

Intravaginal application of Ovugel[®], a product containing the GnRH agonist triptorelin acetate (TA), stimulates LH secretion in gilts

¹R.R. Kraeling, ²M.E. Swanson, ³R.V. Knox, ²S.K. Webel

¹L&R Research Associates, Watkinsville, Georgia, USA; ²JBS United Animal Health II LLC, Sheridan, Indiana, USA; ³University of Illinois, Urbana, Illinois, USA

Intravaginal administration of Ovugel[®], a proprietary gel formula containing the GnRH agonist, triptorelin acetate (TA), effectively synchronizes ovulation in weaned postpartum sows, which allows for fixed-time artificial insemination. GnRH stimulates LH release from the pituitary, thereby stimulating ovulation. Two trials with an ovariectomized (OVX) estradiol (EB)-treated gilt model and one trial with gilts after last feeding of MATRIX[®] were conducted to determine the optimum viscosity of the gel preparation and concentration of TA to induce surge like secretion of LH and ovulation. Estradiol treatment, in OVX gilts, initially suppresses LH secretion followed by a preovulatory-like LH surge 48-72 h later (Asonavich *et al.*, 1998, Britt *et al.* 1991, Elsaesser *et al.* 1998). Thus, serum LH was assayed (Kraeling *et al.*, 1982, 1998) to characterize the LH response to TA. Response parameters were: 1) magnitude (maximum serum LH concentration), 2) time to maximum serum LH concentration (T-Max) and 3) area under the LH response curve (AUC: 0-30 h). Treatments were administered during EB induced suppression of LH secretion.

Trial 1 was designed to determine which of three gel formulations having differing viscosities optimized LH release; 16 gilts about 200 d of age were OVX and fitted with jugular vein cannulae. Estradiol benzoate (15 $\mu\text{g}/\text{kg}$ BW) was injected i.m. and 48 h later 4 gilts each received 2 ml of: 1) 0 μg TA in Viscosity B (Control), 2) 100 μg TA in Viscosity A, 3) 100 μg TA in Viscosity B or 4) 100 μg TA in Viscosity C intravaginally. Sequential blood samples were taken for 48 h after treatment. The proportion of gilts, which responded to TA within 2 h was 4/4, 2/3 and 1/3 for treatment 2, 3 and 4, respectively. LH surge secretion was captured in 3/4 Control, 4/4 treatment 2, 3/4 treatment 3, and 3/4 treatment 4 gilts. T-Max for Controls and treatments 2, 3 and 4 was 14.0 ± 3.6 , 7.0 ± 5.8 , 5.3 ± 5.8 , and 9.3 ± 4.6 h, respectively. Magnitude was 3.4 ± 1.2 , 9.7 ± 4.4 , 8.0 ± 0.4 , 8.7 ± 5.3 and AUC was 69.8 ± 18.8 , 94.1 ± 30.7 , 87.6 ± 28.1 and 87.6 ± 28.1 for Controls, and treatments 2, 3, and 4, respectively. Viscosity A gel was selected for subsequent dose titration trials. Two wks. later, in trial 2, the same gilts were prepared as in trial 1 and 4 each received 2 ml of Viscosity A gel containing 1) no TA (Control), 2) 25 μg TA, 3) 50 μg TA or 4) 100 μg TA intravaginally. Blood samples were taken for 30 h after treatment and evaluated as in trial 1. The proportion responding to TA within 2 h was 0, 33, 100 and 100% for Controls and treatment 2, 3 and 4, respectively. LH surge secretion was captured in 0/4 Control, 3/4 treatment 2, 4/4 treatment 3, and 4/4 treatment 4 gilts. T-Max for Controls and treatments 2, 3 and 4 was 16.0 ± 1.6 , 7.0 ± 7.0 , 3.5 ± 1.7 , and 3.0 ± 0.0 h, respectively. Magnitude was 1.8 ± 0.7 , 5.4 ± 4.9 , 13.4 ± 4.8 , 12.9 ± 2.4 and AUC was 16.5 ± 3.5 , 46.6 ± 18.6 , 52.8 ± 23.5 and 62.9 ± 11.6 for Controls, and treatments 2, 3, and 4, respectively. Number of gilts responding increased with TA concentration; 100 μg dose resulted in 100% response. All TA treatments decreased T-Max and increased AUC. T-Max was shortest and least variable in treatment 4 gilts. The optimum dose for further dose titration trials was 100 μg .

In trial 3, sexually mature gilts were individually fed 15 mg MATRIX[®]/d for 14 d and received: (Control) vehicle gel (n=8) or gel containing (1) 100 μg (n=6), (2) 200 μg (n=7), or (3) 400 μg

(n = 6) of TA at 120 h after last feeding of MATRIX®. Sequential blood samples were taken for 48 h after treatment. Ovaries were examined by ultrasound (Knox *et al.* 2001) every 8 h for 72 h, starting 24 h before treatment, to monitor follicle development and ovulation. Treatments were administered near the approximate time that estrus was expected, about 120 h after last feeding of MATRIX®. LH surge secretion was captured in 5/8 Control, 5/6 treatment 2, 5/7 treatment 3, and 5/6 treatment 4 gilts. Onset of the LH surge and T-Max were earlier in TA-treated gilts than in Controls. Magnitude followed a dose response pattern. Duration was greater for Controls than TA-treated gilts. Gilts in which a LH surge was not captured were either completing a surge at time of treatment or surged before treatment. Although LH surge secretion was not captured in all gilts, 63% of Controls and 100% of TA-treated gilts ovulated by 48 h after treatment. Doses of 100 to 400 µg of TA were equally effective for inducing ovulation when administered 120 h following the last MATRIX® feeding.

Perhaps LH surge secretion was not captured in all animals because of variation in the time at which the hypothalamo-pituitary unit begins to function after an injection of EB in OVX gilts or after last feeding of MATRIX® in cycling gilts. These and subsequent results in postpartum sows (Stewart *et al.* 2010; Webel *et al.* 2013) support the conclusion that by controlling LH secretion, OvuGel® synchronizes ovulation and facilitates fixed-time AI when administered to sows at 96 h following weaning or 120 h following the last feeding of MATRIX®.

Reference

- Asanovich, K. M., B. Johnson, W. J. Chang, C. R. Barb, G. B. Rampacek, and R. R. Kraeling. 1998. Delay of estradiol-induced surge secretion of LH in gilts by intracerebroventricular injection of morphine. *Domest. Anim Endocrinol.* 15:45-53.
- Britt, J. H., K. L. Esbenshade, and A. J. Ziecik. 1991. Roles of estradiol and gonadotropin-releasing hormone in controlling negative and positive feedback associated with the luteinizing hormone surge in ovariectomized pigs. *Biol. Reprod.* 45:478-485.
- Elsaesser, F., N. Parvizi, and G. Foxcroft. 1998. Ovarian modulation of the oestradiol-induced LH surge in prepubertal and sexually mature gilts. *J. Reprod. Fertil.* 113:1-8.
- Knox, R. V. and S. L. Rodriguez-Zas. 2001. Factors influencing estrus and ovulation in weaned sows as determined by transrectal ultrasound. *J. Anim Sci.* 79:2957-2963.
- Kraeling, R. R., G. B. Rampacek, N. M. Cox, and T. E. Kiser. 1982. Prolactin and luteinizing hormone secretion after bromocryptine (CB-154) treatment in lactating sows and ovariectomized gilts. *J. Anim Sci.* 54:1212-1220.
- Stewart, K. R., W. L. Flowers, G. B. Rampacek, D. L. Greger, M. E. Swanson, and H. D. Hafs. 2010. Endocrine, ovulatory and reproductive characteristics of sows treated with an intravaginal GnRH agonist. *Anim. Reprod. Sci.* 120:112-119.
- Kraeling, R. R., B. Johnson, C. R. Barb, and G. B. Rampacek. 1998. Evidence for a luteinizing hormone surge center in the hypothalamus of the pig. *Biol. Reprod.* 58:1199-1205.
- Webel, S.K., M. Johnston, R. Kraeling and M. Swanson. 2013. Effectiveness of OvuGel® in commercial swine herds in the United States. Proceedings of the 44th Annual Meeting of the American Association of Swine Veterinarians, San Diego, CA, March 2-5, pp 119-121.