Estrogen and Progesterone Differentially Regulate the Levels of Cystic Fibrosis Transmembrane Regulator (CFTR), Adenylate Cyclase (AC), and Cyclic Adenosine Mono-Phosphate (cAMP) in the Rat Cervix

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SUMMARY

The consistency of the cervical mucus changes with the reproductive cycle, which we hypothesized involved changing levels of cystic fibrosis transmembrane regulator (CFTR), adenylate cyclase (AC), and cyclic adenosine mono-phosphate (cAMP). We therefore measured the abundance of each in the rat cervix under estrogen and progesterone influence to determine if the activity of these components could explain the changes in the consistency of cervical mucus. Ovariectomised adult female rats were treated with three days of either estrogen (1 μg/kg/day) or progesterone (20 mg/kg/day), or three days of estrogen followed by two days of either vehicle or progesterone or estrogen plus progesterone. In some groups, mifepristone (7 mg/kg/day) was concurrently given with progesterone. Animals were then sacrificed, and the cervix was harvested for protein and mRNA expression analyses by Western blot and real-time PCR, respectively. The distribution of proteins was investigated by immunohistochemistry, and levels of cAMP were determined by enzyme-linked immuno-sorbent assay (ELISA). CFTR mRNA, AC protein, and cAMP levels in cervical homogenates as well as the tissue distribution of CFTR and AC in endocervical epithelia were highest under estrogen influence; the opposite pattern was seen under progesterone influence. Cervical lumen circumference was highest under estrogen and lowest under progesterone. The effects of progesterone were antagonized by mifepristone. Therefore, increased abundance of CFTR, AC, and CAMP under estrogen influence could account for the increased fluid accumulation within the cervical lumen, which would contribute to lower cervical mucus consistency, whereas progesterone reverses this effect at the molecular and organ level.