2004

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Ability of CIDRs or Melengestrol Acetate to Initiate Estrous Cycles in Early Postpartum Beef Cows.

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BEEF 2004 – 15

Summary

Postpartum anestrous interval in beef cows is a major factor contributing to reproductive failure during a defined breeding season. Our objectives were to determine the ability of a controlled internal drug-releasing device (CIDR), or melengestrol acetate (MGA) to induce ovulation and to eliminate short estrous cycles. Multiparous beef cows (n = 75) were equally assigned by age, days postpartum, body condition, and body weight to one of three treatments: CIDR, MGA, or control. All cows were fed carrier (2 lbs•cow^{-1}•day^{-1}) with MGA (0.25 mg/lb) or without MGA for 7 days (day -6 to 0). On day -6, CIDR were inserted and were removed on d 0. Estrous behavior was monitored continuously from day -6 until 29 using HeatWatch electronic mount detectors. Blood was collected three times weekly from day -6 to 29. Treatment influenced (P = 0.03) the percentage of cows that were detected in standing estrus. Beginning on d 2, more CIDR-treated cows had exhibited standing estrus compared to control cows, but CIDR- and MGA-treated cows did not differ. The percentage of CIDR-treated cows that had ovulated was greater (P < 0.05) than the percentage of MGA-, or control-treated cows beginning on day 4. The percentage of cows that exhibited standing estrus before the first postpartum ovulation (CIDR = 65%, MGA = 57%, control = 30%) did not differ (P = 0.09) among treatments. Luteal lifespan following the first ovulation postpartum and the percentage of cows with a normal luteal lifespan (progesterone > 1 ng/mL for ≥ 10 d) was greater (P < 0.01) in CIDR-treated cows (14.0 ± 0.8 days; 20/20, 100%) compared with MGA- (6.2 ± 1.0 days; 3/13, 23%), or control-treated cows (6.1 ± 0.9 days; 4/17, 24%). In the present study, treatment of early postpartum suckled beef cows with CIDR-induced ovulation and initiated estrous cycles with a normal luteal lifespan in more cows than treatment with MGA, and treatment with MGA did not induce ovulation earlier than control cows.

Introduction

The anestrous postpartum interval is a major contributing factor to cows failing to become pregnant and calving on a yearly interval. In addition, a short luteal phase can further delay the interval from calving to conception and usually occurs following the first postpartum ovulation. Treatment with some progestins can induce ovulation in postpartum anestrous cows, shortening the anestrous postpartum interval (Yavas and Walton, 2000; Lucy et al., 2001), and treatment with some progestins before the first postpartum ovulation reduced or eliminated the occurrence of a short luteal phase (Smith et al., 1987; Zollers et al., 1989). Therefore, many estrous synchronization protocols have included progestin treatment; however, all progestins do not have the same biological response. More specifically, 46% of anestrous beef cows fed melengestrol acetate (MGA), an orally active progestin, before GnRH-induced ovulation had a normal luteal phase, compared with 100% of cows exposed to progesterone for the same time period (Smith et al., 1987). Because different progestins have been used interchangeably in estrous synchronization protocols, the objectives of the present study were to determine the ability of progesterone or MGA to induce ovulation in postpartum anestrous beef cows, and to determine the ability of each to decrease or eliminate the occurrence of a short luteal phase following ovulation.

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Materials and Methods

Experimental Design. Postpartum multiparous (n = 75) crossbred beef cows at the Fort Keogh Livestock and Range Research Laboratory were divided equally into three treatment groups [MGA (0.5 mg•cow^{-1}•day^{-1}), controlled internal drug-releasing device (**CIDR**; 1.9 g of progesterone; InterAG, Hamilton, NZ), and control] according to age (range 4 to 11 yr), days postpartum (range 9 to 45 days), cow body condition score (1 = emaciated and 9 = obese; range 4 to 6.5), and post calving body weight (range 445 to 704 kg). Calves were maintained with cows at all times and allowed to suckle without restriction. Cows that had initiated estrous cycles before the start of treatment were removed from the study (MGA = 7; CIDR = 3; control = 3). In addition, one animal in the MGA group ovulated during MGA treatment and was removed from the study, but animals that exhibited standing estrus but did not ovulate were left in their respective treatment.

Cows were fed carrier (wheat middlings pellets, United Agri Products, Miles City, MT) 2 lbs•cow^{-1}•d^{-1} with MGA (0.25 mg/lb) or without MGA for 7 days (day -6 through day 0). Controlled internal drug-releasing devices (1.9 g progesterone per device) were inserted into the vagina of cows on the first day of treatment (day -6) and were removed on day 0. All cows were individually fitted with estrous detection transmitters and monitored for estrous behavior continuously from day -6 until day 29 with the HeatWatch Estrous Detection System (DDx, Inc., Denver, CO). Cows were considered to be in standing estrus when three mounts of 2 seconds or longer in duration were recorded within a 4-hour period.

Blood samples were collected via puncture of a tail vessel three times weekly for determination of concentrations of progesterone. Blood was allowed to clot, stored a 4°C for 24 hours, centrifuged at 2000 x g for 30 minutes and serum collected. Serum was stored at -20°C untilled assayed for progesterone.

Statistical Analysis. Luteal lifespan was analyzed for an effect of treatment by ANOVA using SAS (proc GLM; SAS Inst. Inc., Cary, NC). When the F statistic was significant ($P < 0.05$), a mean separation was performed using the least significant difference test. The percentage of cows exhibiting estrus before an increase in progesterone and the percentage of cows with a normal length luteal lifespan (progesterone > 1 ng/mL for ≥ 10 days) were analyzed for and effect of treatment using categorical data modeling in SAS (Proc Catmod). To determine differences in the distribution of the response to the different treatments, the percentage of animals detected in standing estrus, and the percentage of animals with elevated progesterone (> 1 ng/mL) were analyzed for an effect of treatment, day, and treatment by day interaction using analysis of repeated measures of categorical data.

Results and Discussion

There were no significant differences among treatments in days postpartum, body condition score, or weight at the initiation of treatment (Table 1). A greater ($P < 0.05$) percentage of CIDR-treated cows had exhibited standing estrus on day 2 after treatment withdrawal compared with control-treated cows, but beginning on day 14 no significant difference was detected between CIDR- and control-treated cows. There was a tendency ($P = 0.07$), from day 4 through 10, for the percentage of CIDR-treated cows that had exhibited estrus to be greater than the percentage of MGA-treated cows that had exhibited estrus. The percentage of MGA- and control-treated cows that exhibited standing estrus did not differ on any day of the experiment.

Peripubertal beef heifers treated with MGA for 8 days, increased proportion of heifers that initiated estrous cycles following treatment withdrawal compared with untreated controls (Imwalle et al., 1998). In contrast, when postpartum anestrous beef cows were treated with MGA for 14 days only 13% ovulated within 7 days of treatment withdrawal (2/16, Perry et al., 2002). In the present study, ovulation was defined as occurring 4 days before circulating concentrations of progesterone were greater than 1 ng/mL. The percentage of CIDR-treated cows that ovulated was greater ($P < 0.05$) than the percentage of MGA-, or control-treated cows that ovulated beginning on day 4 after treatment withdrawal. On day 18, the cumulative percentage of CIDR- and control-treated cows that had ovulated did not differ ($P = 0.08$), and no difference was detected between CIDR-treated cows and MGA- ($P = 0.19$) treated ($P = 0.58$) cows on day 22 (Figure 2). The

percentage of cows that ovulated was not different between control- and MGA-treated cows on any day of the experiment (Figure 2).

Differences in the response of early postpartum anestrous beef cows to different progestins may be explained by the ability of progestins to increase LH pulse frequency and cause the formation of a persistent follicle. When early postpartum anestrous non-suckled (Williams et al., 1983) and anestrous suckled (Garcia-Winder et al., 1986) beef cows were treated with low doses of a progestin LH pulse frequency increased compared to non-treated controls. In addition, exposure of peripubertal heifers to a low dose of norgestomet increased LH pulse frequency, stimulated follicular development, and resulted in formation and ovulation of persistent follicles (Anderson et al., 1996). Treatment of peripubertal heifers with MGA (0.5 $mg \bullet cow^{-1} \bullet d^{-1}$) for 7 days increased LH pulse frequency following treatment withdrawal (Imwalle et al., 1998), but feeding MGA (0.5 $mg \bullet cow^{-1} \bullet d^{-1}$) for 14 days to early postpartum anestrous beef cows did not result in formation of persistent follicles (Perry et al., 2002). In contrast, treatment of early postpartum anestrous dairy cows with low concentrations of progesterone (CIDR) resulted in increased LH pulse frequency compared with untreated controls (Rhodes et al., 1997).

A more synchronous rise in concentration of progesterone occurred following treatment in CIDR-treated cows compared with other treatments (Figure 3). However, no difference (P = 0.32) was detected among treatments in the percentage of cows that exhibited standing estrus before an increase in progesterone (65%, 57%, and 30% for CIDR, MGA, and control, respectively).

Progesterone treatment is necessary for establishment of the normal timing of uterine $PGF_{2\alpha}$ secretion. In the present study, only cows that had progesterone > 1 ng/mL were used to determine luteal lifespan and the percentage of cows with a normal length luteal lifespan (progesterone > 1 ng/mL for $\geq$ 10 days). Following the first ovulation postpartum, CIDR-treated cows had a longer luteal lifespan than MGA- or control-treated cows (Table 2), and the percentage of cows that had a normal length luteal phase ($\geq$ 10 days) was greater (P < 0.01) in CIDR-treated cows than in MGA- or control-treated cows (Table 2).

Treatment-induced ovulation was defined as ovulation occurring within 5 days of treatment withdrawal (increase in concentration of progesterone > 1 ng/mL on days 5 to 10) for CIDR- and MGA-treated cows and all ovulations in control treated cows. Following treatment-induced ovulation, a longer luteal lifespan (P < 0.01) was detected in CIDR-treated cows than in MGA- or control-treated cows (Table 2). The percentage of cows with a normal ($\geq$ 10 d) luteal lifespan following treatment-induced ovulation was greater (P < 0.01) in CIDR-treated cows than MGA- or control-treated cows. This is consistent with previous reports in which treatment of anestrous postpartum beef cows with 0.5 $mg \bullet cow^{-1} \bullet d^{-1}$ of MGA for 5 days before GnRH-induced ovulation resulted in only 46% of cows having a normal luteal phase, but treatment with progesterone for 5 days before GnRH-induced ovulation resulted in 100% of cows having a normal luteal phase (Smith et al., 1987). Thus, the normal dose of MGA (0.5 $mg \bullet cow^{-1} \bullet d^{-1}$) is not adequate to prevent the earlier secretion of uterine $PGF_{2\alpha}$ following the first postpartum ovulation.

Implications

The anestrous postpartum period and the occurrence of short estrous cycles are major factors in cows not conceiving during a defined breeding season, and treatment with some progestins before the breeding season can successfully induced ovulation and eliminated the occurrence of short estrous cycles. However, in the current study MGA was not as effective at inducing ovulation in early postpartum anestrous beef cows as CIDR treatment. In addition, treatment with a CIDR resulted in a normal luteal lifespan following ovulation compared with a short luteal phase in cows treated with MGA. Therefore, not all progestins are equally effective at inducing ovulation and eliminating short estrous cycles in early postpartum anestrous cows.

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Table 1. Days postpartum, body condition score, and weight at the initiation of treatment

	CIDR[a]	MGA[b]	Control
No. of cows	22	17	22
Days postpartum (range)	31 ± 1.7 (12 to 42)	30 ± 2.0 (12 to 45)	30 ± 1.5 (9 to 39)
Body condition score (range)[c]	4.9 ± 0.2 (4 to 6)	4.9 ± 0.2 (3.5 to 6.5)	4.9 ± 0.2 (3.5 to 6)
Weight, kg (range)	581 ± 16.4 (477 to 684)	583 ± 17.3 (475 to 704)	571 ± 16.4 (445 to 692)

[a]Controlled internal drug–releasing device.
[b]Melengestrol acetate (0.5 mg MGA•cow^{-1}•d^{-1}).
[c]Body Condition Score – scale 1 to 9

Table 2. Effect of treatment on luteal lifespan and percentage of cows with a normal luteal lifespan following their first ovulation postpartum and ovulation within 5 days of treatment withdrawal

	First postpartum ovulation					
	CIDR[a]	MGA[b]	Control[d]	CIDR vs MGA	CIDR vs Control	MGA vs Control
No. of cows	20	13	17	- - - - - - - - P-value - - - - - - - -		
Luteal lifespan, days[e]	14.0 ± 0.8	6.2 ± 1.0	6.1 ± 0.9	< 0.01	< 0.01	= 0.98
Cows with normal luteal lifespan, %[f]	100	23	24	< 0.01	< 0.01	= 0.97

	Ovulation within 5 days of treatment withdrawal					
	CIDR[a]	MGA[b]	Control[c]	CIDR vs MGA	CIDR vs Control	MGA vs Control
No. of cows	20	5	17	- - - - - - - - P-value - - - - - - - -		
Luteal lifespan, days[d]	14.0 ± 0.8	4.4 ± 1.1	6.1 ± 0.9	< 0.01	< 0.01	= 0.29
Cows with normal luteal lifespan, %[e]	100	0	24	< 0.01	< 0.01	= 0.15

[a]Controlled internal drug–releasing device.
[b]Melengestrol acetate (0.5 mg MGA•cow^{-1}•day^{-1}).
[c]Control animals
[d]Interval from first day of concentrations of progesterone were > 1 ng/mL to day concentrations of progesterone decreased to < 1 ng/mL.
[e]Percentage of animals with a luteal lifespan (i.e., concentrations of progesterone > 1 ng/mL) of 10 days or longer.

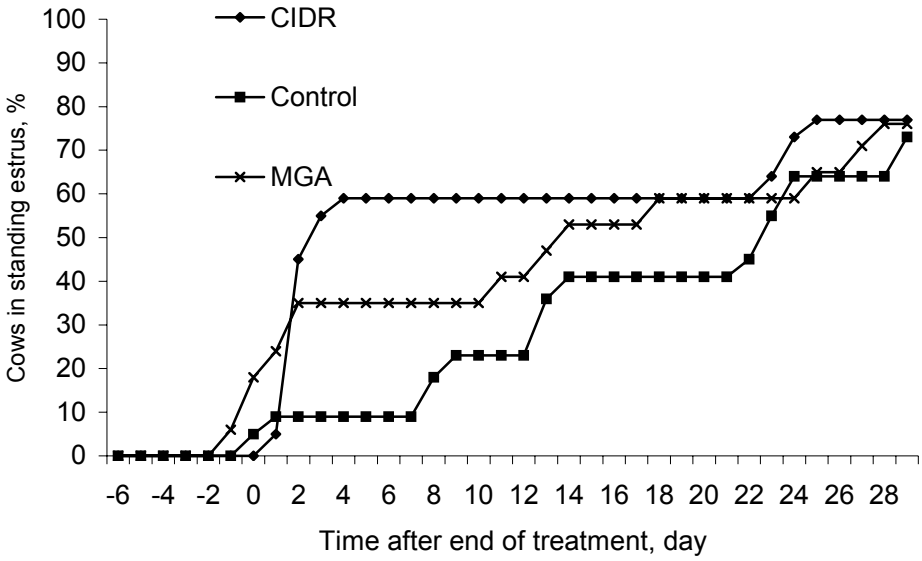

Figure 1. Effect of treatment on cumulative percentage of cows detected in standing estrus by day of treatment (day 0 = last day of feeding melengestrol acetate [MGA], and day of controlled internal drug-releasing device [CIDR] removal). Treatment $P = 0.03$; Day $P < 0.01$; Treatment x Day $P < 0.01$.

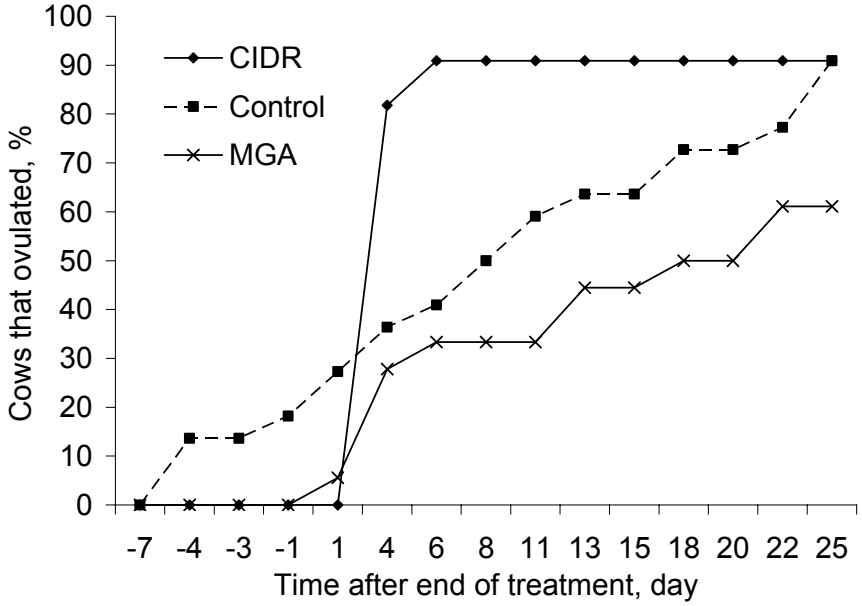

Figure 2. Effect of treatment on the cumulative percent of animals that had ovulated (ovulation is shown as having occurred 4 days before the first day circulating concentrations of progesterone were > 1 ng/mL) by day of treatment (day 0 = last day of feeding melengestrol acetate [MGA], and day of controlled internal drug-releasing device [CIDR] removal). Treatment $P < 0.01$; Day $P < 0.01$; Treatment x Day $P < 0.01$.

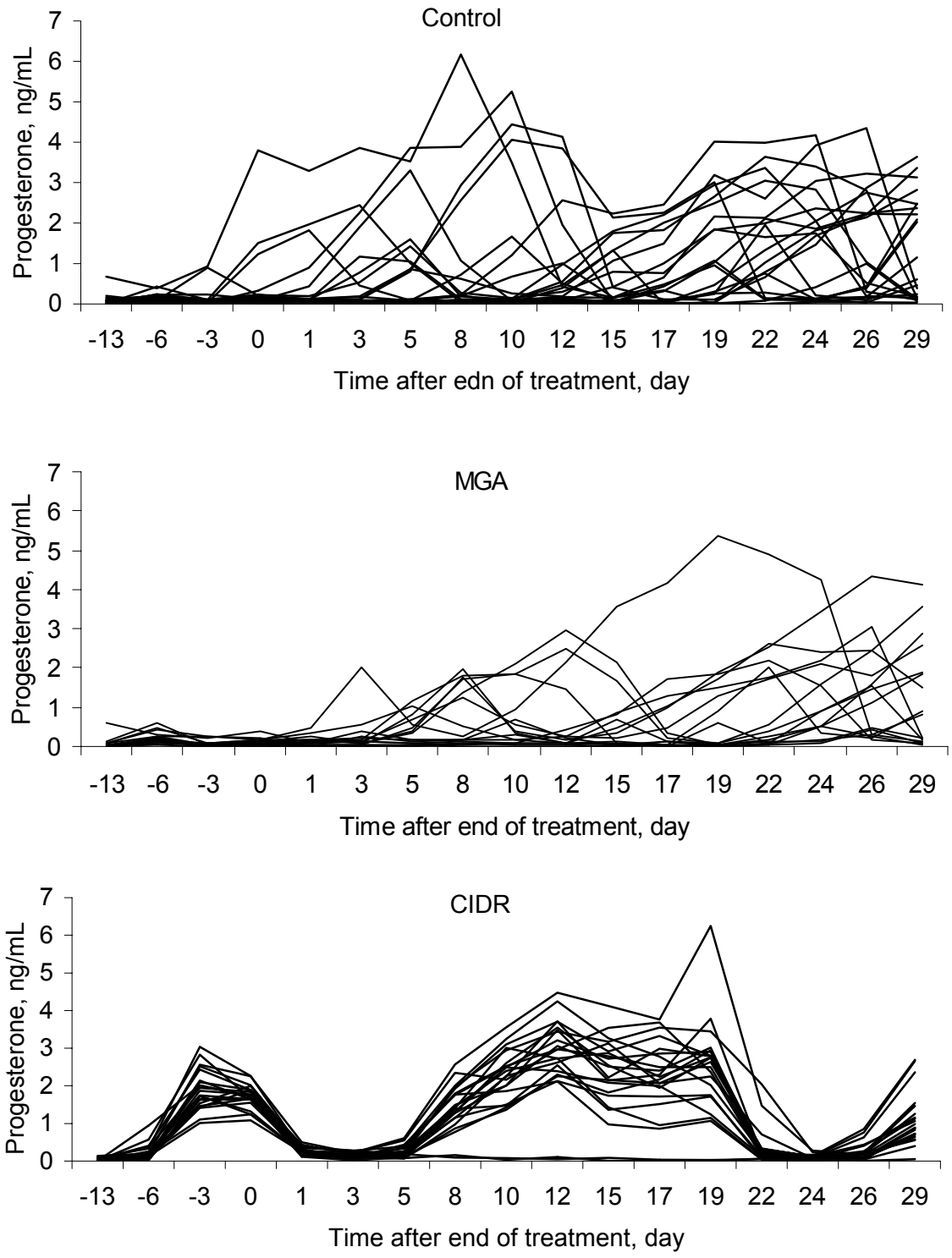

Figure 3. Circulating concentrations of progesterone (collected three times weekly) for cows receiving no treatment (control), 0.5 mg MGA•cow^{-1}•day^{-1} (MGA), or controlled internal drug-releasing device (CIDR; from day –6 to 0). Day 0 = last day of feeding MGA and day of CIDR removal.