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Effects of Luteinizing Hormone Releasing Hormone Antagonist On The Bovine Corpus Luteum

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Pulsatile luteinizing hormone release during the follicular phase of the estrous cycle affects size and function of the corpus luteum and is important in achieving optimal cattle pregnancy rates.

Summary

The size and function of the corpus luteum were examined after administration of luteinizing hormone releasing hormone antagonist. Luteinizing hormone releasing hormone antagonist was administered to three animal groups starting: 1) 2 days before the preovulatory luteinizing hormone surge inducing ovulation; 2) at initiation of the preovulatory surge; and 3) 2 days after the preovulatory surge. Although size and function of the corpus luteum were suppressed in all treated groups, the greatest developmental suppression occurred when luteinizing hormone release was blocked 2 days before the preovulatory surge of LH inducing ovulation. Therefore, optimal pregnancy rates in cattle may depend on pulsatile release of LH during the follicular phase of the estrous cycle in addition to that secreted during and after ovulation.

Introduction

The corpus luteum (CL) develops from an ovarian follicle following ovulation and secretes the progesterone required to support pregnancy. It has been widely observed that luteinizing hormone (LH) is essential for the maintenance of progesterone production by bovine luteal cells and recently shown that LH pulse frequency is greater during the follicular phase than the midluteal phase of the estrous cycle. It has also been shown LH secretion is not required to maintain luteal function during the late luteal phase of a cow's estrous cycle.

It is apparent the CL requires a specific endocrine environment and deviations from this can be detrimental for normal development of structure and function of luteal tissue. Presently, information is scarce concerning the role of LH secretion on luteal development and function during the follicular phase and the periovulatory stages of the reproductive cycle. Treatment with luteinizing hormone releasing hormone (LHRH) antagonist to inhibit LH pulses enables the role of LH pulses before, during and after the preovulatory surge of LH on CL development and function to be assessed.

Procedure

Experimental Protocol

This study used 21 postpubertal heifers of composite breeding (1/4 Hereford, 1/4 Angus, 1/4 Redpoll, 1/4 Pinzgauer; 972 lbs). Estrous synchrony was achieved with two injections of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) administered 11 days apart. Heifers were randomly assigned to one of the following treatments: 1) 5% mannitol injections serving as a control; 2) LHRH-Antagonist (LHRH-Ant) starting 2 days before initiation of the preovulatory LH surge; 3) LHRH-Ant at initiation of the preovulatory LH surge; and 4) LHRH-Ant starting two days after the preovulatory LH surge. LHRH-Ant is a synthetic peptide which selectively blocks LH secretion. It was administered subcutaneously to all treated groups every 24 hours at 10μg/kg body weight until day 7 of the estrous cycle. Preovulatory surges of LH were experimentally

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induced in all heifers by intravenous administration of purified bovine LH (preovulatory LH surge = day 0) every 20 minutes for 3 hours beginning 48 hours after the second injection of $PGF_{2\alpha}$ in order achieve an initial concentration of 100 ng/mL and to maintain a concentration of 50 ng/ml. All follicles larger than 5 mm were ablated by transvaginal procedures four days prior to the second treatment of $PGF_{2\alpha}$ utilizing an ultrasonography probe equipped with a needle guide attachment. This ensured synchrony of the waves of ovarian follicular development and that dominant follicles were at the same developmental stage at corpus luteum regression.

Measurements and Sample Collection

Ovulation and development of the CL (size in mm) were monitored by ultrasonography daily until day 12 of the estrous cycle and every other day until day 28. Ovulation was identified as the disappearance of a large ovarian follicle between two consecutive days of ultrasonography. Starting at the time of the second treatment of PGF_{2a} plasma was obtained from blood samples collected every 12 hours until day 28 or the time of subsequent behavioral estrus detection, whichever occurred first. Concentrations of progesterone in plasma were analyzed by radioimmunoassay (RIA). To verify accuracy of exogenous LH treatment, serum was obtained from blood samples collected every 20 minutes starting 2 hours before the first LH treatment and ending 2 hours after the last injection. Serum concentrations of LH were analyzed by RIA.

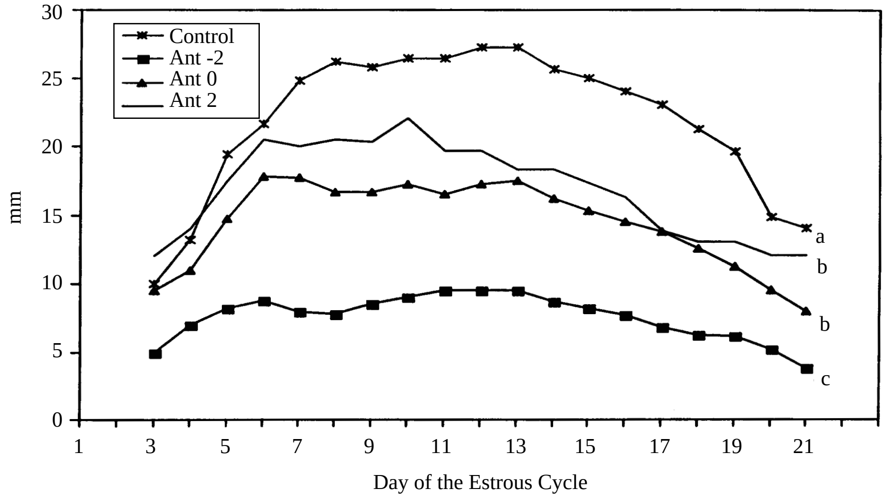

Figure 1. Size of the corpus luteum in heifers treated with LHRH antagonist at different times relative to the preovulatory surge of LH and untreated controls (a,b,c=p<0.01).

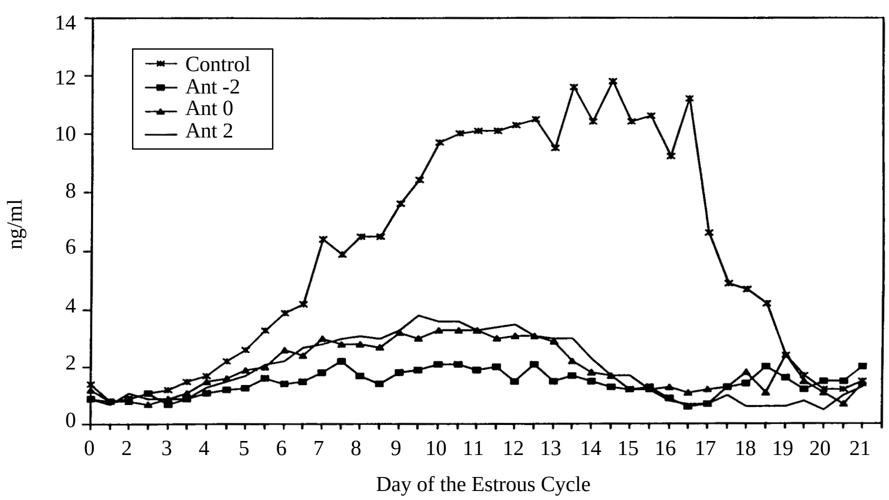

Figure 2. Mean concentrations of progesterone in plasma from heifers treated with LHRH-antagonist at different times relative to the preovulatory surge of LH and untreated controls. Control group is different from treated groups (P<0.01).

Results

Size of Corpus Luteum

Size of the CL was largest (P<.01) in control group heifers and smallest in heifers in which LH release was blocked starting 2 days before the preovulatory surge of LH (Figure 1). Size of the CL in heifers in which LH release was blocked, starting coincident with or 2 days after the preovulatory surge of LH, was less than controls but greater (P<.01) than in heifers in which LH suppression started 2 days before the preovulatory surge of LH. There was no difference (P>.1) in size of the CL among heifers in which LH suppression started coincident with the preovulatory surge of LH or 2 days after the preovulatory surge of LH. Average size of CL was 9.5, 17.5, 21.6 and 28.8 mm (pooled SE = 0.43) for heifers in which LH secretion was blocked starting 48 hours before, at time of initiation or 48 hours after the preovulatory surge of LH and control heifers, respectively.

Progesterone Concentrations

Compared with secretion of progesterone (area under the curve) from the control group, secretion of progesterone was less (P<.01) in heifers where LH release was suppressed prior to, during or after the LH surge (Figure 2). Arbitrary units under the progesterone release curve for heifers in which LH secretion was blocked starting 48 hours before, at the time of initiation or 48 hours after the preovulatory surge of LH and the control group were 19.6, 41.6, 43.6 and 142.2, respectively. There was no difference in function of the CL (P>.1) as determined by arbitrary units of progesterone of heifers in the three groups in which LH secretion was blocked.

Conclusions

Results from this study indicate LH pulses subsequent to the preovulatory LH surge are necessary for development of a CL with similar size and functionality as those observed in control heifers. The influence of LH secretion during late ovarian follicular maturation and early luteal development appear to be additive in developing CL of typical structural size. LH appears to have a differential effect on development and function of the CL in cattle. The effects of LH on luteal function, as evaluated by circulating concentrations of progesterone, appear to be more dramatic than the influence of LH pulses on development of a CL of typical structural size.

Inadequate numbers of LH receptors on both granulosa and thecal cells, due to the absence of LH pulses prior to the preovulatory surge, may account for the smaller luteal structure in which release of LH was blocked 48 hours before the LH surge. Alternatively, the smaller CL in these heifers may be the result of altered populations of luteal cells. Small luteal cells possess functional LH receptors. Large luteal cells do not possess functional LH receptors; however, they will secrete large amounts of progesterone in the absence of LH stimulation. Therefore, it is possible that, in the absence of pulsatile LH secretion during the late stages of ovarian follicular maturation and early luteal development, small luteal cells do not receive the proper stimulus to secrete progesterone and without LH support are not able to develop into large luteal cells that will secrete larger amounts of progesterone. Thecal, granulosal and luteal cells require pulsatile LH support during the periovulatory stages of the estrous cycle for development of a luteal structure with typical size and steroidogenic capacity in cattle.

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