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The use of a deslorelin implant (GnRH agonist) during the late embryonic period to reduce pregnancy loss

J.A. Bartolome [a,b], S. Kamimura [a], F. Silvestre [a], A.C.M. Arteche [a], T. Trigg [c], W.W. Thatcher [a,*]

[a] *Department of Animal Sciences, University of Florida, Gainesville, FL 32610, USA*
[b] *Facultad de Ciencias Veterinarias, Universidad Nacional de La Pampa, Argentina*
[c] *Peptech Animal Health, North Ryde, Australia*

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Abstract

Embryonic and fetal mortality reduce reproductive performance of lactating dairy cows. The objectives of this study were to reduce pregnancy loss by administering a deslorelin implant (GnRH agonist) during the late embryonic period, to reduce follicular growth, induce accessory corpora lutea, and increase plasma progesterone concentrations. Lactating dairy cows received an implant containing 2.1 mg of deslorelin (Deslorelin group; $n = 89$) or no treatment (Control group; $n = 92$) on Day 27 of pregnancy. Pregnancy, ovarian structures and plasma progesterone concentrations were determined on Days 27 and 45, and pregnancy was re-confirmed on Day 90. On Day 45, mean $\pm$ S.E.M. numbers of class 2 (6–9 mm; 0.72 ± 0.19) and class 3 ($\geq$10 mm; 0.86 ± 0.12) follicles for cows in the Deslorelin group were lower ($P < 0.01$) than the numbers of class 2 (1.90 ± 0.18) and class 3 (1.92 ± 0.12) follicles for cows in the Control group. On Day 45, the number of accessory corpora lutea for cows in the Deslorelin group (1.80 ± 0.07) were greater ($P < 0.01$) than for cows in the Control group (1.31 ± 0.07). On Day 45, plasma progesterone concentration was increased ($P < 0.01$) for cows in the Deslorelin group (8.03 ± 0.33 ng/mL) compared to cows in the Control group (6.40 ± 0.31 ng/mL). Pregnancy losses did not differ between Days 27 and 45 and Days 45 and 90 for cows in the Control (15.2 and 11.0%, respectively) and Deslorelin groups (20.2 and 10.5%, respectively). However, in the Deslorelin group, pregnancy loss between Days 45 and 90 was lower

* Corresponding author. Tel.: +1 352 392 5590; fax: +1 352 392 5595.
E-mail address: thatcher@animal.ufl.edu (W.W. Thatcher).

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($P < 0.05$) for cows that formed an accessory CL (0%) compared to cows that did not form an accessory CL (16.1%).

Keywords: Deslorelin implant; Corpus luteum; Ovarian follicle; Pregnancy loss; Cattle

1. Introduction

Embryonic and fetal mortality are important factors influencing reproductive efficiency in lactating dairy cows. Embryonic mortality refers to the losses that occur between fertilization and Day 45 of gestation (completion of embryo differentiation) [1]. Embryonic losses can be further classified as early embryonic mortality when cows return to estrus within 25 days after fertilization, and late embryonic mortality when losses occur between Days 25 and 45 of gestation [2]. Fetal loss or abortions are used to describe pregnancy losses between Days 45 and 260 of gestation [3].

In a recent review paper, late embryonic mortality averaged 12.8% for different studies that evaluated losses between Days 27 and 31 and Days 38 and 50 of gestation in lactating dairy cows [4]. Fetal loss was estimated to be 10.7% between Days 38 and 90 [5], 8.3% between Days 45 and 90 [6] and 9.6% between Days 41 and 120–150 of gestation [7]. The risk of pregnancy loss decreases during the third trimester of pregnancy [3].

Several factors, including genetic predisposition, nutrition, age, climate, insemination time, semen quality, infectious agents, and endocrine balance, have been associated with pregnancy losses [1]. Late embryonic and early fetal losses evaluated between Days 28 and 84 of gestation were 7.2% in pasture-based dairy herds [8]. However, pregnancy losses were 19% between Days 28 and 98 of gestation [9] and 14.6% between Days 34 and 74 of gestation [10] in high-producing, intensively managed dairies. Endocrine imbalances or abnormal hormonal profiles including progesterone and estrogen may be associated with embryonic mortality [1]. For example, high-producing dairy cows may experience low progesterone concentrations during the luteal phase of the estrous cycle, due to an increased blood flow to the liver which can result in a higher rate of steroid metabolism [11], and may contribute to higher pregnancy losses. Excessive follicular development and high estradiol concentrations during the luteal phase can be detrimental to embryo survival [12–14]. Factors including heat stress [15–17], high milk production and administration of bovine somatotropin [18] affect follicular dominance, which may result in greater follicular development during pregnancy. Interestingly, follicular growth is suppressed in the ovary ipsilateral to the pregnant uterine horn during the late embryonic period [19–21]. Consequently, pharmaceutical suppression of follicular development may be beneficial to embryo survival.

A deslorelin implant (GnRH agonist) has been used to induce both ovulation [22,23] and accessory corpora lutea [24] and to suppress follicular development without affecting the lifespan of the CL. The hypothesis of this study was that a deslorelin implant administered at Day 27 of pregnancy will induce formation of accessory corpora lutea, increase plasma progesterone concentrations, suppress follicular growth and reduce late embryonic and early fetal losses in lactating dairy cows. Day 27 of gestation was chosen to administer the deslorelin implant, since this begins the period of measured late embryonic losses as determined by ultrasound and subsequent transrectal rectal palpation at Day 45 [4], and follicular development is sustained on the ovary contralateral to the uterine horn of pregnancy at this stage [27]. The objectives were to evaluate ovarian structures and pregnancy losses at Day 45 and pregnancy losses at Day 90 in lactating dairy cows given a 2.1 mg deslorelin implant at Day 27 of pregnancy.

2. Materials and methods

The study was conducted in a large commercial dairy with 3200 milking cows. The herd was located in north central Florida and is divided into 14 lots according to levels of production and stage of lactation. Cows from all lots were included in the study. Cows were housed in free stall barns and dry lots and fed a total mixed ration (TMR) three times daily. The TMR was formulated to meet or exceed requirements for lactating cows [25]. Cows were milked three times a day, and had a rolling herd average for milk production of 10,700 kg. Beginning at 60-day postpartum, cows were given bovine somatotropin (Posilac®, 500 mg sometribove zinc, subcutaneously; Monsanto, St. Louis, MO, USA) every 14 days during the remainder of lactation. Reproductive management consisted of a voluntary waiting period of 75 days that incorporated a Presynch–Ovsynch program [10] for first service. Subsequent services were conducted either after detection of estrus using visual observation and a computerized pedometer system (Afimilk®; S.A.E. Afikim, Kibbutz Afikim, Israel), or after detection of non-pregnant cows by transrectal palpation of the genital tract and resynchronization using various protocols including insemination at detected estrus or timed insemination.

The study included pregnant cows detected by ultrasonography (Aloka 500 V with a linear-array 5 MHz transrectal transducer; Corometrics, Wallingford, CT, USA) on Day 27 after artificial insemination, according to previously described criteria [26]. In lactating dairy cows, pregnancy losses between Days 27 and 45 are approximately 17% for large herds [4]. With induction of an accessory CL, suppression of ovarian follicular development, or both, a reduction of pregnancy losses to 5% was expected. Therefore with 95% confidence and 80% power for the test, 82 cows per group were required. A total of 181 pregnant cows were assigned randomly to receive either a 2.1 mg, SQ biodegradable deslorelin implant (Ovuplant®, Peptech, Animal Health, North Ryde, Australia; Deslorelin group; $n = 89$) on Day 27, or no treatment (Control group; $n = 92$).

A real-time transrectal ultrasonographic examination was done on Days 27 and 45 to record the presence of a normal embryo (heartbeats), number of class 2 (6–9 mm) and class 3 ($\geq$10 mm) ovarian follicles, and corpora lutea. A cow was considered to develop accessory CL if the number of CL at Day 45 was greater than the number of CL on Day 27. On Day 90, cows were re-examined for pregnancy using transrectal palpation [27]. Cows pregnant at Day 27 and inseminated at estrus between Days 27 and 90 were also considered a pregnancy loss.

Blood samples were collected into vacuum tubes containing sodium heparin (Vacutainer®, BD, Franklin Lakes, NJ, USA), by puncture of the median coccygeal vein or artery on Days 27 and 45 of gestation. Upon collection, samples were immediately placed on ice, and centrifuged within 12 h (3000 rpm for 20 min). Plasma was separated and stored at -20 °C until assayed. Plasma progesterone concentrations were determined using a solid-phase, no-extraction RIA (Coat-a-Count Progesterone, DPC®, Diagnostic Products Corporation, Los Angeles, CA, USA). Accuracy of the assay procedure was determined previously [28]. The standard curve was composed of four tubes for total counts and coated tubes for non-specific binding and 100 μL of increasing concentrations of progesterone (0.1, 0.25, 0.5, 2, 5, 10, 20, and 40 ng/mL). Serum from ovariectomized and cows in estrus (low reference) and from cows in diestrus (high reference) were utilized in the assays. Sensitivity of the assay was 0.1 ng/mL. Intra- and inter-assay coefficients of variation for the luteal phase reference were 12.7 and 4.5%, respectively.

On the day of enrollment, information for month of the year (June, July and August), parity (1, 2, 3+), number of services (first, second, third and four or more) and insemination type (standing estrus, pedometer response or timed insemination) were recorded.

Outcome (dependent) variables were pregnancy losses between Days 27 and 45 and between Days 45 and 90 (yes/no), number of class 2 and class 3 follicles and number of corpora lutea at Day 45, plasma progesterone concentrations (ng/mL) at Day 45, follicular suppression at Day 45 (yes = absence of class 2 and 3 follicles) and accessory corpora lutea formation at Day 45 (yes = number of corpora lutea at Day 45 greater than the number of corpora lutea at Day 27). Explanatory (independent) variables were treatment (deslorelin implant), parity (1, 2, 3+), month (June, July and August), number of services (first, second, third and four or more) and insemination type (standing estrus, pedometer response or timed insemination). Accessory corpora lutea formation and follicular suppression were used as an explanatory variable for pregnancy loss between Days 45 and 90. Baseline comparison for parity, number of services, insemination type and month was conducted using Chi-square (Proc FREQ, SAS/STAT®, SAS Institute Inc., Cary, NC, USA).

Data for the number of class 2 and 3 follicles and corpora lutea were analyzed by analysis of variance to obtain the least square means and standard errors (Proc Mixed, SAS) and the counted data procedures, using a Poisson distribution (Proc GENMOD, SAS), to evaluate significance. The presence of accessory corpora lutea and follicular suppression were evaluated using Chi-square (Proc FREQ, SAS). Plasma progesterone concentration was analyzed by analysis of variance (Proc Mixed, SAS) considering treatment, day, treatment × day, parity, season, number of services, and insemination type [29]. Cow was considered as a random variable. The backward elimination procedure [30] of Logistic Regression (Proc GENMOD, SAS) was used to evaluate the effect of treatment on pregnancy loss between Days 27 and 45 and Days 45 and 90. Explanatory variables (i.e., group, parity, insemination type, number of services, accessory corpus luteum and follicular suppression) and their higher order interactions remained in the model if $P < 0.15$. Treatment differences were considered significant if $P \leq 0.05$.

3. Results

There were no significant differences in the distributions of cows by parity, number of services, and type of artificial insemination in both groups (Table 1). On Day 45, the

Table 1
Distribution of dairy cows by parity, number of services, and type of artificial insemination in the Control (no treatment) and Deslorelin (2.1 mg of deslorelin on Day 27 of pregnancy) groups

Variable	Control group		Deslorelin group		*P*-value
	%	No.	%	No.	
Parity					0.65
1	55.4	36/65	44.6	29/65	
2	47.8	22/46	52.2	24/46	
3+	48.6	34/70	51.4	36/70	
Services					0.07
First	45.7	16/35	54.3	19/35	
Second	62.2	23/37	37.8	14/37	
Third	35.7	15/42	64.3	27/42	
Four+	56.7	38/67	43.3	29/67	
Insemination type					0.10
Standing estrus	70.0	7/10	30.0	3/10	
Pedometers	45.5	55/121	54.5	66/121	
Timed AI	60.0	30/50	40.0	20/50	
Month					0.55
June	38.9	7/18	61.1	11/18	
July	51.4	37/72	48.6	35/72	
August	52.7	48/91	47.2	43/91	

numbers of class 2 and class 3 follicles for cows in the Deslorelin group were lower ($P < 0.05$) than the numbers of class 2 and class 3 follicles for cows in the Control group (Table 2). On Day 45, the number of corpora lutea for cows in the Deslorelin group was higher ($P < 0.01$) than that for cows in the Control group (Table 2).

The rise in plasma progesterone concentrations from Days 27 to 45 tended to be higher ($P < 0.10$) for cows in the Deslorelin group (Table 2). On Day 27, plasma progesterone concentrations were similar for cows in the Control and Deslorelin groups. On Day 45, plasma progesterone concentrations were higher ($P < 0.01$) for cows in the Deslorelin group compared to cows in the Control group (Table 2). There also was an interaction

Table 2
Least square means (LSM) and standard errors (S.E.M.) for the number of class 2 and 3 follicles, number of corpora lutea (CL) and plasma progesterone (Prog.) concentrations (ng/mL) on Days 27 and 45 for dairy cows in the Control (no treatment) and Deslorelin (2.1 mg of deslorelin on Day 27 of pregnancy) groups

Response	Day 27		Day 45		D	T	D × T
	Control	Deslorelin	Control	Deslorelin			
Class 2	3.10 (±0.22)	2.56 (±0.23)	2.10 (±0.22)	0.85 (±0.23)	$P < 0.01$	$P < 0.01$	$P < 0.05$
Class 3	2.02 (±0.15)	1.93 (±0.15)	1.78 (±0.15)	0.69 (±0.15)	$P < 0.01$	$P < 0.01$	$P < 0.01$
CL	1.44 (±0.10)	1.53 (±0.10)	1.31 (±0.10)	1.80 (±0.10)	NS	$P < 0.01$	$P < 0.01$
Prog.	6.44 (±0.44)	7.09 (±0.45)	6.34 (±0.44)	7.93 (±0.47)	NS	$P < 0.01$	$P < 0.10$

Values are represented as LSM (±S.E.M.). D: day; T: treatment; class 2 = 6–9 mm follicles; class 3 = ≥10 mm follicles.

between treatment and accessory corpora lutea formation on plasma progesterone concentrations at Day 45 ($P < 0.01$). In the Deslorelin group, plasma progesterone concentration was higher for cows that formed an accessory CL (10.7 ng/mL) compared to cows that did not form an accessory CL (5.5 ng/mL). In contrast, plasma progesterone concentration was not different for cows in the Control group with (7.8 ng/mL) or without (6.3 ng/mL) an accessory CL on Day 45.

Data for ovarian structures from six cows (three in each group) were not available either on Day 27 or Day 45 to evaluate follicular suppression and accessory corpora lutea. Follicular suppression was more pronounced ($P < 0.01$) for cows in the Deslorelin group (23.3%; 20/86) than for cows in the Control group (1.1%; 1/89). Accessory corpora lutea formation also was higher ($P < 0.01$) for cows in the Deslorelin group (45.4%; 39 [2 non-pregnant; 37 pregnant]/86) than for cows in the Control group (10.1%; 9 [2 non-pregnant; 7 pregnant]/89). Among the 39 cows that formed an accessory CL in the Deslorelin group, 56.4% (22/39) of the accessory corpora lutea were ipsilateral to the pregnant horn (i.e., as determined on Day 27) and 43.6% (17/39) were in the contralateral ovary.

At Day 27, 87.3% of the cows had a follicle greater than 12 mm (158/181). Average sizes of the largest follicle for Control and Deslorelin groups on Day 27 were 15.3 and 15.8 mm, respectively. There were two or three follicles in most cows, and it was not possible with a single ultrasound evaluation to know which follicle was the dominant follicle. Although the deslorelin implant induced a greater frequency of accessory CL at Day 27 (i.e., 43.6%), there was no statistical difference in the frequencies of accessory CL formation in cows with follicles smaller than 12 mm (i.e., 0/13, 0% in the Control group and 5/10, 50% in the Deslorelin group) compared to cows with follicles greater than 12 mm (i.e., 9/79, 11.4% in the Control group; 34/79, 43.0% in the Deslorelin group). In the 10 cows with follicles less than 12 mm in the Deslorelin group, two had 9 mm follicles, four had 10 mm follicles, and four had 11 mm follicles. Among the five cows that ovulated, two had a 10 mm follicle and three had an 11 mm follicle.

Among non-pregnant cows on Day 45, in the Deslorelin group only 61.1% (11/18) had at least one CL while in the Control group 85.7% (12/14) had at least one CL ($P < 0.12$). On Day 45, among non-pregnant cows, follicular suppression was higher ($P < 0.01$) for cows in the Deslorelin group (50%; 9/18) than for cows in the Control group (0%; 0/14).

Pregnancy losses between Days 27–45 and 45–90 and overall pregnancy losses (Days 27–90) were not different for cows in the Control and Deslorelin groups (Table 3). In the

Table 3
Pregnancy losses between Days 27–45 and Days 45–90 for dairy cows in the Control (no treatment) and Deslorelin (2.1 mg deslorelin implant on Day 27 of pregnancy) groups

Response	Control group		Deslorelin group		*P*-value
	%	No.	%	No.	
Pregnancy loss Days 27–45	15.2	14/92	20.2	18/89	0.37
Pregnancy loss Days 45–90	11.0	8/77	7.1	5/70	0.48
Total pregnancy loss Days 27–90	23.9	22/92	25.8	23/89	0.76

Note: one cow in each group was culled between Days 45 and 90.

multivariate analysis for pregnancy loss between Days 27 and 45, only the number of services was significant; therefore, group and number of services were included in the final model. Pregnancy loss between Days 27 and 45 was 31.4% (11/35) in first service cows, 13.5% (5/37) in second service cows, 19.5% (8/42) in third service cows and 11.9% (8/67) in cows with four or more services. The risk of pregnancy loss was higher (adjusted odds ratio = 15.6; 95% CI = 1.5–167.4; $P = 0.02$) in first service cows compared to cows with four or more services (11.9%, 8/67). There was no difference in pregnancy loss between cows in the Control and the Deslorelin groups (adjusted odds ratio = 0.78; 95% CI = 0.35–1.72; $P = 0.54$).

In the multivariate analysis for pregnancy loss between Days 45 and 90, there was an interaction between treatment group and accessory CL formation ($P < 0.01$). Since there were only seven pregnant cows with accessory corpora lutea in the Control group on Day 45, pregnancy loss for cows with and without accessory corpora lutea was evaluated only in the Deslorelin group. In the Deslorelin group, pregnancy losses between Days 45 and 90 was lower ($P < 0.05$) for cows that formed an accessory CL (0%; 0/36) compared to cows that did not form an accessory CL (16.1%; 5/31). The reduction in pregnancy losses between Days 45 and 90 in cows with accessory CL was consistent regardless whether there was one CL at Day 27 (i.e., no accessory CL at Day 45: 3/10 lost pregnancy between Days 45 and 90; accessory CL at Day 45: 0/22 lost pregnancy between Days 45 and 90) or more than one CL at Day 27 (i.e., no accessory CL at Day 45: 2/20 lost pregnancy between Days 45 and 90; accessory CL at Day 45: 0/15 lost pregnancy between Days 45 and 90).

4. Discussion

A deslorelin implant (2.1 mg) on Day 27 of pregnancy in lactating dairy cows increased the number of corpora lutea, increased plasma progesterone concentrations, reduced ovarian follicular growth, but did not reduce pregnancy loss as a treatment main effect. However, deslorelin treatment did affect pregnancy loss depending upon formation of accessory corpora lutea (i.e., presence of additional CL on Day 45 not present at Day 27). Cows treated with the deslorelin implant on Day 27 that formed accessory corpora lutea had a reduced pregnancy loss between Days 45 and 90 compared to treated cows without an accessory CL.

In the present study, a deslorelin implant on Day 27 increased the number of corpora lutea and increased plasma progesterone concentrations on Day 45, compared to untreated control cows. Cows in the Deslorelin group with an accessory CL had higher plasma progesterone concentrations on Day 45 than cows in the Control group (10.7 versus 6.3 ng/mL, respectively). However, only 45% of the cows in the Deslorelin group had accessory corpora lutea. In beef cows that had the contralateral ovary and the original CL removed on Day 26 of pregnancy, a single injection of hCG between Days 28 and 31 induced a CL in the remaining ovary ipsilateral to the pregnant horn in 50% of the cases [14]. Cows that did not respond were treated again after Day 36 and 90% formed a CL. Pregnancy was maintained in 100% of the cows treated with hCG after Day 36, but only 50% of pregnancies were maintained if CL induction was before Day 36. Maintenance of pregnancy was associated with higher progesterone concentrations in serum. The present study examined effects of additional accessory CL not replacement of the original CL. However, cows treated with a deslorelin implant that formed accessory CL had no pregnancy losses and a higher concentration of progesterone at Day 45 compared to those cows that did not form an accessory CL. Administration of different doses of a deslorelin implant, including the 2.1 mg implant, 5 days after ovulation resulted in ovulation of the first wave dominant follicle and induced accessory corpora lutea in all the cows [24]. The occurrence of accessory corpora lutea probably would have occurred with a greater frequency if the deslorelin implant had been inserted around Day 23 after insemination, according to the distribution of estrus after insemination in lactating dairy cows [31]. In high-producing, lactating dairy cows with three follicular waves, the third wave starts at Day 20 and estrus is observed at Day 25 [32]. These cows would likely be responsive to the deslorelin implant when given at Day 23. The disadvantage of administering the deslorelin implant on Day 23 is that current technology, including ultrasonography, does not allow for an accurate diagnosis at this stage such that all cows would have to be implanted.

Use of the GnRH agonist implant was to downregulate follicle development and induce accessory CL. Suppression in follicle development cannot be achieved with a single injection of GnRH [33]. Whether steroidogenic differences exist between CL induced by GnRH versus a deslorelin implant cannot be determined from this study. In the present study, follicular growth, as evaluated by the numbers of class 2 and class 3 ovarian follicles, was reduced in cows treated with a deslorelin implant compared to untreated control cows. The suppression of follicular growth was in agreement with previous studies using the same deslorelin implant dose during the early postpartum period [33] or at 5 days after ovulation [24] or when smaller doses of the deslorelin implant were used for induction of ovulation [22,23]. However, in the present study, only 20% of the cows had follicular suppression (complete absence of class 2 and class 3 follicles) on Day 45, and follicular suppression did not affect pregnancy losses between Days 45 and 90. Follicular development can also be influenced by location of the CL of pregnancy. The number of class 2 follicles was reduced in the ovary containing the CL ipsilateral to the pregnant uterine horn after Day 22 of gestation, and size of the largest follicle was greater in the ovary contralateral to the CL-bearing ovary [21,34,35]. Thus, a localized suppression in follicular development of pregnant cows also may have contributed to the lower rate of accessory CL formation (i.e., 45%) in response to the deslorelin implant.

Among cows non-pregnant at Day 45 within the Deslorelin group, almost 40% of the cows did not have a CL and 50% had follicular suppression as compared to 85.7 and 0%, respectively, for the non-pregnant control group. A higher percentage of the deslorelin treated cows appeared to regress their CL spontaneously and had not yet ovulated due to the continued suppression of follicular development by the deslorelin implant. Suppression of follicular development after administration of a 2.1 mg deslorelin implant delays return to estrus [23] and would further increase the calving to conception interval in cows that lost a pregnancy. In a prior study, administration of a 2.1 mg deslorelin implant on Day 5 after ovulation was associated with a persistent second wave dominant follicle; the third-wave ovulatory follicle was not selected until approximately Day 37. Consequently the interestrous interval was extended [24].

Overall, administration of a 2.1 mg deslorelin implant on Day 27 of gestation did not reduce pregnancy loss between Days 27 and 45 or between Days 45 and 90 of pregnancy in lactating dairy cows. Because accessory corpora lutea formation was not evaluated acutely after treatment (i.e., at Days 27 or 29), it was not possible to compare pregnancy losses between Days 27 and 45 in cows with and without accessory corpora lutea. For example, a cow that formed an accessory CL but retuned to heat prior to Day 45 would not be detected as a cow with an accessory CL. However, because accessory corpora lutea were evaluated on Day 45, pregnancy losses were evaluated between Days 45 and 90 in cows with and without accessory corpora lutea. Cows that formed accessory corpora lutea, when treated with a 2.1 mg deslorelin implant on Day 27 of pregnancy and were pregnant at Day 45, had a reduced pregnancy loss at Day 90 (0%) compared to cows that did not form accessory corpora lutea (16.1%). This finding was in agreement with a previous study in which 49 lactating dairy cows carrying singletons and that had two corpora lutea did not experience any pregnancy loss between Days 38 and 90 of pregnancy [5]. In addition, progesterone supplementation for 28 days starting between Days 36 and 42 of gestation reduced pregnancy losses when evaluated at Day 90 in lactating dairy cows [36]. In contrast, cows with two CL retained fewer pregnancies than those with one CL [38]. However, there was no difference in progesterone concentrations between cows with two versus one CL; although, retention of pregnancies to Week 9 was associated positively with serum progesterone concentrations at Week 5. Occurrences of accessory corpora lutea in pregnant cows of the control group at Day 45 (i.e., 7/87 or 8%) in the present study could have been due to a mistake in diagnosis of accessory corpora lutea. Alternatively, the incidence of estrus during pregnancy was reported to be 5.7% but not associated with an ovulation or metestrous bleeding [39]. Whether spontaneous ovulation, with or without expression of estrus, is a possibility in today's high-producing dairy cow is an intriguing question.

There seems to be a local relationship between the fetal/placental unit and the ovary bearing the CL. Maintenance of pregnancy after removal of the natural CL was more efficient when a CL was induced in the ovary ipsilateral to the pregnant uterine horn [14,37]. In cows of the Deslorelin group, that formed accessory corpora lutea and were examined for pregnancy at Days 45 and 90, 56.4% of the accessory corpora lutea occurred in the ovary ipsilateral to the pregnant horn and 43.6% in the contralateral ovary, but all the cows with accessory corpora lutea maintained pregnancy. Therefore, no difference in pregnancy loss could be detected between cows that formed accessory corpora lutea in the contralateral versus the ipsilateral ovary.

In summary, administration of a 2.1 mg deslorelin implant on Day 27 of pregnancy in lactating dairy cows increased the number of corpora lutea, increased plasma progesterone concentrations, and reduced follicular development on Day 45 but failed to reduce pregnancy losses between Days 27 and 45 or Days 45 and 90. However, cows treated with the deslorelin implant that had accessory corpora lutea at Day 45 had a reduced pregnancy loss at Day 90. Further research is warranted to evaluate the effect of inducing accessory CL development in a higher proportion of treated cows to minimize late embryonic and early fetal losses. Follicular suppression did not appear to be beneficial and delayed ovulation in non-pregnant cows at Day 45.

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