Regulation of prostaglandin synthesis in bovine uterine stromal cells : Role of progesterone, estrogen and epidermal growth factor

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In the ruminants, prostaglandin (PG) E_2 and $F_{2\alpha}$ of uterine origin play a major role in the regulation of corpus luteum function. Although epidermal growth factor (EGF) is shown to increase uterine PG production in some species, the role of EGF in PG production in the bovine uterus is not known. The present study examined the role of EGF in PGE_2 and $PGF_{2\alpha}$ production in the uterine endometrial stromal cells in conjunction with progesterone (P) and estradiol-17β (E_2) pretreatment.

In experiment 1, conditions of trypsin treatment in 2-step enzymatic uterine cell isolation procedure with collagenase and deoxyribonuclease I (DNase I) were examined. The uterine stromal cells were isolated at a high purity (85%), when the endometrial tissues were first processed with 4,000 U/ml trypsin at 4℃ for 1 h, followed by 650 U/ml trypsin at 37℃ for 45 min in combination with collagenase (180 U/ml) and DNase I (400 U/ml). In experiment 2, the effect of P and E_2 on PGE_2 and $PGF_{2\alpha}$ production in stromal cells at the luteal phase (putative day 5-10 of the estrous cycle) was examined. Treatment with P alone increased PGE_2 and $PGF_{2\alpha}$ production, while treatment with E_2 alone had no effect on the production of the PGs. The ratio of PGE_2 and $PGF_{2\alpha}$ production was not affected by any steroid hormone treatments. In experiment 3, the effect of EGF on the production of PGs was examined in the stromal cells pretreated with P and/or E_2. Expression of PGF synthase (PGFS) and cyclooxygenase-2 (COX-2) mRNA was examined after 6 h of EGF treatment. EGF increased PGE_2 and $PGF_{2\alpha}$ production in all groups at 6 and 12 h. This effect of EGF differed among pretreatment groups and was maximal in the P and E_2 cotreatment group. The fold of increase in $PGF_{2\alpha}$ production by EGF treatment was consistent in all pretreatment groups. EGF increased the ratio of PGE_2 and $PGF_{2\alpha}$ production in the stromal cells pretreated with P. However, the degree of increase in the ratio of PGE_2 and $PGF_{2\alpha}$ production was reduced in the presence of E_2 during the pretreatment period. EGF increased COX-2 expression in all the groups. In contrast, the rate of increase in the expression of PGFS by EGF treatment was reduced when stromal cells were pretreated with P.

In conclusion, P and E_2 had regulatory effect on PGE_2 and $PGF_{2\alpha}$ production in bovine uterine stromal cells obtained between 5 and 10 days after estrus. The results of the present study also suggest that EGF increases the ratio of PGE_2 and $PGF_{2\alpha}$ production in the stromal cells that have been sensitized to P, whereas the presence of E_2 during the sensitization period suppresses the effect of EGF.