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Kisspeptin receptor agonist (FTM080) increased plasma concentrations of luteinizing hormone in anestrous ewes
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Kisspeptin (KP) and the KP receptor (Kiss1r) are integral to central regulation of the gonadotropic-axis. The demonstration that intravenous infusion of KP can stimulate gonadotropin secretion and ovulation in seasonally anestrous female sheep offers a means of manipulating the reproductive axis. However, KP may be of limited clinical use because of the short circulating half-life. Kiss1r agonists with increased half-life and similar efficacy to KP in vitro potentially may provide beneficial applications in breeding management of many species. However, many of these agonists have not been tested in vivo. This study was designed to test and compare the effects of a Kiss1r agonist (FTM080) and KP on luteinizing hormone (LH) in vivo. Sheep (n = 4 per treatment) were treated with KP (500 pmol/kg BW), one of three dosages of FTM080 (500, 2500, or 5000 pmol/kg BW), or sterile water (VEH) in a 2-ml bolus via jugular catheter. Serial blood samples were collected every 15 minutes before (1 hr) and after (4 hr) treatment. Plasma concentrations of LH were tested for effect of treatment, time, and treatment by time interaction using ANOVA procedures for repeated measures. Area under the curve (AUC) of LH in the period from 0 to 60 min (post-treatment) following KP was greater than (P < 0.05) all other treatments and the post-treatment AUC of LH following high-dose FTM080 (5000 pmol/kg BW) was greater than (P < 0.05) all treatments except KP. The AUC of LH in the post-treatment period was greater than (P < 0.05) the AUC of LH in the pre-treatment period (-60 to 0 min) for the low-dose FTM080 (500 pmol/kg) and middle-dose FTM080 (2500 pmol/kg). In conclusion, these data provide evidence to suggest that FTM080 stimulates the gonadotrophic axis of sheep in vivo. Any increased half-life and comparable efficacy of FTM080 to KP in vitro does not appear to translate to in vivo.

Keywords: Kisspeptin, agonist, luteinizing hormone, sheep