Theriogenology 83 (2015) 257–265

Contents lists available at ScienceDirect

Theriogenology

journal homepage: www.theriojournal.com

Effect of progesterone supplementation on fertility responses of lactating dairy cows with corpus luteum at the initiation of the Ovsynch protocol

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ARTICLE INFO

Article history:
Received 8 July 2014
Received in revised form 11 September 2014
Accepted 12 September 2014

Keywords:
CIDR
Corpus luteum
Dairy cow
Progesterone
Reproduction

ABSTRACT

The objectives of this study were to determine the effects of supplemental progesterone on fertility responses of lactating dairy cows with a CL at the initiation of the timed artificial insemination (AI) program. Holstein cows were subjected to the Ovsynch protocol (Day −10 GnRH, Day −3 $PGF_{2\alpha}$, Day −0.7 GnRH, and Day 0 timed AI). Ovaries were scanned by ultrasonography on Day −10 and cows with CL were blocked by pen and assigned randomly to receive no supplemental progesterone (control, n = 863) or to receive a controlled internal drug-release (CIDR) insert containing progesterone from Days −10 to −3 (1CIDR, n = 862). Cows were observed for signs of estrus beginning on Day −9 based on removal of tail chalk and those in estrus received AI on the same day. Blood sampled from a subset of cows was analyzed for progesterone concentrations on Days −10, −9, −7, −5, −3, 0, 6, 13, and 19. Pregnancy was diagnosed on Days 32 and 60 after AI. Supplementation increased ($P < 0.01$) progesterone concentrations between Day −9 and −3 compared with control (7.5 vs. 6.2 ng/mL). Treatment had no effect on the ovulatory response to the first and final GnRH injections of the Ovsynch protocol, the proportion of cows that maintained their CL until the day of $PGF_{2\alpha}$ injection, or the diameter of the ovulatory follicle before AI. Although the overall proportion of cows in estrus at AI did not differ between treatments, progesterone supplementation prevented ($P < 0.01$) cows from coming into estrus from Days −9 to −3 (0.0% vs. 4.7%), whereas it increased ($P = 0.02$) the proportion of cows inseminated in estrus from Days −2 to −1 (7.1% vs. 4.5%). Pregnancy per AI (P/AI) tended to be reduced ($P = 0.06$) by supplemental progesterone on Day 32 (40.5% vs. 45.0%), but not on Day 60 after AI (36.6% vs. 39.7%). A tendency for an interaction ($P = 0.09$) between treatment and the presence of CL at the $PGF_{2\alpha}$ injection was observed for P/AI on Day 32 in cows that received timed AI because progesterone supplementation reduced P/AI in cows that maintained their CL until Day −3 (40.3% vs. 46.7%); however, it increased P/AI in those that did not have a CL at $PGF_{2\alpha}$ (38.1% vs. 27.7%). Treatment did not affect pregnancy loss between Days 32 and 60 of gestation. In conclusion, incorporating a single intravaginal insert to the timed AI program increased progesterone concentrations in plasma by 1.3 ng/mL, but did not benefit fertility in dairy cows that have CL at the initiation of the synchronization protocol.

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0093-691X/$ – see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.theriogenology.2014.09.021

1. Introduction

Programs for synchronization of the estrous cycle and timed artificial insemination (AI) increase pregnancy rate by maximizing submission to AI [1], which has stimulated their use for management of reproduction in dairy herds worldwide. Despite the improvement in reproductive performance associated with the use of timed AI over the past decade, individual fertility measured as pregnancy per AI (P/AI) has not changed [2]. This scenario highlights the importance of developing strategies applicable to large groups of cows that benefit the establishment and maintenance of pregnancy. Exposure to insufficient concentrations of progesterone during the growth of the ovulatory follicle is one of the important factors that affect fertility in high-producing dairy cows [3,4]. The decrease in P/AI observed in cows that lack a functional CL at the initiation of the synchronization protocol and the benefits from supplementing progesterone to this cohort of cows have been reported [4–6]. Nevertheless, previous results suggest that cows with CL might also have insufficient circulating progesterone associated with increased catabolism by splanchnic tissues [7] and are expected to benefit from progesterone supplementation during the timed AI program [8–10].

Early studies have shown that progesterone concentrations in blood during the luteal phase preceding the first AI postpartum were 1 to 2 ng/mL less in cows that failed to conceive compared with those that became pregnant [11]. A similar difference in progesterone concentration has been observed between lactating dairy cows and nonlactating heifers, which resulted in larger ovulatory follicles, impaired embryo quality, and reduced P/AI [12,13]. Although the experimental design in many studies does not allow for the establishment of causality [11–13], these results suggest that the circulating concentrations of progesterone maintained by the CL are, in many cases, insufficient to optimize follicle maturation and fertility responses in high-producing dairy cows. The underlying mechanism by which progesterone modulates fertility likely involves a change in the pattern of LH release. Endo et al. [14] depicted a linear trend for the number of LH pulses to decrease concurrently with the increase in progesterone concentrations as the estrous cycle progressed. Data from beef cows also revealed a reduction in LH pulsatility as the concentration of progesterone increased with supplementation using intravaginal inserts [15]. It is reasonable to speculate that these changes in LH pulse frequency are associated with alterations in the process of follicular maturation and subsequent embryo survival [16,17].

In addition to the effects on the development of the ovulatory follicle, supplementation with progesterone is expected to improve the synchrony of the estrous cycle in cows that bear a CL at the initiation of the timed AI program [18]. Cows enrolled in timed AI protocols during late diestrus are likely to undergo spontaneous luteolysis and ovulate before the final GnRH injection is administered [19]. Intravaginal inserts for sustained release of progesterone block the preovulatory surge of LH and have been shown to improve the synchrony of ovulation [18,20,21]. Accordingly, the increase in P/AI observed in cyclic cows supplemented with progesterone was greater among cows that regressed than those that maintained the CL before the injection of $PGF_{2\alpha}$ [8]. Nevertheless, fertility responses to progesterone supplementation during timed AI programs have been inconsistent and, in many cases, the benefits were observed in cows with CL [22].

The hypotheses of the present study were that supplementing progesterone to lactating dairy cows with CL at the initiation of the timed AI program enhances synchrony of the estrous cycle and improves fertility responses. Specific objectives were to evaluate the effects of incorporating a single intravaginal insert to the timed AI protocol on progesterone concentrations in plasma, ovarian responses to the synchronization program, P/AI, and pregnancy loss.

2. Materials and methods

All procedures involving cows in this study were approved by the University of Florida nonregulatory animal research system committee.

2.1. Cows and housing

The study was conducted in four commercial dairy herds located in Hanford, California, USA. A total of 4000, 1500, 1800, and 1450 cows were milked at each site at the initiation of the study. The yearly rolling herd averages for milk yield were approximately 12,700 kg for all herds. Cows diagnosed with clinically abnormal reproductive tract (adhesions, abscesses, etc.) were excluded from enrollment. All inseminations were performed from October 10, 2013 to February 21, 2014. The number of cows enrolled in herds 1, 2, 3, and 4 were 684, 377, 335, and, 329, respectively. Primiparous ($n = 727$) and multiparous ($n = 998$) Holstein cows were housed separately in free-stall barns equipped with sprinklers and fans in herds 1, 2, and 3, or in dry lots provided with shades in herd 4, and pens in all herds had soakers for evaporative cooling in the feedlane. Cows were restrained in headlock stations during all experimental procedures.

2.2. Reproductive management

All cows were subjected to the standard Ovsynch timed AI protocol (Fig. 1), of which 718 were enrolled for the first postpartum AI and 1,007 were enrolled during a resynchronized insemination after diagnosed as nonpregnant. Cows receiving the first AI postpartum had their estrous cycle presynchronized with injections of 25 mg $PGF_{2\alpha}$ intramuscularly (5 mL of Lutalyse Sterile Solution, dinoprost tromethamine, equivalent to 5 mg dinoprost per milliliter; Zoetis, Madison, NJ, USA) administered 14 days apart, at 38 ± 3 and 52 ± 3 days in milk (DIM) in herds 1, 2, and 4, or at 44 ± 3 and 58 ± 3 DIM in herd 3. Cows not observed in estrus after the second injection of $PGF_{2\alpha}$ were enrolled in the timed AI protocol 11 days later. Cows receiving resynchronized inseminations were enrolled in the timed AI program after a nonpregnancy diagnosis at 35 ± 3 days after the previous insemination. The timed AI program consisted of an intramuscular injection of 100 μg of GnRH on study Day −10 (2 mL of Cystorelin, gonadorelin diacetate tetrahydrate equivalent to 43 μg of gonadorelin per milliliter; Merial Ltd., Duluth, Georgia), followed by an injection of $PGF_{2\alpha}$ 7 days later (study Day −3), and a final