J. Dairy Sci. 101:1–12
https://doi.org/10.3168/jds.2017-14058
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Effect of human chorionic gonadotrophin administration 2 days after insemination on progesterone concentration and pregnancy per artificial insemination in lactating dairy cows

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ABSTRACT

The aim of this study was to examine the effect of a single administration of human chorionic gonadotrophin (hCG) during the establishment of the corpus luteum (CL) on progesterone (P4) concentration and pregnancy per artificial insemination (P/AI) in lactating dairy cows. Postpartum spring-calving lactating dairy cows (n = 800; mean ± SD days in milk and parity were 78.5 ± 16.7 and 2.3 ± 0.8, respectively) on 3 farms were enrolled on the study. All cows underwent the same fixed-time AI (FTAI) protocol involving a 7-d progesterone-releasing intravaginal device with gonadotrophin-releasing hormone (GnRH) administration at device insertion, prostaglandin at device removal followed by GnRH 56 h later, and AI 16 h after the second GnRH injection. Cows were blocked on days postpartum, body condition score, and parity and randomly assigned to receive either 3,000 IU of hCG 2 d after FTAI or no further treatment (control). Blood samples were collected on d 7 and 14 postestrus by coccygeal venipuncture on a subset of 204 cows to measure serum P4 concentration, and pregnancy was diagnosed by ultrasonography approximately 30 and 70 d after FTAI. Administration of hCG caused an increase in circulating P4 concentrations compared with the control treatment on d 7 (+22.2%) and d 14 (+25.7%). The P/AI at 30 d after FTAI was affected by treatment, farm, body condition score, and calving to service interval. Overall, administration of hCG decreased P/AI (46.3% vs. 55.1% for the control). Among cows that did not become pregnant following AI, a greater proportion of control cows exhibited a short repeat interval (≤17 d) compared with cows treated with hCG (8.6% vs. 2.8%, respectively). In addition, the percentages of cows pregnant at d 21 (59.6% vs. 52.0%) and d 42 (78.3% vs. 71.9%) were greater in control than in hCG-treated cows. The overall incidence of embryo loss was 10.7% and was not affected by treatment. There was a tendency for an interaction between treatment and CL status at synchronization protocol initiation for both P4 concentration and P/AI. In conclusion, administration of hCG 2 d after FTAI increased circulating P4 concentrations. Unexpectedly, cows treated with hCG had lower fertility; however, this negative effect on fertility was manifested primarily in cows lacking a CL at the onset of the synchronization protocol.

Key words: human chorionic gonadotrophin, progesterone, timed artificial insemination, pregnancy per artificial insemination

INTRODUCTION

A fundamental goal in seasonal-calving pasture-based systems of dairy production is to achieve a 12-mo calving interval to synchronize grass growth with herd dietary demand (Dillon et al., 1995). Pregnancy loss is one of the major causes of reproductive failure in cattle and leads to extended calving intervals. In a seasonal system, this can have a significant effect on profitability (Shalloo et al., 2014). Despite high fertilization rates (80–90%), many studies have reported that only 30% or less of high-producing lactating cows calve after a single AI (Wiltbank et al., 2016). Most of the loss occurs before maternal recognition of pregnancy, in the period between fertilization and d 16 after insemination (Diskin and Morris, 2008), with a significant proportion occurring before d 7 in high-producing dairy cows (Sartori et al., 2010).

The steroid hormone progesterone (**P4**) plays a key role in the reproductive events associated with the establishment and maintenance of pregnancy (reviewed by Lonergan et al., 2016, and Spencer et al., 2016). Low circulating P4 concentrations in the early postovulatory period have been reported in several studies to have an adverse effect on conceptus elongation (Mann and

Received October 27, 2017.
Accepted February 19, 2018.
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Lamming, 2001; Forde et al., 2011) and the endometrial transcriptome (Forde et al., 2012) and are ultimately associated with reduced fertility in lactating dairy cows (Diskin et al., 2006; Wiltbank et al., 2014). On the other hand, elevated concentrations of circulating P4 in the period immediately after conception have been associated with advanced conceptus elongation (Carter et al., 2008), increased interferon-tau production (Mann and Lamming, 2001; Rizos et al., 2012), and greater pregnancy rates in cattle (Stronge et al., 2005; McNeill et al., 2006) and sheep (Ashworth et al., 1989).

In cattle, human chorionic gonadotrophin (**hCG**) has luteinizing hormone (**LH**)-like activity but has a longer half-life than LH. Administration of hCG has been reported to (1) prolong the life span of the corpus luteum (**CL**; Sianangama and Rajamahendran, 1992), (2) induce ovulation throughout the estrous cycle (Santos et al., 2001), (3) stimulate the emergence of accessory CL (Rajamahendran and Sianangama, 1992), and (4) alter follicular wave dynamics (Diaz et al., 1998). Administration of hCG increases endogenous P4 produced by the CL (for review, see De Rensis et al., 2010; Lonergan, 2011). Typically, hCG is administered around d 5 postestrus to coincide with the first wave dominant follicle, resulting in ovulation and formation of an accessory CL, leading to increased circulating P4 concentrations (Santos et al., 2001; Nascimento et al., 2013b). In addition to forming an accessory CL, hCG administration can lead to hypertrophy of the original CL (Rizos et al., 2012).

Despite its positive effects on circulating P4, the effect of hCG administration on pregnancy rates has been inconsistent (Lonergan, 2011; Wiltbank et al., 2014). An elevation in circulating P4 concentrations occurs 3 d after hCG injection when it is administered on d 5 after AI (Rajamahendran and Sianangama, 1992; Santos et al., 2001; Stevenson et al., 2007; Vasconcelos et al., 2011). In a recent large study, Nascimento et al. (2013a) reported a modest increase of 3% (meta-analysis study; n = 4,397 cows) or 3.5% (manipulative study; n = 2,979 cows) in pregnancy rate following hCG administration 5 d after AI. A beneficial effect on pregnancy per AI has been reported in repeat-breeding dairy cows treated with hCG 6 d after AI (Alnimer and Shamoun, 2015). An early increase in P4 has been associated with improved pregnancy rates in cattle; however, administration of hCG on d 5 to 7 does not affect circulating P4 for several days, partly due to the time required for ovulation and accessory CL formation (Rizos et al., 2012). We previously evaluated the effect of a single administration of hCG on d 1, 2, 3, or 4 after estrus on P4 concentrations in beef heifers and observed that administration of hCG on d 2 resulted in increased CL area from d 6 to 12 and increased P4 in circulation from d 6 (Maillo et al., 2014).

Therefore, the objective of this study was to investigate the effect of hCG administration 2 d after fixed-time AI (**FTAI**) on P4 concentrations and pregnancy per AI (**P/AI**) in lactating dairy cows managed under pasture-based systems. We hypothesized that hCG treatment administered on d 2 after an FTAI program would increase circulating concentrations of P4 during the early luteal phase and thereby enhance fertility in lactating dairy cows.

MATERIALS AND METHODS

All experimental procedures involving animals were licensed by the Department of Health and Children, Ireland, in accordance with Statutory Instrument No. 543 of 2012 (under Directive 2010/63/EU on the protection of animals used for scientific purposes).

Animals and Experimental Design

Lactating Holstein Friesian dairy cows (n = 846) located on 3 commercial spring-calving farms in Ireland were enrolled in this study (78.5 ± 16.7 DIM) conducted between April and August 2016. The average parity was 2.3 ± 0.80 (mean ± SD). Cows that were ≥35 DIM were deemed eligible for enrollment in the study. Estrous cycles were synchronized using a 7-d P4-releasing intravaginal device (**PRID**; containing 1.55 g of P4; PRID E, Ceva Sante Animale, Libourne, France), with administration of $PGF_{2\alpha}$ (Enzaprost, 5 mL equivalent to 25 mg of dinoprost; Ceva Sante Animale) at device removal. Gonadotrophin-releasing hormone containing 0.1 mg gonadorelin diacetate (Ovarelin, Ceva Sante Animale) was administered at PRID insertion (d −10) and at 56 h after PRID removal (d −1) to stimulate ovulation of the dominant follicle. Cows were inseminated 72 h after PRID removal (i.e., 16 h after the second GnRH). Body condition score was recorded at PRID insertion by the same 2 people using a scale from 1 (emaciated) to 5 (fat) according to Ferguson et al. (1994). On d 2 after FTAI (d 0), cows were blocked on parity, DIM, and BCS and randomly allocated to receive 3,000 IU of hCG (Chorulon; Intervet, Dublin, Ireland) by intramuscular injection or no further treatment (Figure 1).

Blood Sampling and P4 Assay

Blood samples were collected by coccygeal venipuncture from a subset of cows (n = 204) from both treatments on d 7 and 14 post-FTAI to measure serum P4

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