Heifer estrous cycle stage impacts luteinizing and growth hormone response to kisspeptin.

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Abstract

The reproductive neuropeptide, kisspeptin (KP), may have a role in regulation of growth hormone (GH) secretion. This study was conducted to determine the effects of KP on plasma concentrations of luteinizing hormone (LH) and GH in pubertal heifers during different reproductive stages. Heifers received a single injection of KP (100 pmole / kg) or saline intravenously during proestrus, estrus, and diestrus, and blood samples were collected for 3 hours to determine the response of both LH and GH. Concentrations of LH were increased ($P < 0.05$) by KP during proestrus and diestrus but not estrus. However, area under the LH curves following KP were increased ($P < 0.05$) during all reproductive stages. Mean concentrations of GH were unaffected by treatment. Kisspeptin increased ($P < 0.05$) area under GH curves during proestrus and diestrus but not estrus. Thus, KP can stimulate concentrations of LH and GH in pubertal heifers and functional reproductive stage affects the gonadotropic and somatotropic responses.

Introduction

Kisspeptin is integral to central regulation of the gonadotropic-axis [1]. Recent evidence suggests that KP may have a role in regulating GH [2]. The somatotropic axis and the KP-system are clearly influenced by sex steroids [3]. Studies in ovariectomized adult cattle treated with sex steroids [4] showed that KP increased both LH and GH. Despite considerable progress in the field, few studies on the reproductive roles of the KP-system have been conducted in cyclic females. Moreover, effects of KP on GH during different stages of the estrous cycle of the female have yet to be reported. The present study was undertaken to determine LH and GH responses to KP during different stages of the estrous cycle in heifers.

Materials and Methods

All procedures were approved by the Auburn University Institutional Animal Care and Use Committee.

Fourteen cyclic Holstein heifers [13.5 ± 0.3 (SEM) months; 336.3 ± 13.8 kg body weight] were used in a study of KP-10 (human Metastin 45-54, 4389-v, Peptide Institute Inc., Osaka, Japan) effects on LH and GH during different stages of the estrous cycle. Heifers were group housed at Auburn University (Auburn, AL) and exposed to ambient temperatures and photoperiod throughout the experiment.

Estrous cycles were synchronized by insertion of a single controlled internal drug release device (CIDR, 1.38 g progesterone, Pharmacia Animal Health, Kalamazoo, MI, USA) and simultaneous administration of Cystorelin® [(gonadorelin diacetate tetrahydrate); 100 µg; IM; Merial, Essex, England]. Seven days later all CIDR devices were removed and $PGF_{2\alpha}$ was administered to all heifers. Estrous cycles were synchronized three different times so treatments could be given one day after luteolysis ("proestrus"), two days after luteolysis ("estrus"), and day 11 of the estrous cycle ("diestrus"). The day before treatment heifers were fitted with jugular catheters. On the day of an experiment blood was collected and progesterone concentrations were determined. During each "stage" of estrous heifers were treated intravenously with saline (Veh) or 100 pmole/kg BW (130 ng/kg) KP-10. Blood was collected and plasma was harvested until 180 min after injection.

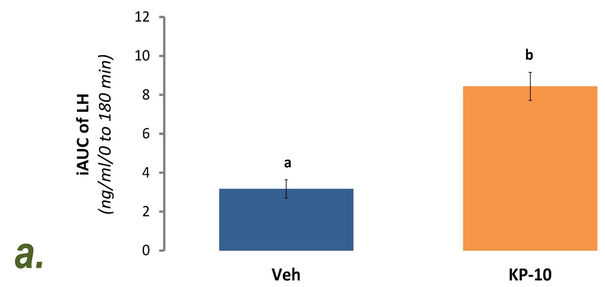
Plasma GH and LH concentrations were assayed by radioimmunoassay (RIA) as previously described [5]. Plasma progesterone concentrations were determined using the Coat-a-Count® Progesterone RIA kit (Siemens, Los Angeles, CA) [6].

Data were subjected to least-squares analysis of variance with repeated measures using the MIXED procedures of SAS (SAS, 2003). If a significant ($P<0.05$) treatment by time interaction was detected, effects of treatment within time were compared using the SLICE option of the LSMEANS statement of SAS. Mean concentration and incremental area under the curve (iAUC) for plasma LH and GH at fixed periods were subjected to generalized least squares ANOVA with repeated measures.

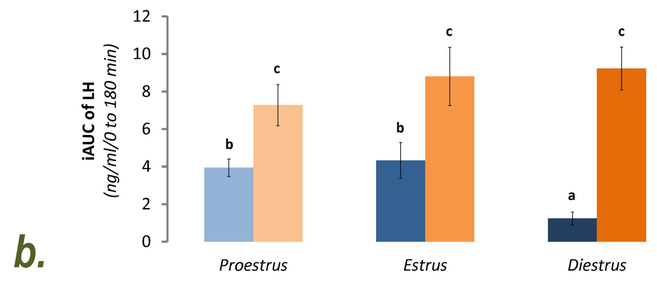
Results

- Plasma progesterone concentrations were 0.76 ± 0.10 (SEM), 0.51 ± 0.08, and 6.20 ± 0.32 for heifers classified here as proestrus, estrus, and diestrus, respectively.
- There was a stimulatory effect ($P < 0.05$) of KP on the combined LH concentrations in heifers ***(Figure 1-a).*** The iAUC for LH from 0 to 180 min was approximately 3-fold greater ($P < 0.05$) following KP than with Veh.
- There was a stimulatory effect ($P < 0.05$) of KP on LH concentrations in heifers during each stage of the estrous cycle ***(Figure 1-b).*** To the extent that iAUC reflects the magnitude of response from baseline, there was no effect of estrous cycle stage on magnitude of the LH response to KP.
- There was no effect of KP on concentrations of GH during any of the stages of the estrous cycle tested. Treatment with KP did increase iAUC for GH ***(Figure 2-a).*** . The GH response to KP-10 from 0 to 180 min after treatment across all stages of the estrous cycle (as assessed by iAUC) was almost 2-fold greater than ($P < 0.05$) the GH response to treatment with Veh ***(Figure 2-b).*** .

Figure 1. *Effects of intravenous (IV) KP-10 on iAUC of LH concentrations in cyclic heifers.*

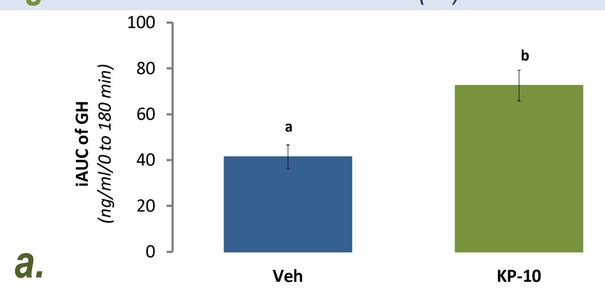


Effect of IV saline (Veh) or KP-10 (100 pmole/kg) on iAUC of LH concentrations (n = 14) from 0 to 180 min following treatment (mean ± SEM). iAUCs with different superscripts differ ($P < 0.05$).

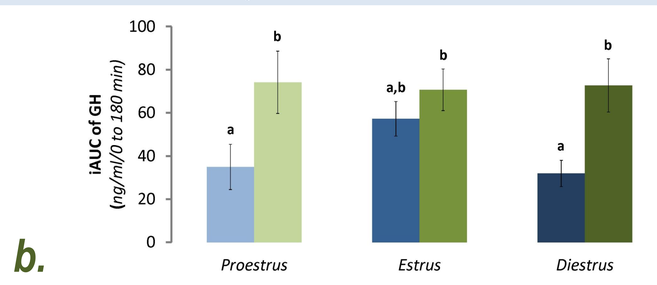


Effect of IV Veh or KP-10 (100 pmole/kg) on iAUC of LH concentrations in post-pubertal heifers (n = 7) during proestrurs, estrus, and diestrus from 0 to 180 min after injection (mean ± SEM). iAUCs with different superscripts differ ($P < 0.05$).

Figure 2. *Effects of intravenous (IV) KP-10 on iAUC of GH concentrations in cyclic heifers.*



Effect of IV saline (Veh) or KP-10 (100 pmole/kg) on iAUC of GH concentrations (n = 14) from 0 to 180 min following treatment (mean ± SEM). iAUCs with different superscripts differ ($P < 0.05$).



Effect of IV Veh or KP-10 (100 pmole/kg) on iAUC of GH concentrations in post-pubertal heifers (n = 7) during proestrurs, estrus, and diestrus from 0 to 180 min after injection (mean ± SEM). iAUCs with different superscripts differ ($P < 0.05$).

Summary

- ✓ Peripheral administration of KP increased LH and GH release in pubertal Holstein heifers.
- ✓ Effects of KP on gonadotropic and somatotropic axes varies depending on the functional reproductive stage at the time of treatment.
- ✓ Data support links between KP and both reproductive and growth axes in cattle.

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