Effect of Prepartum Administration of Growth Hormone-Releasing Factor on Somatotropin, Insulin-Like Growth Factor I, Milk Production, and Postpartum Return to Ovarian Activity in Primiparous Beef Heifers

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ABSTRACT: Forty-one primiparous beef heifers were used over 2 yr to evaluate the effect of prepartum administration of a growth hormone-releasing factor analog (GRF-A) or growth hormone-releasing factor (GRF(1-29)-NH₂) on somatotropin (ST), insulin-like growth factor I (IGF-I), milk production, heifer BW, and postpartum (PP) return to ovarian activity. Beginning on d -11 from parturition, heifers were administered (s.c.) GRF-A ([desNH₂-Tyr¹,D-Ala²,Ala¹₅]GRF(1-29)-NH₂, 2.5 µg/kg; Yr 1) or GRF(1-29)-NH₂ (12.5 µg/kg; Yr 2) (GRF; n = 17) or vehicle (CON; n = 24) for seven consecutive days. Blood samples were collected at 20-min intervals from -60 to 300 min from the first and fourth injections. Samples were also collected at 20-min intervals for 6 h on d 25 and 69 ± 1 PP. Area under the curve of ST (nanograms·minute⁻¹·milliliter⁻¹) was greater (P < .01) in GRF than in CON heifers (9,671 ± 677 vs 2,611 ± 237). Increases in ST after GRF-A or GRF(1-29)-NH₂ were similar. On d 25 ± 1 PP, frequency of ST release (pulses per 6 h) was greater (P < .01) in CON (3.3 ± .2) than in GRF (2.1 ± .2) heifers. Milk production was similar (P > .1) for the two treatments. Heifer BW loss from d -16 to 81 after parturition was greater (P < .01) in GRF (88 ± 5) than in CON (68 ± 5) heifers. Postpartum return to ovarian activity (progesterone > 1 ng/mL for two consecutive weeks) was delayed (P < .05) in GRF (97 ± 14) vs CON (71 ± 8) heifers. After accounting for variation due to treatment and year, a negative (P < .02) correlation (r = -.39) was detected between concentrations of IGF-I during the first 30 d PP and PP interval to ovarian activity. These results indicate that prepartum administration of GRF altered the release pattern of ST after parturition and was associated with greater PP BW loss and delayed PP return to ovarian activity in heifers.

Key Words: Heifers, Growth Hormone-Releasing Factor, Somatotropin, Insulin-Like Growth Factor, Body Weight, Postpartum Interval


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Introduction

The stimulatory effect of somatotropin (ST) on milk yield in dairy cows is well documented (Machlin, 1973; Peel et al., 1981; McCutcheon and Bauman, 1986). Administration of growth hormone-releasing factor (GRF) has also been shown to increase milk yield in dairy cows (Baile and Buonomo, 1987; Enright et al., 1988; Lapierre et al., 1988; Dahl et al., 1990, 1991).

Milk production in beef dams exerts a major impact on the preweaning growth of calves. Milk yield of the dam accounts for approximately 65% of the variance in calf ADG from birth to weaning (Glededdie and Berg, 1968; Jeffrey et al., 1971; Rutledge et al., 1971). Administration of ST has been shown to increase milk production in beef (Bines et al., 1980) and in dual-purpose (Schams et al., 1991) breeds of cattle. Given the importance of milk production in beef cattle production, further investigation into the potential benefits of elevated ST concentrations on milk production in beef cows is warranted.

Most research with GRF and ST has involved elevating ST during lactation. Delivery of compounds during the prepartum period could be combined with other practices and provide a practical alternative to administration during lactation. Chew et al. (1984) infused arginine into Holstein cows for seven consecutive days before parturition and observed approximately a 10% increase in milk production during the first 22 wk of lactation. Administration of human GRF from d 105 to 115 of gestation increased milk production during the subsequent lactation in the ewe (Kann et al., 1988). Stelwagen et al. (1990) observed an increase in milk production during the first 100 d of lactation in Holstein heifers that received recombinant bovine ST (20 mg/d) for 84 d during the late gestation.

The objectives of this study were to evaluate the effect of prepartum administration of a GRF analog or GRF(1–29)-NH₂ on serum concentrations of ST, insulin-like growth factor I (IGF-I), insulin (INS), milk production, BW, calf weaning weight, and postpartum (PP) return to ovarian activity in primiparous beef heifers.

Materials and Methods

Forty-one primiparous Simmental heifers were used to evaluate the effect of prepartum administration of a growth hormone-releasing factor analog (GRF-A) or growth hormone-releasing factor (GRF(1–29)-NH₂) on ST, IGF-I, INS, milk production, 205-d adjusted weaning weights of calves, and PP return to ovarian activity. The study was conducted over 2 yr (Yr 1 = 1988, n = 19, 515 ± 7 kg BW; Yr 2 = 1989, n = 22, 507 ± 7 kg BW). In Yr 1, GRF heifers received GRF-A [desNH₂-Tyr¹,D-Ala²,Ala¹⁵] GRF(1–29)-NH₂ (2.5 µg/kg BW), a potent analog (Mowles et al., 1987). In Yr 2, GRF heifers received GRF(1–29)-NH₂ (12.5 µg/kg BW; Hoffmann-La Roche, Tom Mowles, Nutley, NJ). Doses were calculated to produce a similar increase in ST. Heifers were blocked by sire and expected calving date and randomly assigned to treatment. Heifers received (s.c.) either GRF-A (n = 7) or GRF(1–29)-NH₂ (n = 10) for Yr 1 and 2, respectively, or vehicle (CON; n = 24) for seven consecutive days beginning 11 ± 1 d before parturition.

Blood samples were collected at 20-min intervals for 6 h (-60 to 300 min from injection, 1000 to 1600) on the 1st (d 0) and 4th (d 3) d of injection and were analyzed for serum concentration of ST. Samples collected at -60, 60, and 300 min from injection were analyzed for serum concentration of IGF-I, INS, nonesterified fatty acids (NEFA), and plasma glucose (GLU). On d 25 and 69 ± 1 PP, samples were also collected at 20-min intervals for 6 h (1000 to 1600) for determination of serum ST. Samples taken at 1000, 1200, and 1600 on these days were also analyzed for serum concentration of IGF-I, INS, NEFA, and plasma GLU.

To facilitate frequent blood sampling, cannulas were inserted into the vena cava via the jugular vein approximately 18 h before initiation of sampling. During the frequent sample collection period, heifers were maintained in individually partitioned, stationary chutes (183 × 76 cm). Single blood samples were collected at 7-d intervals from d 21 ± 1 to 88 ± 1 in Yr 1 and to 184 ± 1 PP in Yr 2 for determination of serum progesterone (P₄) and IGF-I. Postpartum return to ovarian activity was defined as the first date in which serum P₄ exceeded 1 ng/mL for 2 consecutive weeks.

Blood samples were collected into plain glass tubes (ST, NEFA, INS), evacuated glass tubes (Vacutainer Tube, Becton-Dickinson, Rutherford, NJ; P₄, IGF-I), or glass tubes containing sodium fluoride (Vacutainer Tube, Becton-Dickinson; GLU). Samples were stored at 4°C until centrifugation at 1,500 x g for 30 min on the day of P₄, GLU, IGF-I or the day after (ST, INS, NEFA) collection. Serum or plasma was stored at -20°C until it was analyzed.

In Yr 1, heifers were managed as a single group and given ad libitum access to corn silage (8.8% CP and 71.1% TDN, DM basis) plus .45 kg of soybean meal per heifer daily. Feed intake was not recorded in Yr 1. In Yr 2, treatment groups were fed separately a diet consisting of 93% corn silage and 7% alfalfa haylage (DM basis). Feed intake was measured during a 49-d interval (from d 8 to 57 PP).
Minerals were provided on a free-choice basis during both years. Cow and calf BW and cow body condition scores (BCS) were recorded before initiation of treatments and at 28-d intervals through approximately d 210 PP. The BCS were based on the system described by Richards et al. (1986) with a range of 1 = emaciated to 9 = extremely fat. Calf BW were adjusted for sex and age in calculating adjusted 205-d weaning weights. Milk production estimates were carried out at approximately 28-d intervals. 

Milk production in Yr 1 was estimated via a weigh-suckle-weigh procedure. Calves were separated from their dams at 0800 on the 1st d, and at 1600 they were allowed to nurse their dams to empty the udders. Calves were then separated from their dams until 0800 the next day, at which time they were weighed, allowed to nurse, and reweighed. Calves and dams were again separated until 1600, at which time the weigh-suckle-weigh procedure was repeated.

In Yr 2, milk production was measured via machine milking. Milk was obtained by the procedures described by Chenette and Frahm (1981), with modifications. Cows were milked in the morning and afternoon. Immediately after being restrained in a squeeze chute, cows were given (orally) approximately 15 mg of the tranquilizer Acepromazine maleate (10 mg/mL). Immediately before milking, cows were administered (i.v.) oxytocin (20 IU; 1 mL) to induce milk letdown. Milking continued until milk flow had visibly ceased; each quarter was stripped by hand to ensure complete milkout. After the morning milking, cows were separated from their calves and kept in drylot with access to water. Six hours elapsed between the morning and afternoon milking and cows were milked in the same order in the afternoon as in the morning. Twenty-four-hour milk yield was estimated by multiplying the afternoon milk weight by four. Subsamples were collected in duplicate for determination of fat, protein, and somatic cell count.

Assays. Serum concentrations of P4 were determined by a solid-phase RIA (Diagnostic Products, Los Angeles, CA). Average intra- and interassay CV were 5.1 and 9.1%, respectively, for 12 assays. Sensitivity of the P4 assay, defined as 90% of total binding, was .10 ng/mL.

Serum concentrations of ST were determined as described by Armstrong and Spears (1988). Average intra- and interassay CV for nine assays were 10.2 and 19.7%, respectively. Sensitivity of the assay, as described previously, was 1.0 ng/mL.

Serum INS concentrations were analyzed via the procedures of Hales and Randle (1963) with modifications as described by Jones et al. (1991). Average intra- and interassay CV were 16.4 and 18.7%, respectively, for two assays. Assay sensitivity was 1.7 μU/mL. Plasma GLU was analyzed by an automated GLU oxidase method (Glucose Analyzer 2, Beckman Instruments, Brea, CA). Serum NEFA were determined via an enzymatic, colorimetric method (WAKO Chemicals USA, Dallas, TX).

Serum IGF-I concentrations were determined using rabbit anti-IGF-I serum as detailed by Houseknecht et al. (1991) with modifications (Jones et al., 1991). The average intra- and interassay CV were 7.1 and 11.5%, respectively, for five assays. Sensitivity of the assay was 5.0 ng/mL.

Statistical Analyses. All analyses were conducted using the GLM procedure (SAS, 1985). Hormone and metabolite data were analyzed using a model containing treatment (GRF vs CON), year, treatment x year, heifer within treatment x year, period, treatment x period, year x period, period x heifer within treatment x year, time, treatment x time, year x time, period x time, and treatment x year x period. Effects of treatment, year, and treatment x year were tested using the heifer within treatment x year mean square as the error term. Effects of period, treatment x period, and year x period were tested using the period x heifer within treatment x year mean square as the error term. For the prepartum analyses, days of injection (d 0 and 3) were treated as separate periods. For the postpartum analyses, ST data were analyzed within period (d 25 and 69 ± 1 PP).

Frequency (pulses per 6 h) and amplitude (nanograms per milliliter) of ST release were determined for individual heifers during the 6-h sampling period. Criteria used to define an ST pulse were as follows: 1) the pulse had to occur within 40 min of the previous nadir, 2) it had to be at least 50% greater than the previous nadir, and 3) the amplitude of the pulse had to be greater than the sensitivity of the assay. Basal ST was determined after deleting peaks of ST and all observations associated with an episode of ST release. Frequency, amplitude, and basal ST were analyzed within period (d 25 and 69 PP) using a model including treatment, year, and treatment x year.

Because milk estimation procedures differed between years, milk production data were analyzed separately for each year using a model containing treatment, period, and the treatment x period interaction. In Yr 1, the mean (± SEM) days PP for the respective 30-d periods were d 22 ± 2, 45 ± 2, 74 ± 2, 106 ± 2, 136 ± 2, 166 ± 2, 193 ± 2, and 218 ± 2. In Yr 2, the mean (± SEM) days PP for the respective 30-d periods were d 34 ± 2, 49 ±...
In a similar manner, to facilitate analyses of treatment and period effects on serum IGF-I concentrations during lactation, the PP period was divided into 30-d periods within each year. In Yr 1, the mean (± SEM) days PP for four respective periods were 22 ± 1, 44 ± 1, 73 ± 1, and 101 ± 2. Those values (days PP) for seven respective periods in Yr 2 were 22 ± 1, 45 ± 1, 74 ± 1, 103 ± 1, 137 ± 3, 158 ± 1, and 192 ± 2.

Analyses for BW and BCS changes and PP return to elevated P4 (days) used a model consisting of treatment, year, and treatment × year. Because year significantly affected PP return to elevated P4, the median days PP for each year (across treatments) was used to facilitate further analysis of this variable using the chi squared procedure (SAS, 1985). The median was d 45 PP for Yr 1 and d 110 PP for Yr 2.

Multivariate analysis of variance (MANOVA) under the GLM procedure (SAS, 1985) was used to evaluate the relationship between concentrations of IGF-I during the first two 30-d periods of lactation and PP return to elevated P4. This allowed comparisons between these variables after accounting for differences that were due to treatment and year.

Table 1. Serum concentrations of insulin-like growth factor I (IGF-I; ng/mL) on days 0 and 3 of injection period in heifers that received prepartum administration of a growth hormone-releasing factor analog [GRF-A; Yr 1], GRF(1-29)-NH2 [Yr 2], or vehicle [CON].

<table>
<thead>
<tr>
<th>Item</th>
<th>Day 0</th>
<th>Day 3</th>
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<tr>
<td></td>
<td>Yr 1</td>
<td>Yr 2</td>
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<tr>
<td>GRF-A</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>48 ± 4&lt;sup&gt;cd&lt;/sup&gt;</td>
<td>85 ± 4</td>
</tr>
<tr>
<td>CON</td>
<td>52 ± 6&lt;sup&gt;e&lt;/sup&gt;</td>
<td>64 ± 3</td>
</tr>
<tr>
<td>GRF(1-29)-NH2</td>
<td>65 ± 5</td>
<td>62 ± 3</td>
</tr>
<tr>
<td>CON</td>
<td>40 ± 4</td>
<td>49 ± 3</td>
</tr>
</tbody>
</table>

<sup>a</sup>Injections of GRF-A (Yr 1), GRF(1-29)-NH2 (Yr 2), or vehicle were given for seven consecutive days beginning on d -11 ± 1 from parturition.

<sup>b</sup>Year × treatment × day of injection interaction (P < .05).

<sup>c</sup>Mean ± SEM.

<sup>d</sup>In GRF heifers, day of injection and the year × day of injection interaction contributed (P < .01) to variation in serum IGF-I.

<sup>e</sup>In CON heifers, year, day of injection, and the year × day of injection interaction were not significant (P > .1).

Results

Prepartum Hormone Responses

Serum concentrations of ST increased (P < .01) within 20 min after injection of GRF and remained elevated for the entire 5-h postinjection period (Figure 1). This increase was similar across days and years; thus, the response of ST during the injection period was pooled across both sampling days and years. Area under the curve (nanograms .minute⁻¹ .milliliter⁻¹) of ST for the 5-h postinjection sampling period was greater (P < .01) in GRF (9,671 ± 677) than in CON (2,611 ± 237) heifers.

A year × day of injection interaction (P < .01) was detected in GRF, but not in CON, heifers regarding the chronic response of serum IGF-I to GRF during the injection period (three-way interaction, P < .05; Table 1). In Yr 1, serum concentrations of IGF-I in GRF-A heifers increased from d 0 to 3 of the injection period. However in Yr 2, no such increase in IGF-I concentrations was observed in GRF(1-29)-NH2 heifers during this time. In contrast, neither year, day of injection, nor the year × day of injection interaction contributed (P > .1) to variation in IGF-I concentrations in CON heifers.

The treatment × day of injection interaction (P < .05) was the primary factor contributing to variation in concentrations of INS during the injection period. Concentrations (µU/mL) of INS in GRF heifers did not change from d 0 to 3 of injection, whereas INS concentrations decreased...
in CON heifers during this time (4.4 ± .3 to 4.9 ± .6 vs 4.9 ± .4 to 3.5 ± .3, respectively).

A significant effect of year was observed regarding plasma GLU during the injection period. Concentrations of GLU (milligrams per deciliter) were higher (P < .05) in Yr 1 (52 ± .5) than in Yr 2 (49 ± .5). Neither treatment nor day of injection affected plasma concentrations of GLU during the injection period.

As was observed with GLU, year also affected serum concentrations (microequivalents per liter) of NEFA during the injection period. Across treatments, serum NEFA were lower (P < .02) during Yr 1 (458 ± 27) than during Yr 2 (633 ± 34). As with GLU, variation in NEFA during the injection period was not attributable to treatment, day of injection, or any interactions.

Postpartum Hormone Responses

Concentrations and characteristics of ST release on d 25 and 69 ± 1 PP are given in Table 2. On d 25 ± 1 PP, frequency of ST release was less (P < .01) in GRF than in CON heifers, and amplitude of ST release tended (P = .06) to be greater in GRF than in CON heifers. Neither year (P > .3) nor the treatment x year interaction (P > .4) contributed to variation in frequency or amplitude of ST release on d 25 ± 1 PP. An effect of year was observed for mean and basal ST concentrations (nanograms per milliliter) on d 25 ± 1 PP, respectively; those variables were lower (P < .01) in Yr 1 (6.8 ± .4 and 5.0 ± .2) than in Yr 2 (12.8 ± .6 and 10.3 ± .5). On d 69 ± 1 PP, effects of treatment, year, or the treatment x year interaction did not contribute to variation in ST concentrations or release pattern.

Treatment and period effects and a year x period interaction were detected (P < .01) for serum concentrations of IGF-I during the PP period (Figure 2). In Yr 1, GRF (71 ± 5) heifers had lower (P < .01) concentrations (nanograms per milliliter) of IGF-I than CON (89 ± 4) heifers during PP period two. In Yr 2, the same pattern was observed: GRF heifers had lower (P < .01) concentrations of IGF-I than CON heifers during PP periods two and three (33 ± 2 and 51 ± 4 vs 45 ± 3 and 72 ± 4, respectively).

Across treatments, serum concentrations of IGF-I were higher during PP periods one, two, and three in Yr 1 (80 ± 4, 82 ± 3, and 90 ± 3) than during these periods in Yr 2 (40 ± 3, 40 ± 2, and 62 ± 3). By PP period 4, IGF-I concentrations were similar (P > .1) for the two years (97 ± 6 and 97 ± 4 for Yr 1 and 2, respectively).

Concentrations (microunits per milliliter) of INS were similar (P > .1) between GRF and CON heifers during the PP period (3.2 ± .2 vs 3.9 ± .4, respectively). Neither year, period, nor any interactions involving these variables contributed to variation in INS concentrations during the PP period.

A year x period interaction (P < .05) was detected for plasma GLU concentrations (milligrams per deciliter) during the PP period; GLU concentrations across treatments increased from d 25 ± 1 (53 ± .9) to d 69 ± 1 (55 ± 1.4) in Yr 1, but they did not change during this period in Yr 2 (remained at 52 ± .5 for both days).

Table 2. Frequency and amplitude of somatotropin (ST) release and mean and basal concentration [ng/mL] of ST on days 25 and 69 ± 1 postpartum in heifers that received prepartum administration of growth hormone-releasing factor (GRF) or vehicle (CON)a

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Pulse frequencyb</th>
<th>Pulse amplitudec</th>
<th>Meandon</th>
<th>Basaldn</th>
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</thead>
<tbody>
<tr>
<td>GRF</td>
<td>2.1 ± .2e</td>
<td>10.3 ± 3.8f</td>
<td>10.7 ± .6</td>
<td>8.2 ± .5</td>
</tr>
<tr>
<td>CON</td>
<td>3.3 ± .2</td>
<td>7.7 ± 1.6</td>
<td>9.1 ± .4</td>
<td>7.1 ± .3</td>
</tr>
<tr>
<td>GRF</td>
<td>2.4 ± .2</td>
<td>9.3 ± 1.5</td>
<td>9.9 ± .4</td>
<td>7.6 ± .3</td>
</tr>
<tr>
<td>CON</td>
<td>2.9 ± .3</td>
<td>9.8 ± 2.1</td>
<td>9.9 ± .5</td>
<td>7.4 ± .3</td>
</tr>
</tbody>
</table>

aInjections of GRF or vehicle were given for seven consecutive days beginning on d -11 ± 1 from parturition.
bPulses of ST/6 h.
cSomatotropin, nanograms per milliliter; pulse amplitude = difference between peak and previous nadir; mean concentration determined from 19 samples/heifer; basal ST = mean concentration after samples associated with episodes of ST release were omitted.
dMean ± SEM.

*GRF vs CON heifers (P < .01).

1482 SIMPSON ET AL.
Year and the year × period interaction contributed to variation in serum concentrations (microequivalents per liter) of NEFA during the PP period. Across treatments and PP sampling days, serum NEFA were lower \((P < .01)\) in Yr 1 \((232 \pm 28)\) than in Yr 2 \((487 \pm 28)\). In Yr 1, NEFA concentrations decreased from \(402 \pm 43\) to \(212 \pm 15\) between d 25 and 69 in PP. In Yr 2, NEFA increased from \(363 \pm 34\) to \(616 \pm 35\) during this same time interval. Treatment had no effect \((P > .1)\) on PP concentrations of NEFA.

Performance-Related Variables

During the 49-d period (d 8 to 57 PP) of Yr 2 when feed intakes (kilograms of DM·heifer\(^{-1}·\text{day}^{-1}\)) were recorded, no difference \((P > .1)\) was detected between GRF \((10.3 \pm .2)\) and CON \((10.1 \pm .2)\) heifers.

Heifer BW (kilograms) were similar \((P > .1)\) for GRF \((508 \pm 6)\) and CON \((513 \pm 7)\) heifers at the initiation of the study. However, from –16 to 52 ± 1 d after parturition, GRF heifers lost more \((P < .01)\) BW than did CON heifers \((83 \pm 6\) vs \(54 \pm 6\), respectively). This difference was maintained further into lactation: GRF heifers continued to lose more \((P < .01)\) BW than CON heifers from d –16 to 81 and 110 ± 1 PP \((88 \pm 5\) and \(81 \pm 6\) vs \(68 \pm 5\) and \(59 \pm 6\), respectively).

As was observed with BW, heifer BCS at the initiation of the study were similar \((P > .1)\) between GRF \((5.4 \pm .2)\) and CON \((5.6 \pm .2)\) heifers. Heifer BCS on d 81 ± 1 PP were lower \((P < .05)\) for GRF \((4.5 \pm .2)\) than for CON \((5.0 \pm .1)\) heifers. However, the changes in BCS from d –16 to 52 or 81 ± 1 were not different \((P > .1)\) between treatment groups. Across treatments, year contributed to the change in BCS from d –16 to 81 ± 1: BCS decreased more \((P < .01)\) in Yr 1 \((1.3 \pm .2)\) than in Yr 2 \((3 \pm .2)\).

Neither treatment nor the treatment × period interaction contributed to variation in milk production in either year. A period effect \((P < .01)\) was detected for milk production in each year. In Yr 2, milk composition was not affected \((P > .1)\) by treatment. Across years, adjusted 205-d weaning weights (kilograms) were similar \((P > .1)\) for GRF \((253 \pm 8)\) and CON \((249 \pm 5)\) calves. The PP intervals (days) to elevated P₄ for each year of the study are depicted in Figure 3. Treatment \((P < .05)\) and year \((P < .01)\) contributed to the variation in PP return to elevated P₄ (treatment × year interaction, \(P > .1)\). In Yr 1, a greater \((P = .07)\) percentage of CON heifers exhibited elevated P₄ by d 45 PP than of GRF heifers \((44 \%\) vs \(11\%\), respectively). Likewise, in Yr 2, 45% of CON heifers resumed ovarian activity by d 110 PP vs 10% of the GRF heifers \((P < .01)\). Multivariate analysis of variance revealed a negative \((P < .02)\) correlation \((r = –.39)\) between concentrations of IGF-I during the first 30 d PP and PP interval to elevated P₄.

Discussion

In the present study, prepartum administration of GRF-A or GRF(1–29)-NH₂ had no effect on milk production in primiparous beef cows. Also, weaning weights of calves were not affected by treatment in either year of the study.

The timing of GRF injections and duration of the present study were based on the results of Chew et al. (1984), who administered arginine for 7 d during late gestation and observed transitory increases in prolactin, ST, and INS, with a subsequent 10% increase in milk production during the first 22 wk of lactation. Also, Kann et al. (1988) gave GRF to heifers.
Mechanisms for such an increase may have been observed in ewes twice daily from d 105 to 115 of gestation and reported an increase in milk production during wk 5 and 6 of lactation. They speculated that the mechanism for such an increase may have been stimulation of mammogenesis or improved maintenance of mammary epithelial cells. Likewise, Stelwagen et al. (1990) gave daily injections of recombinant bovine ST (20 mg/d) to nulliparous Holstein heifers during the last trimester of gestation and observed an increase in milk production over that of control animals.

Concentrations of ST were substantially increased in GRF heifers during the injection period and remained elevated for at least 5 h after each injection, based on the frequent blood samples collected on the 1st and 4th d of injection. Administration of GRF-A and GRF(1-29)-NH₂ yielded similar increases in ST concentration.

The increase in serum IGF-I observed in GRF heifers by d 3 of the injection period during Yr 1 is consistent with previous reports involving administration of GRF (Abribat et al., 1990) and ST (Cohick et al., 1989; Elsasser et al., 1989; McShane et al., 1989). However, an increase in serum IGF-I from d 0 to 3 of injection was not observed in GRF heifers during Yr 2, which probably reflects the lower plane of nutrition. The stimulatory effect of ST on serum IGF-I is absent in nutritionally restricted animals (Breier et al., 1986, 1988a,b).

Although not reflected in the subjective BCS, the level of nutrition was higher during Yr 1 than during Yr 2 of the study. This statement is supported by detection of lower mean and basal ST on d 25 ± 1 PP in Yr 1, lower NEFA and higher IGF-I during the early PP period of Yr 1, and a shorter PP interval to elevated P₄ in Yr 1 compared with Yr 2. Also, the observation that heifers across both treatments lost more body condition after parturition in Yr 1 than in Yr 2 indicates that heifers in Yr 1 had more fat stores available for utilization during early lactation than those in Yr 2.

An unexpected finding was the treatment difference in release pattern of ST during the early PP period. On d 25 ± 1 PP, heifers that had received GRF for 7 d before parturition had a lower frequency of ST release and a tendency for higher amplitude of ST release than CON heifers. This alteration in the release pattern of ST in GRF heifers is somewhat consistent with previous reports concerning GRF effects on ST release. Long-term treatment with GRF enhances the responsiveness to subsequent administration of GRF in humans and rodents (Heiman et al., 1984). Schriock et al. (1984) reported that a prolonged absence of endogenous GRF may decrease later responsiveness to GRF in ST-deficient humans. Conceivably, the 7-d treatment with exogenous GRF before parturition could have enhanced the response of somatotropes to the endogenous GRF released during early lactation.

Another possible explanation for the difference between treatments in ST release on d 25 ± 1 PP is the apparent difference in metabolic status between heifers of the two treatments. Treatment with GRF and the resulting elevation of ST concentrations for 7 d possibly shifted the GRF heifers into a more negative energy balance just before parturition, which persisted during early lactation. Evidence for this condition includes the greater loss of BW and lower serum concentrations of IGF-I during the early PP period in GRF heifers and the delayed PP return to ovarian activity in GRF heifers. These treatment differences were observed in each year of the study. Breier et al. (1986) found that reduced feeding of young steers resulted in an increased amplitude of ST pulses. Although no difference in feed intake was detected between treatments in the present study, we suggest that prepartum administration of GRF altered metabolism through d 25 PP.

In both years, PP interval to elevated P₄ was delayed in GRF heifers. This observation provides further evidence that prepartum administration of GRF may have heightened the catabolic state of these primiparous cows after parturition. The higher pulse amplitude of ST observed in GRF

![Figure 3](image-url)
heifers on d 25 ± 1 PP is indicative of metabolic stress and agrees with Carstairs et al. (1980), who reported a positive correlation \( r = .51 \) between PP concentrations of ST and the number of days PP to elevated \( P_4 \) in primiparous Holstein cows. Wettemann et al. (1987) infused GRF into beef cows from d 25 to 45 of lactation but found no effect on PP return to ovarian activity.

In both years, CON heifers maintained greater serum concentrations of IGF-I than GRF heifers during the early PP period. Even in Yr 1, when serum IGF-I was elevated in GRF heifers on d 3 of injection, IGF-I concentrations remained higher in CON than in GRF heifers to d 44 PP.

The higher PP concentrations of IGF-I in CON heifers are of particular interest because these animals also exhibited a shorter PP interval to ovarian activity than GRF heifers. Possible roles for IGF-I in reproductive function have been advanced in recent years (reviews by Hammond et al., 1988; Carson et al., 1989; Hammond et al., 1991). Concentrations of IGF-I in follicular fluid collected from ovaries of gilts increased during follicular growth (Hammond et al., 1985). Adashi et al. (1985) discussed the possibility that IGF-I may be a factor in the selection and maintenance of the dominant follicle during early follicular development. Spicer et al. (1988) observed a positive relationship between concentrations of progesterone and IGF-I in bovine follicular fluid. Serum concentrations of IGF-I were positively correlated to serum concentrations of progesterone in Holstein cows (Spicer et al., 1990). Beef heifers that were actively immunized against GRF maintained lower serum concentrations of IGF-I and exhibited delayed onset of puberty compared with control heifers (Simpson et al., 1991). Multivariate analysis of variance revealed that, after accounting for treatment and year effects, a negative relationship existed between serum IGF-I during the first 30 d PP and the number of days after parturition to elevated \( P_4 \). This observation adds further credence to the possibility that IGF-I may be involved in reproductive function. In contrast, Rutter et al. (1989) found no apparent relationship between serum IGF-I and days to first ovulation in mature, Hereford-cross cows. It is possible that energy balance and overall metabolic state differed between cows of these two studies, because of differences in parity and age of the animals. It is also possible that the metabolic actions of IGF-I might vary at different levels of energy balance.

The observation that heifers given GRF lost more BW than CON heifers during the period from late gestation to the early PP period gives rise to speculation that either 1) GRF heifers were producing more milk than CON heifers but the difference was not detected with these milking procedures or 2) administration of GRF and subsequent elevation of ST concentrations for 7 d during late gestation shifted these primiparous heifers into a catabolic state just before parturition, which continued under a heightened state of metabolic stress during the early PP period. The latter possibility would be supported by the observation of lower frequency and a tendency for greater amplitude of ST release in GRF heifers on d 25 ± 1 PP, as well as lower concentrations of serum IGF-I during the early PP period in GRF heifers.

It seems that the greater BW loss in GRF compared with CON heifers from d -16 to 52 and 81 after parturition may have been a factor involved in the extended PP interval to ovarian activity. Previous investigators have studied the impact of BW and BCS changes during the late gestation and early PP period on PP reproductive performance. Rasby et al. (1991) reported that nutrition and BCS influence the release of LH from the anterior pituitary gland and speculated that the effects of BCS on reproductive efficiency may be mediated via secretion of LH. Rutter and Randel (1984) found that Brangus cows that maintained BCS after parturition had shorter PP intervals to estrus and greater release of LH than cows that lost body condition after parturition.

In conclusion, prepartum elevation of ST in response to GRF treatment in primiparous Simmental heifers altered release of ST and increased BW loss in the early PP period, long after cessation of treatment. Heifers receiving GRF before parturition also exhibited a longer PP interval to ovarian activity. Across treatments and years, serum IGF-I during the first 30 d PP was inversely related to number of days from parturition to elevated \( P_4 \). Neither milk production nor 205-d adjusted weaning weights of calves were affected by prepartum administration of GRF.

**Implications**

Administration of growth hormone-releasing factor to primiparous beef heifers was used to elevate concentrations of somatotropin before parturition. This treatment altered the release of somatotropin during early lactation, caused heifers to lose more body weight during early lactation, and delayed the onset of ovarian activity following parturition. Milk production and calf weaning weights were not influenced by prepartum treatment with growth hormone-releasing factor. Across treatments, serum insulin-like growth factor I was inversely related to the length of postpartum anestrus.


