Effects of GnRH Administration in the Prepubertal Heifer and Post-Partum Cow

A. R. Peters,* J. P. Jagger *and* **G. E. Lamming**
AFRC Group on Hormones and Farm Animal Production
University of Nottingham, School of Agriculture
Sutton Bonington, Loughborough, Leicestershire, U.K.
**Meat and Livestock Commission,*
Queensway House, Bletchley
Milton Keynes, U.K.

Summary

Common features of the anovulatory state in post-partum cows and prepubertal heifers are low mean plasma LH concentrations and infrequent episodes of LH release. We have studied both animal models giving low doses of GnRH. Post-partum cows received 1, 2.5 or 5 mcg GnRH iv. per 2h for 48h either as pulsed injections or continuous infusion. Preovulatory LH surges occurred in 17/33 cows and 20 slowed luteal activity. Cows exhibiting LH surges had higher oestradiol-17B and lower FSH concentrations during the pretreatment period. 23 × 4-month old beef heifers received either 0.25, 0.5 or 2.5 mcg GnRH per h for up to 120h by continuous i.v. infusion. A further 12 received 5.0 mcg GnRH per h for 120h by s.c. infusion with or without progesterone pretreatment. Only 9/35 heifers showed luteal function and the pituitary response was again related to oestradiol concentrations. A pulsatile pattern of LH release continued during and after constant GnRH infusion. We suggest that the pituitary/ovarian response to GnRH treatment is governed by the follicular status before treatment.

Introduction

Common features of the anovulatory state in post-partum cows and prepubertal heifers are low mean plasma LH concentrations and infrequent episodes of LH release (4, 8). During the preovulatory period the frequency of LH episodes increases together with rising plasma concentrations (5, 8) culminating approximately 24 hours before ovulation in the preovulatory LH surge.

Many studies have been carried out where animals have been challenged with large dose so-called bolus injections of GnRH i.e. between 100 and 500 mcg (1, 2, 7). Whilst this treatment is effective in inducing a preovulatory gonadotrophin surge, any ovulation response is presumably dependent on there being a follicle present which is already at the appropriate state of development. The aim of later treatment regimes, particularly in the post-partum cow, have been to use repeated injections of low doses of GnRH to stimulate an increase in tonic gonadotrophin release thereby inducing follicular development. In terms of inducing ovulation, these experiments have varied in their success rate (3, 6, 9).

The present studiess were carried out to examine the endocrine responses to a range of doses of GnRH administered by different methods.

Paper presented at the 14th World Congress on Cattle Diseases, Dublin, Ireland, Aug. 26-29, 1986.

Materials and Methods

1. Thirty three Hereford x Friesian cows were used starting between 9 and 26 days *post-partum*. Blood samples were taken at frequent intervals for 84 h periods commencing 12 h before treatment. Three groups of six cows each received either 1.0, 2.5 or 5.0 mcg GnRH by i.v. injection at 2 h intervals for 48 hr. Three further groups of five cows each received exactly the same dose rate but by continuous intravenous infusion.
2. A second study was carried out in four month old prepubertal heifers. Groups of six heifers received either 0.25, 0.5 or 2.5 mcg GnRH by continuous intravenous infusion for 48 hours. A further group of five heifers received 1.25 mcg GnRH by continuous i.v. infusion for 120 h.
3. Following an initial dose response study to compare the potency of i.v. versus s.c. infusion, a further group of 12 heifers received 5 mcg GnRH s.c. for 120 h with or without a 14-day progesterone pretreatment.

Results

1. Cow study.
   Episodes of LH occurred in response to virtually all GnRH injections although the amplitude varied. At the two lower-dose levels, they were within the physiological range, whilst they were higher than natural episodes at the highest dose level. Three cows in each group exhibited preovulatory-type LH surges (see Table 1) and ten appeared to ovulate as determined by a significant increase in plasma progesterone occurring within 7 day

TABLE 1. Effect of GnRH administration in post-partum cows.

Method	Dose (mcg/2h)	Number of cows Total	LH Surge	Ovulated
Repeated injection	1.0	6	3	3
	2.5	6	3	4
	5.0	6	3	3
Continuous infusion	1.0	5	0	0
	2.5	5	5	5
	5.0	5	3	3

of the end of treatment.

Significant increases in plasma LH concentrations occurred in all cows during constant infusion of GnRH (see Table 1) although these were rather transient in the lower dose group. Eight of the cows in the two highest dose groups exhibited preovulatory-type OH surges and ten appeared to have ovulated within the 7-day period.

There was a highly significant difference between the timing of the surges between the repeated injection and infused groups, 30.6± 5.1 hours as compared to 3.3± 0.7 hours after the beginning of the treatment.

With the exception of the lowest-dose group of the continuously infused cows, neither the GnRH dosage nor the mode of administration affected the proportion of cows exhibiting LH surges or rises in progesterone concentrations. Therefore plasma hormone concentrations were compared across all doses between cows showing or not showing preovulatory LH surges.

In the cows receiving repeated injection, FSH concentrations tended to be lower throughout the sampling period in those cows showing preovulatory surges, but differences were not significant. Oestradiol concentrations tended to be highes during most of the sampling period but were only significantly so during the period of the LH surge.

In the infused cows, LH concentrations were significantly different only at the time of the surge. However FSH concentrations were significantly lower in the cows which produced an LH surge, during the pretreatment period and between 12 and 24 h of treatment (P 0.05). Oestradiol concentrations were significantly higher during the pretreatment period and first 12 h of treatment (P 0.05).

2. The response of heifers to continuous intravenous infusion of GnRH are shown in Table 2. Only 5 heifers of a total of 23 exhibited preovulatory LH surges and ovulated.

TABLE 2. The response to GnRH infusion in prepubertal heifers.

Dose (mcg/h)	Treatment period (hours)	N	LH surges	Ovulated
0.25	48	6	0	0
0.50	48	6	0	0
2.50	48	6	3	3
1.25	120	5	2	2

Hormone concentrations in heifers receiving 2.5 mcg GnRH were compared for those showing and those not showing LH surges. There were no significant differences in FSH concentrations. However oestradiol concentrations were significantly lower in those not showing surges in the pretreatment period and for the first 12 h after the beginning of treatment (see Table 3).

TABLE 3. Plasma oestradiol concentrations (pg/ml) in heifers receiving 2.5 mcg GnRH per hour.

	Pretreatment period	First 12 hours of treatment
LH Surge	1.85 ± 0.10	3.01 ± 0.44
No LH Surge	1.22 ± 0.1	1.78 ± 0.28
Significance	* $P<0.05$	* $P<0.05$

3. In this group of 12 heifers receiving GnRH by s.c. infusion for 120 h, LH surges/ovulation occurred in only 4 animals.

Discussion

It is concluded that

1. We are unable to consistently induce LH surges and ovulation in post-partum cows and prepubertal heifers using GnRH despite a range of doses and methods of administration. However 8/10 cows receiving the two highest infusion doses of GnRH ovulated, an encouraging response.
2. The occurrence of preovulatory LH surges was associated with lower FSH concentrations (cows) and higher oestradiol concentrations (cows and heifers).
3. It is therefore apparent that pituitary responsiveness to GnRH treatment is dependent on the ovarian follicular status at the time of treatment and that the state of unresponsiveness is not overcome by 120 h of GnRH treatment.
4. Commercial development of slow-release formulations of GnRH for the induction of ovulation may therefore require continuous release for well in excess of 120 h.

References

1. Britt, J.H., J. Kittock and S. Harrison: 1974 J. Anim. Sci., 39, 915. 2. Bulman, D.C. and G.E. Lamming: 1978 J. Reprod. Fert. 54, 447. 3. Edwards, S., J.F. Roche and G.D. Niswender: 1983 J. Reprod. Fert, 69, 65. 4. Lamming, G.E., D.C. Wathes and A.R. Peters: 1981 J. Reprod. Fert. suppl. 30, 155. 5. Rahe, C.H., R.E. Owens, J.L. Fleeger, H.J. Newton and P.G. Harms: 1980 Endocrinology 107, 498. 6. Riley, G.M., A.R. Peters and G.E. Lamming: 1981 J. Reprod. Fert. 63, 559. 7. Schams, D., F. Hofer, B. Hoffman, M.L. Ender and H. Karg: 1973 Acta endocr. Copenh. suppl. 177, 296. 8. Schams, D., E. Schallenberger, S. Gombe and H. Karg: 1981 J Reprod. Fert. suppl. 30, 103. 9. Walters, D.L., R.E. Short, E.M. Convey, R.B. Staigmiller, T.G. Dunn and C.C. Kaltenbach: 1982 Biol. Reprod. 26, 655.