

EFFECTS OF RELAXIN ON ESTROGEN RECEPTOR AND VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION IN THE CERVIX AND VAGINA OF NEONATAL PIGS

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While the trophic effects of relaxin on the reproductive tract mimic estrogen action, the means by which relaxin promotes growth is unclear. Studies in rats and neonatal gilts indicate that uterotrophic actions of relaxin are estrogen receptor (ER)-dependent. However, in the cervix and vagina at postnatal day (PND) 0, prior to the appearance of the ER, relaxin increased tissue wet weight by 86% while estradiol-17 β (E₂) failed to show any trophic effect. These data suggest that relaxin-induced cervical and vaginal growth is ER-independent. However, the impact of relaxin on ER expression is unknown. Thus, the first objective of this study was to investigate the effects of relaxin and E₂ on ER α expression in the neonatal cervix and vagina. In human endometrial cells, relaxin stimulates vascular endothelial growth factor (VEGF) expression, an important angiogenic factor in regulating reproductive growth. To determine the mechanism by which relaxin promotes cervical and vaginal growth, the second objective was to study the effects of relaxin and E₂ on VEGF expression. At PND 0 and 12, gilts were given E₂ (50 μ g/kg BW, ip every 24 h for 48 h) or porcine relaxin (30 μ g - PND 0; 100 μ g - PND 12, ip every 6 h for 48 h). Three h after the last injection, gilts were sacrificed and tissues collected. Protein extracts were subjected to Western blot analysis. Results in PND 0 gilts showed that after two days of treatment with either relaxin or E₂, ER α expression in the cervix and vagina was significantly increased by 254% and 195% when compared to controls ($p=0.010$, $p=0.014$, respectively). Likewise, in PND 0 gilts both relaxin and E₂ significantly increased VEGF expression when compared to controls ($p=0.001$, $p=0.002$, respectively). However, at PND 12, when cervical and vaginal tissue is ER α -positive, neither relaxin nor E₂ were effective in altering ER α levels. In conclusion, these data show that at PND 0 both relaxin and E₂ are effective in inducing ER α and VEGF expression in the ER-negative cervix and vagina. To our knowledge, this is the first time that relaxin is reported to induce ER α and VEGF expression in vivo. Although both relaxin and E₂ have similar effects on ER α and VEGF, only relaxin induces cervical and vaginal growth at this developmental stage. These data suggest that, in addition to ER α and VEGF, other signaling events are involved in relaxin-induced cervical and vaginal growth. (Supported by USDA-99-35203-7812).

Key Words: relaxin, estrogen receptor, vascular endothelial growth factor, neonatal gilts