

Public Abstract

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Title:EFFECT OF RU486, A PROGESTERONE ANTAGONIST, ON UTERINE PROGESTERONE RECEPTOR, CONCEPTUS DEVELOPMENT AND OVARIAN FUNCTION DURING EARLY PREGNANCY IN PIGS

Pigs will lose approximately 20 to 46% of conceptuses before term. The majority of conceptuses are lost between day (d) 7 and d 20 of pregnancy. Factors that allow the conceptus to attach to the uterus and establish pregnancy may be to blame. Progesterone (P4), the hormone of pregnancy, down-regulates the progesterone receptor (PGR) specifically in the uterine epithelium during both the estrous cycle and early pregnancy in the pig. Down-regulation of the PGR is considered necessary for the conceptus to attach to the uterus and establish pregnancy. How P4 down-regulates the PGR is not fully understood. It has been suggested that P4 may increase expression of a cytokine, receptor activator for nuclear factor-kappa B ligand (RANKL), in the uterine epithelium that can then activate nuclear factor-kappa B (NF-kB). Nuclear factor kappa B is a transcription factor that is thought to enter the epithelial cell nucleus and block expression of the PGR, resulting in PGR down-regulation and conceptus attachment. To test this hypothesis, we used the P4 antagonist, RU486, to block P4 action. Gilts were injected with RU486 on d 3, 4 and 5 (T1) or on d 6 and d 7 (T2) of pregnancy. The uterus was removed on d 8 or d 12 of pregnancy. We then measured endometrial PGR and RANKL expression as well as activation of NF-kB in the epithelium. Conceptuses were also flushed from the uterine horns to monitor conceptus development. Injections of RU486 increased endometrial PGR expression, indicating that P4 does down-regulate the PGR. Endometrial expression of RANKL was greater in gilts injected with RU486 (d 8 and d 12) and activation of NF-kB was not different between treatments on d 8, indicating that RANKL and NF-kB may not be involved in PGR down-regulation. Activation of NF-kB did increase on d 12 in treatments that were conducive to normal conceptus development. Activation of NF-kB on d 12 may be a result of conceptus elongation and release of the cytokine interleukin-1 beta (IL-1B). RU486 also increased ovarian follicular diameter, number of corpora lutea, and plasma estradiol concentrations during early pregnancy in T1 gilts. Numerous oocytes were collected from the uterine horns of T1 gilts on d 12 of pregnancy indicating that treatment of pigs with RU486 resulted in ovulation.