

The Effect of a Sustained-Release Injection of Human Chorionic Gonadotropin on Corpus Luteum Formation and Progesterone Secretion in Beef Heifers

D. J. Kesler* and R. J. Favero

Department of Animal Sciences, University of Illinois, Urbana,
Illinois 61801

ABSTRACT

A sustained-release injection of human chorionic gonadotropin (HCG) was administered to Syncro-Mate B® synchronized beef heifers 12 hours after estrus. The sustained-release formulation doubled the ovulation rate, increased corpora lutea size, increased the incidence of cystic corpora lutea, and tended to increase progesterone concentrations. Sustained release of HCG produced effects similar to larger doses and/or multiple aqueous injections of HCG. The doubling of multiple ovulations may have been a result of availability of persistent follicles caused by the Syncro-Mate B®. The increase in corpora lutea size was partially caused by the more frequent presence of fluid-filled cavities within the corpora lutea (cystic corpora lutea). In summary, the sustained-release injection of HCG accomplished similar effects as larger doses and/or multiple administrations of nonsustained-release formulations of HCG.

INTRODUCTION

There have been several publications demonstrating that the administration of human chorionic gonadotropin (HCG) during metestrus increases corpora lutea size, progesterone synthesis, and fertility (1-3). The enhancement of fertility, however, has not been observed in all

studies (4-6). In order to obtain an optimal effect, large doses of HCG have been administered over several days. These factors (large quantities of HCG and multiple administration times) decrease the likelihood of commercial use of HCG for fertility enhancement.

In addition to enhancement of fertility, the increased progesterone concentrations posttreatment may increase

*Address correspondence to 1207 W. Gregory Drive, Urbana, Illinois 61801.

fertility at a subsequent estrus (5). Data demonstrate that progesterone secretion during the estrous cycle preceding insemination was greater in cows that conceived than those that did not conceive (7,8). Therefore, the advantages of HCG administration during metestrus may be twofold. However, the therapy must be capable of being implemented at one convenient time in order for the procedure to be realized commercially.

The objective of this study was to determine the effectiveness of a single sustained injection of HCG administered at the time of insemination, when cows are already restrained, on increasing corpus luteum size and progesterone secretion.

MATERIALS AND METHODS

Thirty crossbred beef heifers managed on dry lot at the University of Illinois Beef Unit were included in this study. Heifers were selected for the study from a larger group based on being in good body condition and being detected in estrus the month before initiating the study. All heifers were administered Syncro-Mate B®.* Syncro-Mate B® consisted of administering a hydron ear implant containing 6 mg norgestomet. The implant was subcutaneously implanted on the convex surface of the ear. At the same time, treated females were administered a 2 ml intramuscular injection containing 3.0 mg norgestomet and 5.0 mg estradiol valerate in sesame oil. Implants were removed 9 days after implantation and treated females were expected to be in estrus 24–48 hours after implant removal.

Approximately 12 hours after the first detection of estrus, one-half ($n = 15$) of the heifers were administered a sustained-release injection (2 ml) of human chorionic gonadotropin (HCG). Each ml of the injection contained 750 I.U. of HCG. Therefore, HCG-treated heifers received a total dose of 1500 I.U. of HCG. The sustained-release formulation has been demonstrated to release HCG for 3 days (unpublished data). The other one-half of the heifers received no treatment at the time of HCG treatment and served as controls. All heifers were detected in estrus and all HCG injections were administered 2 days after Syncro-Mate B® implant removal.

Six days after the time of the HCG treatment, heifers were bled and serum was harvested and frozen. Ten days after the time of HCG treatment, all heifers were again bled (and serum harvested and frozen) and all were ovariectomized by a sterile surgical procedure

through the flank (10). Ovaries were examined and follicular number and size (surface diameter), corpora lutea number and size (weight), and number of cystic corpora lutea (corpora lutea with cavities) were recorded. Immediately after surgical removal of the ovaries, heifers were administered a therapeutic dose of an antimicrobial (Liquamycin® LA 200®†).

Blood serum was assayed for progesterone concentrations by a validated enzyme immunoassay (11). All qualitative data were analyzed by chi-square analysis (12) and quantitative data were analyzed by nested analysis of variance (13).

RESULTS

Twenty-seven of the heifers had corpora lutea, indicating that they had ovulated subsequent to the synchronized estrus. For those that did not ovulate, one was a control heifer and two were HCG-treated heifers. For the heifers that ovulated, 9 had multiple corpora lutea. Although not significant ($P > 0.15$), twice as many HCG-treated heifers had multiple ovulations as control heifers (Table 1). All but one heifer with multiple corpora lutea had two corpora lutea. The one exception had four corpora lutea.

Mean corpora lutea weights are reported in Table 1. Corpora lutea of HCG-treated heifers with multiple corpora lutea were heavier ($P < 0.01$) than corpora lutea of control heifers. Although heavier, the variation in corpora lutea weights was greater ($P < 0.05$) for HCG-treated heifers than for control heifers. Progesterone concentrations tended to be higher ($P = 0.075$) for HCG-treated heifers with a single corpus luteum than for control heifers with a single corpus luteum on both days 6 and 10.

As reported in Table 2, HCG-treated heifers tended to have fewer ($P = 0.07$) medium-size follicles than control heifers and more ($P < 0.01$) of the corpora lutea from HCG-treated heifers than control heifers were cystic. In heifers with single and multiple ovulations combined, HCG-treated heifers tended ($P = 0.065$) to have higher progesterone concentrations than control heifers.

On day 6, all heifers that had corpora lutea had progesterone concentrations greater than 1.0 ng/ml. For the heifers that did not ovulate, progesterone concentrations in the control heifer were less than 0.5 ng/ml whereas the HCG-treated heifers had mean progesterone concen-

*Rhone Merieux, Inc., Athens, GA.

†Pfizer, Inc., Animal Health Division, New York, NY.

Table 1

Number and Weight of Corpora Lutea and Serum Concentrations of Progesterone on Days 6 and 10 After the Time of HCG Treatment

	Control		HCG	
	Single	Multiple	Single	Multiple
Number ^a	11 (73%)	3 (20%)	7 (47%)	6 (40%)
Weight				
Mean	2.98 g	1.47 g	4.10 g	3.09 g ^b
Variance	.52	.23	3.94 ^c	2.20 ^c
Progesterone ^d				
Day 6	2.31	2.06	3.50 ^e	2.83
Day 10	4.00	3.38	6.23 ^e	5.87

^aThere were 15 heifers per group. One control heifer and two HCG-treated heifers did not ovulate and no corpora lutea were present.

^bCorpora lutea of HCG-treated heifers had more ($P < 0.01$) mass than control heifers.

^cVariance associated with corpora lutea weights was greater ($P < .05$) for HCG-treated heifers than for control heifers.

^dProgesterone concentrations (ng/ml) in the serum.

^eThere tended to be more progesterone secreted by HCG-treated heifers ($P = 0.075$) than for control heifers.

trations of 1.34 ng/ml. Examination of the follicles of these two HCG-treated heifers revealed luteinization of the follicular wall, which may have been the source of the progesterone (14,15).

Blood progesterone concentrations on day 10 (day of ovariectomy) were not correlated ($r = 0.12$; $P > 0.15$)

with corpora lutea weight. In fact, HCG-treated heifers with corpora lutea two standard deviations or greater than the mean of the control heifers (mean 6.8 g; $n = 6$) had progesterone concentrations (5.6 ng/ml) similar ($P > 0.15$) to those (6.5 ng/ml) of HCG-treated heifers that had corpora lutea of similar size to the control heifers (mean = 3.6 g; $n = 7$).

DISCUSSION

This study demonstrates that a single injection of HCG, in a sustained-release format, enhanced the development of corpora lutea and increased progesterone secretion by the corpora lutea in a similar magnitude to multiple injections. The sustained-release injection used in our study increased corpora lutea weight by about 1½ times that of a conventional injection at a similar time (12 hours postestrus; 22). Further, progesterone concentrations were similarly increased with the sustained-release injection as 3.33 times the dose of HCG by conventional injection (2).

All heifers were synchronized with Syncro-Mate B® prior to HCG administration for convenience. This may have been the cause of the multiple corpora lutea observed in this study. Although Syncro-Mate B® effectively synchronizes estrus and ovulation in beef females (9,16–18), there have been studies reporting the presence of persistent follicles in Syncro-Mate B® treated females (19–21). Our data support the presence of per-

Table 2

Incidence of Follicles and Corpora Lutea Cavities in Heifers 10 Days After the Time of HCG Treatment and Progesterone Concentrations on Days 6 and 10

	Control	HCG
Follicles		
0.5–1.5 cm	2.1	0.9 ^a
> 1.5 cm	0.2	0.8
Cystic corpora lutea	15.8 %	57.9 % ^b
Progesterone ^c		
Day 6	2.25	3.19
Day 10	3.87	6.06 ^d

^aHCG-treated heifers tended to have fewer ($P = 0.07$) 0.5–1.5 cm follicles.

^bHCG-treated heifers had more ($P < 0.01$) corpora lutea with fluid-filled cavities (cystic corpora lutea).

^cProgesterone concentrations (ng/ml) in the serum.

^dThere tended to be more progesterone secreted by HCG-treated heifers than for control heifers ($P = 0.065$).

sistent follicles by the presence of a high number of multiple corpora lutea in both control and HCG-treated heifers. HCG doubled the incidence of multiple corpora lutea, apparently ovulating persistent follicles that normally do not ovulate. In addition, fewer medium-size follicles were observed in the HCG-treated heifers. In the two HCG-treated heifers that did not ovulate, the follicles were luteinized and were synthesizing progesterone, which was not detected in the control heifer that did not ovulate. Gonadotropins have been previously demonstrated to luteinize ovarian follicles (14,15).

Although, both corpora lutea weights and progesterone concentrations were increased, in contrast to a previous report (22) they appeared to be independently increased based on the lack of a positive correlation between corpora lutea size and progesterone concentrations. This may have been caused by the higher percentage of cystic corpora lutea in the HCG-treated heifers. Cystic corpora lutea result from ovulations and maintain pregnancy as effectively as normal corpora lutea (23). However, the presence of the fluid-filled cavities in cystic corpora lutea increases their size and weight without increasing the progesterone synthesizing luteal cells.

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