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Regulation of LH Secretion by Progesterone in Heifers

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Release of LH is regulated more by circulating amount of progesterone than by the magnitude of shift in progesterone. Understanding interactions of reproductive hormones advances development of management tools for producers to control estrous cycles of beef females.

Summary

Heifers experienced either a: 1) large magnitude of change in progesterone; 2) medium magnitude of change in progesterone; or 3) small magnitude of change in progesterone. During the 24 hours following the progesterone shift, heifers with the large magnitude progesterone shift had a greater LH pulse frequency than heifers with a medium or small magnitude of shift in progesterone. Despite the large or medium magnitude progesterone shift, LH pulse frequency did not differ from heifers in which a small change in progesterone occurred. We conclude that amount of progesterone in circulation is more important in regulation of LH secretion than magnitude of shift in amount of progesterone.

Introduction

Secretion of LH is an important component of cattle reproduction because it is necessary for the development of ovarian follicles, estradiol production, ovulation and the formation of corpora lutea. Pattern of LH secretion changes during the estrous cycle of cattle and is influenced by concentration of progesterone and estradiol.

Regulation of LH secretion by progesterone is relatively acute, as within 6 hours following a shift from a small to large dose of progesterone, a significant change in pulse frequency of LH was observed. Understanding the endocrine mechanisms by which reproductive hormones, such as progesterone and LH, interact will enhance development of new management techniques to control estrous cycles of beef cattle.

The objective of this study was to determine whether magnitude of shift in progesterone or circulating amount of progesterone is more important in regulating LH secretion during the 72 hours after the progesterone shift.

Materials and Methods

Seventeen post-pubertal beef heifers (MARC III; 1/4 Hereford, 1/4 Angus, 1/4 Pinzgauer and 1/4 Red Poll) were synchronized to a common day of estrus with two i.m. injections of

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$PGF_{2\alpha}$ (25 mg Lutalyse®; The Upjohn Co., Kalamazoo, MI) given 10 days apart. During the eighth day of their estrous cycle, heifers were injected with a single dose of $PGF_{2\alpha}$ to regress existing corpora lutea and treatments were initiated (day 0). From day 0 to day 4, heifers were treated with various doses of progesterone via progesterone-releasing intravaginal devices (.5 to 2 PRIDs; Sanofi Animal Health Inc., Paris, France) followed by a large dose of progesterone (2 PRIDs) from day 4.5 to day 7. Change in dose of progesterone occurred on the morning of day 4, within 4 hours following collection of the day's blood sample. At this time, PRIDs were removed from each heifer followed by immediate insertion of 2 PRIDs.

Based on mean magnitude of concentration change of progesterone in circulation from day 0 to day 4 relative to day 4.5 to day 7, heifers were placed into one of the following groups: 1) large magnitude of change in concentration of progesterone (3.1 ng/ml; n=6); 2) medium magnitude of change in concentration of progesterone (2.5 ng/ml; n=6); or 3) small change in concentration of progesterone (0.5 ng/ml; n=5).

Blood Collection and Radioimmunoassays

Jugular blood samples were collected every 12 hours from day 0 to day 7 and used to assess circulating concentrations of estradiol and progesterone. Jugular blood samples were also collected via cannulae every 15 minutes from day 3.5 to day 7 to assess concentrations of LH in circulation.

Table 1. Mean concentration of LH, LH pulse frequency and amplitude, and mean magnitude of change in amount of progesterone of heifers with a large, medium, or small magnitude of shift in amount of progesterone.

		Group		
Item		LG	MD	SM
Mean magnitude of change in progesterone (ng/ml)[a]		3.1[b]	2.5[c]	0.5[d]
Mean LH (ng/ml):	Pre-shift -12 to 0 hours	2.1[b]	1.7[c]	1.2[d]
	Post-shift 0 to 24 hours	1.2[b]	1.2[b]	1.0[b]
	Post-shift 24 to 48 hours	1.1[b]	1.1[b]	1.1[b]
	Post-shift 48 to 72 hours	1.2[b]	1.4[b]	1.4[b]
LH pulses/12 h:	Pre-shift -12 to 0 hours	9.7[b]	6.5[c]	3.4[d]
	Post-shift 0 to 24 hours	5.4[bx]	2.8[c]	2.9[bcy]
	Post-shift 24 to 48 hours	3.3[b]	2.9[b]	3.5[b]
	Post-shift 48 to 72 hours	4.3[b]	4.8[b]	5.3[b]
LH pulse amplitude (ng/ml):	Pre -shift -12 to 0 hours	1.4[b]	1.4[b]	1.5[b]
	Post-shift 0 to 24 hours	0.8[b]	0.9[b]	0.8[b]
	Post-shift 24 to 48 hours	0.6[b]	0.5[b]	1.7[c]
	Post-shift 48 to 72 hours	0.9[bx]	1.5[bcy]	1.6c

[a]Mean change in concentration of progesterone from day 0 to 4 relative to day 4.5 to 7 of the experiment.
[b,c,d]Means within a row without common superscripts differ $P \leq .05$.
[x,y]Means within a row without common superscripts differ $P < .10$.

Results

Progesterone, secreted by a corpus luteum, regulated the estrous cycle in cattle such that in the presence of increased concentrations of progesterone, pulse frequency of LH is low and estrus and ovulation are inhibited. Treatment of beef females with doses of commercially used progestins (norgestomet, melengestrol acetate or progesterone) in the absence of a corpus luteum is sufficient to inhibit ovulation. However, it does not regulate pulse frequency of LH like the greater concentrations of progesterone present in circulation during the luteal phase of an estrous cycle. Consequently, LH pulses are more frequent during treatment with small doses of progestins than during the luteal phase of an estrous cycle. Pulse frequency changes affect ovarian follicle development and their secretion of estradiol (see "Prolonged Elevated Concentration of Estradiol Do Not Affect Conception Rates in Beef Cattle" in this NE Beef Report).

Researchers have hypothesized that magnitude of change in progesterone concentration (or dose of progestin) is involved, along with amount of progesterone, in regulation of pulse frequency of LH. This hypothesis was suggested because an evaluation of LH pulse pattern of individual animals from a previous study in our laboratory indicated a possible relationship between magnitude of shift in progesterone dose and duration of cessation of pulsatile LH secretion.

In this study, mean magnitude of change in progesterone concentration from day 0 to day 4 relative to day 4.5 to day 7 differed across groups ($P < .02$; Table 1). There were group x day interactions for mean concentrations of progesterone ($P < .001$; Figure 1) and estradiol ($P < .01$) during treatment (day 0 to day 7). Pulse frequency and mean concentration of LH differed ($P < .05$) across groups during the 12 hours before the shift in progesterone (Table 1). Pulse frequency of LH was greater ($P = .05$) among heifers with the large magnitude of change in concentration of progesterone as compared with the medium during the first 24 hours following the shift in progesterone concentration. Pulse frequency of LH tended to be greater ($P < .10$) during the first 24 hours following the shift in progesterone concentration among heifers with the large magnitude of change as compared with the small magnitude of change. From 24 to 48 hours and 48 to 72 hours following the shift in progesterone concentration, pulse frequency of LH was similar across groups. Mean concentration of LH was similar across groups during the first 24 hours and from 24 to 48 hours and 48 to 72 hours following the shift in progesterone.

Before the shift in dose of progesterone, there was an inverse relationship

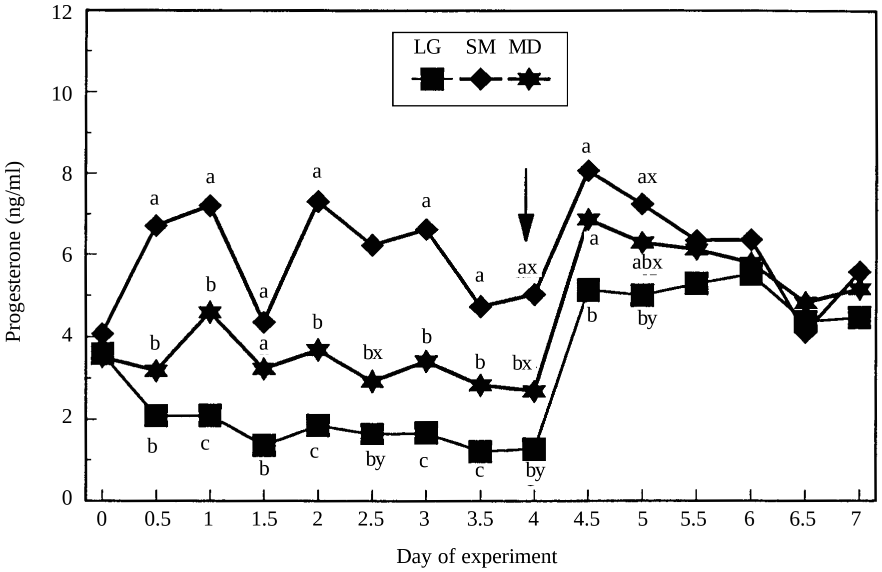

Figure 1. Concentrations of progesterone in circulation of heifers with a large (LG), medium (MD) or small (SM) magnitude of change in concentration of progesterone. Arrow indicates time of shift from various doses to a relatively large dose of progesterone. There was a group x day interaction (P < .01). Differences in progesterone across groups within day are indicated by uncommon superscript letters (^{a,b}P < .05; ^{x,y} P< .10).

between circulating concentration of progesterone and estradiol (data not shown). Heifers with lesser circulating concentration of progesterone and increased pulse frequency of LH (Table 1) likely developed large dominant ovarian follicles, resulting in the increased concentrations of circulating estradiol. Additionally, circulating concentrations of progesterone differed across groups (Figure 1) before the shift in progesterone. Differences in frequency of LH pulses, before the shift in progesterone amount, can likely be attributed to differences in amount of both progesterone and estradiol. Previous research has shown that when both progesterone and estradiol are present in circulation, a greater suppression of LH pulse frequency is achieved than with either steroid alone. Following the progesterone shift, however, concentration of estradiol was similar among the three groups of heifers. Therefore, differences in frequency of LH pulses following the shift may be attributed solely to progesterone and not estradiol.

Heifers experiencing a large magnitude of change in progesterone concentration had less circulating progesterone and, subsequently, greater pulse frequency of LH during the first 24 hours following the shift in progesterone concentration. Apparently, the large magnitude of shift in progesterone concentration in these heifers did not affect pulse frequency of LH, but rather frequency of LH pulses during the first 72 hours following the progesterone shift was regulated by amount of progesterone in circulation and not the magnitude of the shift. Heifers with either medium or small magnitudes of shift in progesterone had similar concentrations of progesterone in circulation following the shift. Subsequently, frequency of LH pulses was similar among heifers of all three groups following the progesterone shift irregardless of the magnitude of the shift. Based on these results, it appears that amount of progesterone, rather than magnitude of shift, is more important in regulation of pulsatile secretion of LH during the 72 hours after the shift in progesterone. An acute shift in amount of progesterone, however, appears to regulate pulsatile secretion of LH to some extent as an acute shift in amount in circulation dramatically affects secretion of LH. This contrasts the gradual changes observed in release of LH during a typical estrous cycle, when changes in progesterone concentration also are relatively subtle and gradual.

Pulse amplitude of LH was similar across groups during the 12 hours before and the first 24 hours following the shift in progesterone (Table 1). From 24 to 48 hours following the shift in progesterone concentration, pulse amplitude of LH was greater (P < .01) among heifers experiencing a small magnitude of change in progesterone as compared with heifers experiencing a large or medium magnitude of change in progesterone. From 48 to 72 hours following the shift, pulse amplitude of LH was greater (P < .05) among heifers with a small magnitude of change in progesterone concentration and tended (P < .10) to be greater among heifers with a medium magnitude of change in progesterone as compared with heifers that had a large magnitude of change in progesterone. These differences in LH pulse amplitude appear to reflect sequential adjustments to the three magnitudes of shift in progesterone. Greater amplitudes of LH pulses resumed earlier following the shift among heifers with the small, followed by the medium and lastly the large magnitude of shift in progesterone.

Results from this study indicate LH pulse frequency appears to be influenced more by amount of progesterone in circulation than by magnitude of shift in progesterone. The LH pulse generator does not appear to be sensitive to different magnitudes of change in amount of progesterone.

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