Theriogenology 110 (2018) 27–33

Contents lists available at ScienceDirect

Theriogenology

journal homepage: www.theriojournal.com

Additional small dose of prostaglandin $F_{2\alpha}$ at timed artificial insemination failed to improve pregnancy risk of lactating dairy cows☆

J.A. Sauls, B.E. Voelz, L.G.D. Mendonça, J.S. Stevenson*

Department of Animal Sciences and Industry, Kansas State University, Manhattan, KS, 66506-0201, USA

ARTICLE INFO

Article history:
Received 24 August 2017
Received in revised form
7 November 2017
Accepted 31 December 2017
Available online 3 January 2018

Keywords:
Artificial insemination
Pregnancy per AI
Prostaglandin $F_{2\alpha}$ at AI

ABSTRACT

Two experiments were performed to test the hypothesis that administering $PGF_{2\alpha}$ concurrent with timed artificial insemination (AI) in lactating dairy cows would enhance pregnancy per AI (P/AI). In experiment 1, lactating Holstein cows (n = 289) in one herd were enrolled after a non-pregnancy diagnosis (30–36 d after AI) to synchronize subsequent ovulation before AI. Cows were assigned randomly to receive (im) 10 mg of $PGF_{2\alpha}$ concurrent with timed AI (Day 0; treatment) or no injection (control). Blood samples were collected on Days −3, 0, and 13 to determine serum concentrations of progesterone. Ovaries were scanned via transrectal ultrasonography to determine follicle diameters (Day −3), subsequent ovulation risk (Day 13), and total volume of luteal tissue (Day 13). Diagnosis of pregnancy occurred on Days 32 and 80 after AI. Ovulation risk post-AI exceeded 90% and did not differ between treatments. In addition, $PGF_{2\alpha}$ treatment only numerically increased progesterone (5.7 ± 0.3 vs. 6.2 ± 0.3 ng/mL) or luteal tissue volume (8.9 ± 0.4 vs. 9.8 ± 0.5 ng/mL) on Day 13 by 8.8% (P = .206) or 10.1% (P = .134) in control and treated cows, respectively. Pregnancy per AI at Days 32 (P = .50) and 80 (P = .33) did not differ between treatments. Cows with progesterone >0.5 ng/mL at timed AI had reduced (P < .001) ovulation risk but risk was unaffected by treatment. In experiment 2, lactating dairy cows (n = 1828) in two commercial dairy herds were enrolled at time of insemination (Day 0), and assigned randomly to treatment or control as described in experiment 1. Initial (Days 32–35) and confirmed (Days 63–68) pregnancy diagnosis revealed no differences in P/AI or pregnancy loss. Pregnancy diagnosis on Days 32–35 produced percentage increases in P/AI for primiparous compared with multiparous cows (20.8%; P = .002), for first-service compared with repeat-service cows (26%; P = .001), and cows in one herd compared with the second herd (36%; P < .001). Pregnancy loss was greater (P = .001) for cows inseminated at first (10.0%) vs. later services (5.3%) but was unaffected by treatment. Cows treated with $PGF_{2\alpha}$ in one herd produced more twins than control cows (11.7 vs. 3.2%), whereas no treatment difference was detected in the second herd (5.6 vs. 5.6%), respectively. We conclude that im treatment of lactating dairy cows with 10 mg of $PGF_{2\alpha}$ concurrent with timed AI did not improve P/AI or embryo survival, but increased twinning in one herd.

1. Introduction

Treatment of domestic livestock with $PGF_{2\alpha}$ administered (iv, im, or iu) concurrent with artificial insemination (AI) to influence conception has been a subject of recurring research since the early 1990s. Pregnancy outcomes have been improved in some bovine studies [1–3], but not in others [4–6]. Furthermore, $PGF_{2\alpha}$ may successfully induce and synchronize ovulation similar to treatments with estradiol benzoate or estradiol cypionate [7]. Prostaglandin $F_{2\alpha}$ is produced by many cells, including endometrial cells, and is considered to be the main luteolysin in farm animals [8]. Because of the various biological activities of $PGF_{2\alpha}$, it has been used in reproductive management of cattle to induce parturition, synchronize estrus, and treat ovarian and uterine disease [9,10]. Administration of $PGF_{2\alpha}$ increased release of luteinizing hormone

☆ Contribution number 18-022-J from the Kansas Agricultural Experiment Station, Manhattan, KS.

* Corresponding author.
E-mail address: jss@ksu.edu (J.S. Stevenson).

https://doi.org/10.1016/j.theriogenology.2017.12.051
0093-691X/

(LH) in postpartum cows that stimulated follicular growth and ovulation [11]. Treatment with a single iv injection of $PGF_{2\alpha}$ concurrent with AI improved synchrony of ovulation, increased ovulation risk, and increased pregnancy risk in dairy cows [2]. In addition, administering $PGF_{2\alpha}$ at the time of AI increased embryo numbers in rabbits [12] and improved farrowing rates and litter size in sows [13].

Approximately 20% of cows exposed to estrus- or ovulation-synchronization programs have delayed or incomplete luteal regression [14]. A review of previous research demonstrated that cows with reduced concentrations of progesterone at AI had increased conception risk [15], in part, because basal concentrations of progesterone at AI are optimal for gamete transport. Administration of $PGF_{2\alpha}$ concurrent with AI could increase pregnancy rate by hastening luteal regression in cows that have delayed or incomplete luteolysis at AI. In addition, administration of $PGF_{2\alpha}$ concurrent with AI increased corpus luteum size and concentrations of progesterone 11 d after treatment and AI in buffaloes [16] and increased the number of cows with a corpus luteum after AI [2].

Sperm transport to the site of fertilization is a critical component to achieve pregnancy. Because smooth muscle contractions are most likely responsible for moving sperm to the uterus [17] as evidenced by limited sperm transport in ewes with reduced uterine contractions moving toward the oviduct [18]. Prostaglandin $F_{2\alpha}$ stimulated myometrial contractions in pigs [19] and cattle [20]. Previous research demonstrated improved sperm transport to the oviduct when compounds such as $PGF_{2\alpha}$, oxytocin, estradiol, phenylephrine, or ergonovine were added to semen or were administered to females [17]. In addition, ewes inseminated with $PGF_{2\alpha}$-supplemented semen or administered $PGF_{2\alpha}$ im at breeding had increased semen in all parts of their reproductive tract [21]. Therefore, administering $PGF_{2\alpha}$ concurrent with AI could increase pregnancy risk by inducing secretion of oxytocin that may stimulate uterine contractions and support semen transport.

The objectives of the present experiments were to test the hypothesis that administering im 10 mg of $PGF_{2\alpha}$ concurrent with timed AI will increase subsequent concentrations of progesterone, luteal volume, and pregnancy outcomes in lactating dairy cows receiving a fixed-time insemination.

2. Materials and methods

Two experiments were conducted under the Kansas State University Institutional Animal Care and Use Committee application #3671 (Manhattan) between January of 2015 through May of 2016.

2.1. Experiment 1

In experiment 1, 289 lactating Holstein cows in the Kansas State University Dairy Teaching and Research Center were enrolled. Cows were housed in sand-bedded free stalls with overhead roofs and fed twice daily a total mixed diet calculated to meet nutritional requirements for lactating dairy cows producing 50 kg of 3.5% milk [22]. The diet consisted of alfalfa hay, corn silage, soybean meal, whole cotton seed, corn or milo grain, corn-gluten feed, vitamins, and minerals. Feedline sprinklers and fans over the free stalls were employed during days in which ambient temperature exceeded 22 °C. Other characteristics of cows enrolled in experiment 1 are summarized in Table 1 including monthly test-day milk.

2.1.1. Experimental design

Cows were enrolled in a completely randomized design with two treatments when diagnosed not pregnant (Day −3) at 30–36 d after AI. Beginning at the not-pregnant diagnosis, cows were exposed to either a 5- or 7-d Ovsynch timed AI program before AI (100 μg GnRH [2 mL Factrel, Zoetis, Kalamazoo, MI, USA] — 5 or 7 d — 25 mg $PGF_{2\alpha}$ [5 mL Lutalyse, Zoetis] — 56 h — 100 μg GnRH — 16 h — AI). A second dose of $PGF_{2\alpha}$ was administered 24 h after the first when the 5-d program was employed. Body condition scores (1 = thin and 5 = fat) were assigned to cows and cows were stratified by parity (primiparous vs. multiparous) and then assigned randomly to receive 10 mg $PGF_{2\alpha}$ (n = 140; 2 mL Lutalyse [dinoprost tromethamine], Zoetis) at timed AI (Day 0) or served as untreated controls (n = 149). The treatment dose of 10 mg $PGF_{2\alpha}$ was chosen because 10 mg, but not 5 mg, increased pregnancy risk at fixed-time AI in one North American Holstein herd [3]. Pregnancy was diagnosed by transrectal ultrasonography (7.5-MHz linear-array transducer, Aloka 500 V; Corometrics Medical Systems Inc., Wallingford, CT) at Day 32 after timed AI.

2.1.2. Measurements

Blood samples were collected 3 d before timed AI (Day −3), at timed AI (Day 0), and at Day 13 to determine progesterone concentrations. Samples were stored on ice and transported to the laboratory for storage at 5 °C until serum was harvested by centrifugation (1200×*g*). Sera samples were stored at −15 °C until assayed for progesterone concentration by radioimmunoassay [23] using ImmuChem Double Antibody progesterone ^{125}I kits (MP Biomedicals, LLC, Orangeburg, NY, USA). Inter- and intra-assay coefficients of variation of 14 assays for a low (1.2 ± 0.1 ng/mL) and high concentration pool (17.4 ± 1.2 ng/mL) were 5.2 and 7.1%, respectively. Assay sensitivity averaged 60 ± 5.0 pg/mL and progesterone standard concentrations in the assay were 0.05, 0.1 0.2, 0.5, 2.0, 5.0, 10.0, and 25.0 ng/mL.

Ovaries were scanned via transrectal ultrasonography at not-pregnant diagnosis (Day -10 or -8) to characterize and map number and diameter of all ovarian follicles and any luteal structure(s). At Day −3, ovaries were re-examined to determine ovarian structures and ovulatory response to GnRH administered at the non-pregnant diagnosis. Ovaries were re-examined on Day 13 to determine ovulation risk (single or multiple) and total volume of luteal tissue ($4/3 \times r3 \times \pi$, where W = largest width and H = largest height of the structure; r = radius [W/2 + H/2]/2, and $\pi = 3.14159$). When a luteal structure contained a fluid-filled cavity, volume of the cavity was subtracted from the total luteal volume.

2.1.3. Statistical analyses

All binomial variables (incidence of single or multiple ovulation [proportion of ovulating cows having more than one luteal structure]), P/AI at Days 32 and 80 after AI, intervening pregnancy loss, and incidence of twin births) were analyzed using procedure GLIMMIX in SAS (SAS Enterprise 6.1, SAS Inst. Inc., Cary, NC, USA). Options used in the model statement included LINK = LOGIT, DIST = BINOMIAL, and the least square means option of ILINK and DIFF. The initial model included the fixed effects of treatment (control vs. 10 mg $PGF_{2\alpha}$ at AI), parity (primiparous vs. multiparous), season of AI (warm = May 1 through September 30 vs. cool = October 1 through April 30), and interactions of treatment with previous fixed effects, in addition to the random effects of days in milk and body condition score at time of enrollment. No interactions were detected, so they were deleted from the final model.

Continuous variables (progesterone and CL volume) were analyzed using the procedure MIXED in SAS to adjust for unequal variances. The REPEATED option added after the model statement, with GROUP = treatment allowed for estimating the individual treatment variances. Furthermore, including the option, DDFM = SATTERTHWAITE, to the MODEL statement adjusted the degrees of freedom for unequal variances. The model consisted of the same independent fixed effects described previously for the