detrimental to the first-service conception rate (FSCR; PVD+: 26 ± 5%; PVD−: 40 ± 3%; P = 0.02). The negative effect of PVD+ was indicated by a hazard ratio of 0.72 (chi-square = 8.58; P < 0.01; 95% confidence interval = 0.56–0.91). Treatment with cephapirin was associated with a significant improvement of the FSCR in PVD+ cows (PVD+ CEPH: 36 ± 5%, PVD+ CONT: 23 ± 5%; P < 0.05), although it did not produce a considerable clinical cure based on the second examination. Thus, a longer period of time following treatment may be needed to properly assess the efficacy of intrauterine treatment in PVD+ cows. In conclusion, cephapirin intrauterine treatment in PVD+ cows at 34 DIM considerably improves reproductive performance compared with untreated PVD+ cows.

1. Introduction

Reproductive performance in dairy cows [1] and farm economic efficiency [2–4] are related to uterine health status at the end of the voluntary waiting period. Uterine diseases affect about half of all dairy cows in the postpartum (PP) period [5,6] causing infertility by disrupting uterine and ovarian functions [7]. In the last decade, uterine diseases have generally been defined based on their clinical presentation and effect on fertility [1]. The prevalence of clinical endometritis in PP cows is about 20% [8]. Clinical endometritis is defined as an inflammation of the endometrium in a normal-sized uterus, associated with purulent vaginal discharge (PVD) after 21 days in milk (DIM), or mucopurulent discharge after 26 DIM in the absence of any

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systemic clinical disease. On the basis of the risk factors and the low correlation between PVD and endometrial inflammation as measured by endometrial cytology, some researchers have proposed that PVD replaces the term clinical endometritis [9]. In general, PVD is associated with a *Trueperella pyogenes* infection in the uterus [7]. Although testing for vaginal discharge is an indirect method of diagnosing inflammation and infection of the uterus, the presence of purulent discharge in the anterior vagina or vaginal opening of the cervix has been consistently associated with reduced fertility in dairy cows [10–13]. However, although the effect of PVD on fertility is well known, there is still considerable controversy about how to best treat the underlying endometrial condition [14].

Historically, two major therapeutic approaches have been used to treat endometritis—antibiotics (intrauterine or systemic) and prostaglandins ($PGF_{2\alpha}$, systemic). Treatment efficacy appears to vary depending on the type of antibiotic used, the calving-treatment interval, the severity of endometrial inflammation, and ovarian status [14]. Antibiotics are assumed to reduce bacterial loads in the uterus and, indirectly, diminish inflammation in the endometrium [15]. Antibiotics are the main treatment prescribed to treat clinical endometritis in dairy cows [14], with the intrauterine route being the most widely recommended treatment protocol [16–18]. The systemic approach has not been well studied. A study of the intramuscular administration of oxytetracycline has shown that this antibiotic reaches the endometrial tissue as required [19]. The use of subcutaneous ceftiofur crystalline free acid on endometritis cows at 26 DIM did not improve the reproductive performance [20].

Prostaglandins ($PGF_{2\alpha}$) are also used to treat endometritis [21]. They cause luteolysis of the corpus luteum and induce estrus, thereby increasing uterine contractility and subsequent clearance of the uterine cavity. During estrus, the local immune response prepares the uterine environment so that it can eventually support embryo development [22] and the establishment of pregnancy. Although many reports on this type of treatment for PVD can be found in the literature, its efficacy is still a matter of some debate [21]. Kauffmann et al. [23] reported that ceftiofur was as effective as prostaglandins at treating clinical endometritis. However, the effects of $PGF_{2\alpha}$ and antibiotics are often confounded [14]. In general, the lack of negative controls, the small number of animals per treatment, the use of multilevel experimental designs, the use of different case definitions, lack of precision in categorization of the vaginal discharge and the use of outcome parameters based on clinical cure instead of reproductive performance, and particularly the first-service conception rate (FSCR), all make it difficult to assess the best evidence-based therapeutic approach.

The objectives of the present study were to compare the clinical cure rate and the FSCR for PVD+ cows treated with an intrauterine infusion of 500-mg cephapirin benzathine with nontreated cows, both groups being submitted to a presynch-ovsynch systematic protocol. It was hypothesized that PP dairy cows with PVD treated with intrauterine cephapirin would demonstrate a clinical cure and show improved reproductive performance.

2. Materials and methods

All procedures conformed to national guidelines for the care and use of laboratory animals and were approved by the Institutional Animal Care Committee of the University of Montreal.

2.1. Herds, facilities, and feeding management

A total of 18 different commercial dairy herds located in Quebec (Canada) were recruited based on convenience. Herd size was from 40 to 250 lactating cows. The reproductive and health data were entered in a databank with health record management software (DSAHR Inc., St-Hyacinthe, Quebec, Canada). The rolling herd average for milk production was 9900 kg. Cows from free stall barns (n = 2) were milked three times daily and cows from tied stall barns (n = 16) were milked twice daily. Cows were fed a total mixed ration formulated mainly with corn and hay silage to meet the dietary requirements for a lactating dairy cow (NRC, 2011). From these selected herds, 1247 Holstein cows were enrolled in a controlled randomized clinical trial.

2.2. Treatment description and group allocation

All cows were systematically enrolled in a synchronization protocol (presynch-ovsynch using dinoprost tromethamine and gonadorelin injection; LUTALYSE and FACTREL; Zoetis Animal Health) during their first genital examination (EXAM1) at 34 (±7) DIM (Fig. 1). Cows that received the first injection of the protocol before 27 DIM or after 41 DIM were excluded from the study. The cows were re-examined 2 weeks later (EXAM2) at 48 (±7) DIM. Reproductive data for the cows were collected for at least 300 DIM. Herd records were compiled in a DSAHR databank.

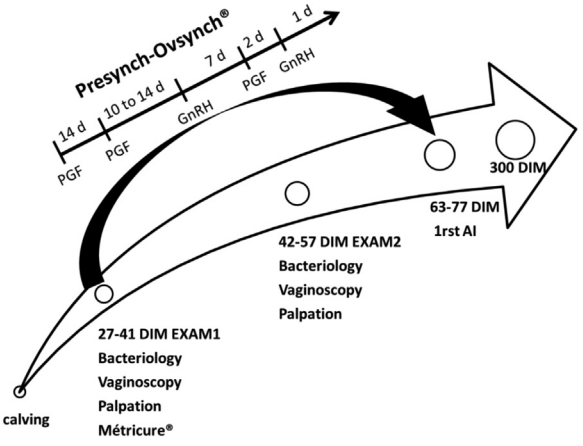

Fig. 1. Synchronization protocol. Timeline for treatment of PVD cows, monitoring of cure, and evaluation of uterine health. At EXAM1, cows were randomly assigned to receive either cephapirin or no treatment. PVD+ cows were defined based on the highest sum of sensitivity and specificity on pregnancy status at 120 DIM. DIM, days in milk; EXAM1, first genital examination; EXAM2, second genital examination; PGF, prostaglandin; PVD, purulent vaginal discharge.