25

The Transport of Estrogens Into The Postmenopausal Human Perfused Uteri

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Twenty human uteri obtained from postmenopausal women undergoing abdominal hysterectomy for cervical carcinoma or leyomyomas were perfused by a machine for the extracorporeal perfusion. ^{3}H and ^{14}C estrogens mixed in 300 µl of human serum were injected during the perfusion. Perfusate samples were collected for 30 minutes and endometrial samples were taken at the end of the perfusate collection. The experiments indicated a preferential uptake of unconjugated estrogens by the organ while the permeability of the endometrial microvessels appears to facilitate the transport of E_1S in the endometrium.

This work was supported by C.N.R. , grant n. 84.00817.96

26

BLOCKAGE OF THE POTENT ESTROGENIC ACTIVITY OF 5-ANDROSTENE-3β, 17β-DIOL (Δ^5-DIOL) AND DEHYDROEPIANDROSTERONE (DHEA) BY THE ANTIESTROGEN LY-156758 IN RAT ANTERIOR PITUITARY CELLS IN CULTURE. Jacques Simard and Fernand Labrie, MRC Group in Molecular Endocrinology, Laval University Medical Center, Québec, G1V 4G2 - CANADA.

Previous studies have shown that the C_{19} adrenal steroid Δ^5-diol, a metabolite of DHEA and DHEA-sulfate (DHEA-S), can act as an estrogen at physiological concentrations in target tissues. Since estrogens are known to exert a specific stimulatory effect on dopamine (DA)-inhibited prolactin (Prl) secretion as well as on intracellular Prl content in lactotrophs, we have investigated the effect of 17β-estradiol (E_2) and C_{19} adrenal steroids on these parameters. Following a 72-h preincubation, the estrogenic effects of E_2, Δ^5-diol, DHEA, and DHEA-S result in a 7-, 8-, 4- and 3.5-fold increase, respectively, in Prl cell content. The effects are exerted at respective ED_{50} values of 0.023, 60, 220 and 2330 nM. LY-156758 (100 nM) completely blocks the stimulatory effect of the steroids up to 1 nM E_2, 1 µM Δ^5-diol, 5 µM DHEA and 10 µM, DHEA-S. The sensitivity of lactotrophs to DA action decreased by 4-fold ($p < 0.01$) after a 48h-pretreatment with either 10 nM E_2, 1 µM Δ^5-diol or 1 µM DHEA. Prl release measured at the end of the 4-h exposure to 30 nM DA was stimulated by 4-fold in cells pretreated with E_2, Δ^5-diol or DHEA at respective K_D values of 0.013, 21 and 143 nM. All the antidopaminergic effects of the steroids are competitively inhibited by simultaneous incubation with LY-156758. In addition, Δ^5-diol and DHEA have 100-, >10000-fold lower affinities, respectively, than E_2, for the estrogen receptor (ER) in rat anterior pituitary and human breast cancer (ER^+) homogenate. The present data suggest that DHEA and its sulfate are metabolized in the anterior pituitary gland into Δ^5-diol, a C_{19} steroid showing a high affinity for the ER, thus supporting the potential role of C_{19} adrenal steroids in estrogen-dependent diseases, especially breast cancer.