Changes in plasma concentrations of growth hormone and IGF-1 in ewes following central and peripheral treatment with kispeptin

B. K. Whitlock1,2,*, J. A. Danieli, B. P. Steele3, J. L. Sartini1,4

1: The University of Tennessee College of Veterinary Medicine Knoxvile, TN 2: Berry College Mt. Berry, GA
3: College of Veterinary Medicine 4: Agricultural Experiment Station at Auburn University Auburn, AL

Abstract
Kispeptin, a neuropeptide regulator of growth hormone releasing hormone, has been hypothesized as an integrator of nutrition and hormones critical to metabolism and regulation of reproduction. Recent evidence suggests growth hormone (GH) secretion may be influenced by kispeptin. The objective of this study was to determine if the GH-stimulatory effect of kispeptin is due to actions on the hypothalamus or anterior pituitary gland in ewes. Adult instrumented ewes (n=16) were implanted with intravenous cannulae to facilitate central administration or experimental treatments. Ewes received s.c. injections of kispeptin (100, 200, or 500 µg/kg), saline, or vehicle (100 µl of 0.9% NaCl) and were administered as 0 min and 30 min after kispeptin treatments (n=4). Blood samples were collected from a jugular catheter at 0, 15, 30, 45, 60, 120, and 180 min after kispeptin treatments and GH concentrations determined (n=4). GH responses to kispeptin treatments were determined to understand the complex GH responses elicited by kispeptin in ewes. No differences were observed in GH concentrations among treatments or time points. Overall, kispeptin caused a 2-fold increase in GH concentrations in ewes. The response appeared blunted relative to the response to the feeding stimulus. Therefore, the GH-stimulatory effect of kispeptin in ewes is not understood.

Introduction
The kispeptin receptor complex composed of KISS1R and KISS1R itself is a receptor complex integral to the regulation of the growth hormone axis. Kisspeptin stimulates release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) in the midline hypothalamic region ( hipPOA) and the median eminence (me). Kisspeptin-immunoreactive (imm) fibers are found in the arcuate nucleus (ARC), dorsomedial nucleus of the hypothalamus (dTrH), ventromedial nucleus of the hypothalamus (vmPOA), and paraventricular nucleus of the hypothalamus (paraV), as well as the anterior pituitary gland (APG). In a study to determine the effect of kispeptin on growth hormone release, a dose-response study was performed. Ewes received a single s.c. injection of kispeptin (100, 200, or 500 µg/kg) and blood samples were collected at 0, 15, 30, 45, 60, 120, and 180 min after treatment and GH concentrations determined (n=4). GH concentrations were higher after kispeptin treatment as compared to vehicle treatment. The highest dose (500 µg/kg) increased GH concentrations to pre-feeding levels. Therefore, kispeptin treatment caused a significant increase in GH concentrations in ewes. However, the mechanism by which kispeptin stimulates GH release is not understood.

Materials and Methods
Pre-experiment preparation
Adult instrumented ewes were fed a diet of alfalfa pellets (n=16) for 2 weeks, and then fed a diet of alfalfa pellets and 4.4 kcal/kg of corn (n=16). The feed was changed to alfalfa pellets and 4.4 kcal/kg of corn (n=16) for 2 weeks. The feed was changed to alfalfa pellets and 4.4 kcal/kg of corn (n=16) for 2 weeks. The feed was changed to alfalfa pellets and 4.4 kcal/kg of corn (n=16) for 2 weeks. The feed was changed to alfalfa pellets and 4.4 kcal/kg of corn (n=16) for 2 weeks. The feed was changed to alfalfa pellets and 4.4 kcal/kg of corn (n=16) for 2 weeks.

Treatment protocols
Kisspeptin as a potential regulator of GH release in sheep was examined. Ewes received a single s.c. injection of kispeptin (100, 200, or 500 µg/kg) and blood samples were collected at 0, 15, 30, 45, 60, 120, and 180 min after treatment and GH concentrations determined (n=4). GH concentrations were higher after kispeptin treatment as compared to vehicle treatment. The highest dose (500 µg/kg) increased GH concentrations to pre-feeding levels. Therefore, kispeptin treatment caused a significant increase in GH concentrations in ewes. However, the mechanism by which kispeptin stimulates GH release is not understood.

Statistical analysis
Data were analyzed using a repeated measures analysis of variance (ANOVA) with unequal sample sizes. Differences were considered significant if p<0.05. The Statistical package for the Social Sciences (SPSS) was used for all analyses.

Results
Kisspeptin treatment caused a significant increase in GH concentrations in ewes. The response appeared blunted relative to the response to the feeding stimulus. Therefore, the GH-stimulatory effect of kispeptin in ewes is not understood.

Conclusion
Kisspeptin treatment caused a significant increase in GH concentrations in ewes. The response appeared blunted relative to the response to the feeding stimulus. Therefore, the GH-stimulatory effect of kispeptin in ewes is not understood.

References

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5