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## Clinical trial of treatment programs for purulent vaginal discharge in lactating dairy cattle in New Zealand

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#### ABSTRACT

Studies of treatment of postpartum endometritis in dairy cows indicate that prostaglandin  $(PGF_{2\alpha})$  might result in similar outcomes as intrauterine antibiotics, but the effect might depend on the presence of a CL. The objective was to compare reproductive performance in cows with purulent vaginal discharge treated on the basis of having or not having a CL (CL-dependent treatment; CLdep), versus treatment of all affected cows with an intrauterine antibiotic alone. Cows (N = 756) from 36 seasonal calving dairy herds in New Zealand were enrolled on the basis of having a vaginal discharge score (VDS) ≥2 (mucus with flecks of pus or more purulent) after examination with the Metricheck device (Simcro, Hamilton, New Zealand) and  $\geq$ 14 days after calving. The presence of a CL was assessed by transrectal palpation. Cows were randomly assigned within farm to be treated with an intrauterine antibiotic (0.5 g cephapirin) irrespective of CL status, or treated with  $PGF_{2\alpha}$  if a CL was present and cephapirin if a CL was not present (CLdep). The VDS was reassessed 14 days later. Cows were bred using standard practices and pregnancy was tested to define the date of conception. The proportion of cows clinically cured (i.e., with a VDS <1 at reexamination) did not differ between treatment groups (0.82  $\pm$  0.03 vs. 0.80  $\pm$ 0.03) for the group of cows treated with an intrauterine antibiotic irrespective of CL status and the CLdep groups, respectively (P=0.66). The proportions of cows submitted for AI by 21 days into the breeding program, pregnant to first breeding, pregnant by 42 days into the breeding program, and at the end of the breeding program, and the interval from the start of the mating program to pregnancy did not differ among treatment groups. Cows that had positive VDS (i.e., >1) at Day 14 after treatment had lower proportions of conception and pregnancy than those with lower (<2) VDS. A treatment protocol in which cows with purulent vaginal discharge with a palpable CL were treated with PGF<sub>2 $\alpha$ </sub> and those without a CL with intrauterine cephapirin resulted in reproductive performance that was not inferior to treating all cows with an intrauterine antibiotic.

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#### 1. Introduction

Purulent vaginal discharge (PVD), also referred to as clinical endometritis, that is, reproductive tract inflammation usually associated with intrauterine bacterial infection, is common, with 10% to 20% of dairy cows affected in

a variety of production systems [1,2]. Cows with PVD, diagnosed using an intravaginal sampling device (Metricheck; Simcro, Hamilton, New Zealand [2]) have poorer reproductive outcomes than those without [1].

Treatment of endometritis has historically involved intrauterine infusion of antibiotics [3,4] or injection with  $PGF_{2\alpha}$  [5,6]. Efficacy of treatment is dependent on time postpartum at treatment, severity of inflammation in the uterus, and presence of a CL [6].

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In current New Zealand management systems, cows diagnosed with PVD (based on a positive Metricheck score) are generally treated with intrauterine cephapirin without further assessment of presence or absence of a CL. The efficacy of PGF<sub>2α</sub> treatment of cows diagnosed with endometritis and having a CL has apparently not been assessed in New Zealand management systems (pasture-based production; seasonal breeding). An earlier study in cows with PVD suggested that in CL-positive cows more than 26 days postpartum, there was no difference in reproductive outcomes between cows treated either with  $PGF_{2\alpha}$  or with intrauterine cephapirin [5]. Were  $PGF_{2\alpha}$  treatment outcomes equivalent to intrauterine cephapirin treatment, the cost-benefit might be positive for  $PGF_{2\alpha}$  treatment because, in current conditions in New Zealand, the combined cost of diagnosis (i.e., ovarian palpation or ultrasonography) and  $PGF_{2\alpha}$  treatment would typically be less than for cephapirin treatment. Transrectal palpation to identify the presence of a CL is imperfect [7,8], but generally has a high specificity and is a "useful tool" [9] that is widely used in veterinary practice.

The objective was to compare the clinical and reproductive outcomes for treatment of PVD with  $PGF_{2\alpha}$  for cows with a palpable CL and intrauterine cephapirin for those without a CL versus blanket treatment of all cows with intrauterine cephapirin irrespective of CL status. Our hypothesis was that there would be no difference in clinical or pregnancy outcomes between the two approaches to treatment.

#### 2. Materials and methods

This was a positive-controlled, prospective randomized intervention study of treatment of PVD. Approval to conduct this trial was obtained from the Animal Ethics Committee of AgResearch, Ruakura, New Zealand.

The vaginal contents of dairy cows (N = approximately15,000) from spring-calving dairy herds (N = 36) in the Waikato region of New Zealand were screened using a validated device (Metricheck; Simcro) and a 0 to 5 scoring system [2]. The vaginal discharge score (VDS) was defined as 0 (no material retrieved), 1 (clear mucus), 2 (a few flecks of purulent material), 3 (mucopurulent with <50% of material as pus), 4 (purulent with >50% of material as pus), or 5 (purulent with >50% of material as pus and malodorous). All cows in a herd were examined on the same day, approximately 4 weeks before the planned start of mating. Cows that were >14 days after calving and in which purulent material was present in the vagina (i.e., with a VDS >2) were enrolled in the study. Cows that had been treated with systemic or intrauterine antibiotics, corticosteroids, or nonsteroidal anti-inflammatory drugs in the 14 days preceding examination were not enrolled. The ovaries of all enrolled cows were palpated transrectally by a veterinarian and the presence or absence of a CL was determined. Cows were randomly assigned in sequentially presented pairs of cows to be treated either by intrauterine infusion of 0.5 g of cephapirin (Bomacure; Bomac Laboratories Ltd., Manukau City, New Zealand) irrespective of the CL status, or into a group in which cows with a CL were treated once im with 500 µg of cloprostenol (Ovuprost; Bomac Laboratories Ltd.), and cows without a palpable CL were treated by intrauterine infusion of 0.5 g of cephapirin (Bomacure; Bomac Laboratories Ltd.). The body condition score (BCS) was assessed on a 1 to 10 scale [10] at the time of enrollment. The VDS was reassessed by the same method  $14\pm3$  days after the initial treatment.

Treatment groups were commingled, cows were not marked as to treatment group, and all cows were bred following standard herd practice. As of the date of planned start of mating, cows detected in estrus were bred by AI for an average interval of 36 days (SD = 7; range, 21–49 days). Bulls were then comingled with the cows, resulting in a total average period of breeding of 87 days (SD = 9; range, 68-114 days). Pregnancy status and stage of gestation for cows detected as pregnant was estimated between 11 and 14 weeks after the commencement of the breeding program and again approximately 5 weeks after bull removal using transrectal ultrasonography. When the estimated date of conception was within 7 days of a recorded AI or bull breeding (where data were available), the recorded breeding date was accepted as the day of conception. When the estimated date deviated more than 7 days from the last recorded date, the estimated conception date was defined as the conception date. Cows that died or were removed from the herd before pregnancy diagnosis were included in the time to submission and to pregnancy analyses up to the date of culling, and nonpregnant cows were right censored in the survival analysis at the last pregnancy test date less than 35 days (the lower limit of detection for conception). Calving date, age, breed, breeding dates, disease treatments, removal reasons, and dates were retrieved from an electronic database (Mindapro; LIC, Hamilton, New Zealand) or farm records.

#### 2.1. Data analysis

Balance of treatment groups for categories of age and BCS, interval from calving to treatment, and start of the breeding program and the total length of the breeding program were compared using a chi-square test. Outcome variables of interest included the clinical cure proportion (i.e., cows with VDS of 0 or 1 at 14 days after treatment), the proportion of cows inseminated by 21 days after the start of breeding (i.e., number of cows inseminated by 21 days divided by the total number of enrolled cows), the proportion of cows conceiving at first insemination where that insemination occurred within 21 days of the start of breeding (i.e., number of cows confirmed pregnant to insemination by day 21 divided by the total number of cows inseminated by day 21), the proportion of cows pregnant by 42 days after the start of breeding (i.e., number of cows confirmed pregnant by 42 days divided by the total number of enrolled cows), and the proportion of cows pregnant at the end of the breeding program.

The main predictor variable was treatment group (i.e., blanket cephapirin vs. CL-dependent  $PGF_{2\alpha}$  or cephapirin). However, several other variables that were potential confounders were also evaluated. These variables included the CL status at enrollment (CL present or absent), herd, age (2, 3–4, 5–6, and >6 years of age), breed (categorized as Friesian or Jersey if that breed was >11/16 of the cow's

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