Rates of luteolysis and pregnancy in dairy cows after treatment with cloprostenol or dinoprost

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Abstract

Our objective was to determine whether rates of luteolysis or pregnancy differed in lactating dairy cows of known progesterone status and either known or unknown luteal status after either cloprostenol or dinoprost was injected as part of a timed-insemination program. In Experiment 1, 2358 lactating dairy cows in six herds were given two injections of $PGF_{2\alpha}$ 14 d apart (Presynch), with the second injection given 12 to 14 d before the onset of a timed AI protocol (Ovsynch). Cows (n = 1094) were inseminated when detected in estrus after the Presynch $PGF_{2\alpha}$ injections. Cows not inseminated (n = 1264) were enrolled in the Ovsynch protocol and assigned randomly to be treated with either cloprostenol or dinoprost as part of the timed-AI protocol. In cows having pretreatment concentrations of progesterone $\geq$ 1 ng/mL and potentially having a functional corpus luteum (CL) responsive to cloprostenol (n = 558) or dinoprost (n = 519), dinoprost increased (P < 0.05) luteal regression from 86.6 to 91.3%. Despite a significant increase in luteolysis, pregnancies per AI did not differ between luteolytic agents (dinoprost = 37.8% and cloprostenol = 36.7%). Fertility was improved in cows of both treatments having reduced concentrations of progesterone at 72 h and in cows showing signs of estrus. In Experiment 2, an ovulation-resynchronization program was initiated with GnRH or saline in 427 previously inseminated lactating dairy cows of unknown pregnancy status in one herd. Seven days later, pregnancy was diagnosed and nonpregnant cows were blocked by number of CL and assigned randomly to be treated with cloprostenol or dinoprost. Compared with cloprostenol, dinoprost increased (P < 0.05) luteal regression from 69.1 to 78.5%, regardless of the number of CL present or the total luteal volume per cow. Pregnancies per AI did not differ between dinoprost (32.8%) and cloprostenol (31.3%). Although dinoprost was more effective than cloprostenol at inducing luteolysis in lactating dairy cows exposed to an Ovsynch or ovulation-resynchronization protocol, resulting fertility did not differ between products.
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1. Introduction

Since the first $PGF_{2\alpha}$ product was introduced in the United States in 1979 (Lutalyse, The Upjohn Co., Kalamazoo, MI, USA), several agonists and generic $PGF_{2\alpha}$ products have become available by prescription. The major difference in available products is between those that are chemically the same as uterine-derived $PGF_{2\alpha}$ (dinoprost) [1] and its agonist (cloprostenol sodium) [2]. The half-life of elimination in blood of 0.5 mg of free acid ^{14}C-cloprostenol is 3 h [2] and is longer than the blood half-life of a few minutes for dinoprost [1], because a benzyl chlorine ring is substituted at position 17 of the fatty-acid structure of $PGF_{2\alpha}$. Whether this property makes the agonist

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cloprostenol more effective in lysing the corpus luteum (CL) is equivocal.

Different physiological responses of bovine females to administration of either cloprostenol or dinoprost have been reported for luteolysis [3], receptor binding [4], changes in intrauterine pressure [5], estrus expression [6–14], conception rates [7,8–10,12–16], and pregnancy rates [7,9,12–16]. An unpublished meta-analysis (A. L. Skidmore, personal communication) of some of these factors did not find significant differences ($\alpha > 0.05$) in conception rate, pregnancy rate, or overall differences in detected estrus. Odds ratios (OR), however, were consistently greater than 1.0, indicating only numerical trends in the combined studies that consistently favored cloprostenol over dinoprost.

Strict timed-AI programs are common place on dairy operations because they are reliable and not wholly dependent on visual or other means of detecting estrus [17]. The Ovsynch protocol (injection of GnRH 7 d before and 48 h or 72 h after treatment with $PGF_{2\alpha}$; timed AI at 72 h) synchronizes follicular maturation and luteal regression [18,19], resulting in approximately 20–30% of cows having at least two luteal structures at the time of $PGF_{2\alpha}$ injection [20]. A good test of luteolytic efficacy between product types (dinoprost vs. cloprostenol) is possible in lactating cows to which the Ovsynch protocol is applied, because a larger proportion of cows have more than one CL to regress at the time of $PGF_{2\alpha}$ injection.

We hypothesized that if one $PGF_{2\alpha}$ product was more effective than another as a luteolytic agent, lactating dairy cows having ancillary luteal structures would be an effective model for testing that difference. Therefore, the present study consisted of two experiments. The objective of the first experiment was to determine the efficacy of luteal regression in response to two chemically different luteolytic products (cloprostenol vs. dinoprost), as determined by changes in blood progesterone concentrations and subsequent pregnancy outcome of lactating dairy cows exposed to either of the two products before first postpartum AI. The objective of the second experiment was similar to that of the first, except the number of CL and total luteal tissue volume were quantified in previously inseminated nonpregnant dairy cows before treatment injections were given.

2. Materials and methods

The Kansas State University (Manhattan, KS) Institutional Animal Care and Use Committee approved all procedures involving cows in this study.

Table 1
Herd characteristics for lactating dairy cows enrolled in Experiments 1 and 2.

Traits	Experiment 1						Experiment 2
	Herd 1	Herd 2	Herd 3	Herd 4	Herd 5	Herd 6	
First and last AI dates	January 30, 2008 to May 13, 2008	January 24, 2008 to May 17, 2008	January 29, 2008 to May 13, 2008	January 28, 2008 to May 13, 2008	January 26, 2008 to May 18, 2008	February 13, 2008 to May 30, 2008	November 8, 2007 to July 10, 2008
Herd	California	California	California	California	California	California	Kansas
Herd size (n)	727	1,162	1,025	1,186	1,759	2,446	248
Milking frequency (times/d)	3	3	3	3	3	3	2
First pregnancy diagnosis (d)	36	36	35	36	36	32	30
Pregnancies per AI[a], % (n)	38.4 (86)	26.0 (181)	38.9 (113)	31.2 (185)	40.6 (192)	33.5 (337)	...
Cows enrolled in experiments (n)	112	163	100	110	257	488	306
Pregnancies per AI [b] (%)	42.0	27.6	26.0	31.8	38.5	42.2	33.3
	Mean ± SD						
Body condition score[c]	2.7 ± 0.2	2.7 ± 0.3	2.7 ± 0.3	2.8 ± 0.6	2.8 ± 0.4	2.7 ± 0.2	2.4 ± 0.5
Test-day milk[d] (kg)	51 ± 10	53 ± 10	54 ± 10	55 ± 10	55 ± 10	43 ± 11	44 ± 11
Days in milk at treatment AI	82 ± 2	83 ± 5	82 ± 2	83 ± 2	82 ± 2	86 ± 2	188 ± 93
Serum progesterone (ng/mL)	Mean ± SEM						
Before treatment	4.0 ± 0.30	3.6 ± 0.20	3.8 ± 0.30	4.5 ± 0.30	3.8 ± 0.20	4.0 ± 0.10	4.6 ± 0.15
48 h	0.6 ± 0.06	0.7 ± 0.07	0.7 ± 0.09	0.8 ± 0.08	0.9 ± 0.07	0.6 ± 0.02	...
72 h	0.6 ± 0.06	0.7 ± 0.06	0.6 ± 0.07	0.7 ± 0.07	1.0 ± 0.07	0.6 ± 0.04	1.0 ± 0.06

[a] Pregnancy outcome after inseminations made upon detected estrus during the Presynch period before enrollment in Experiment 1.

[b] Post-treatment outcome after first service (Experiment 1) or after a repeat service (Experiment 2).

[c] Assessed at treatment injection (1 = thin and 5 = fat).

[d] Average fat (3.5%)-corrected milk (Experiment 1) or energy-corrected milk (Experiment 2) of the test-day milk weight immediately before treatment injection.