53

EFFECTS OF ESTROGEN TREATMENT OR ORCHIDECTOMY ON SERUM STEROIDS, STEROID BINDING AND "STEROID SENSITIVE" PROTEINS IN PROSTATIC CANCER PATIENTS. K Carlström, L Collste, A Eriksson, SA Gustafsson, P Henriksson, Å Pousette, R Stege and B von Schoultz. Huddinge University Hospital, Huddinge and Umeå University Hospital, Umeå, Sweden.

After six months of estrogen treatment of 34 prostatic cancer patients with i.m. polyestradiol phosphate + oral ethinyl estradiol, serum levels of testosterone(T), DHA, DHAS and albumin were significantly reduced to 6±1, 67±9, 62±8 and 88±2 % of their respective pretreatment values (mean ± SEM). Levels of androstenedione(A-4) were unaffected while total cortisol, SHBG and pregnancy associated α_2-macroglobulin(α_2-PAG) levels were significantly increased to 230±10, 556±39 and 3518±47 % respectively. Six months after orchidectomy of another group of 33 patients, T, DHAS, A-4 and estradiol levels were significantly reduced to 4±1, 83±10, 82±7 and 52±4 % respectively. DHA, cortisol, SHBG, α_2-PAG and albumin levels were not affected. Despite the clearcut effects of exogenous estrogens upon the "steroid sensitive" proteins SHBG, α_2-PAG and (indicated by increased total cortisol) CBG, the dramatic change in the endogenous androgen/estrogen balance caused by orchidectomy was without any effect in this respect, indicating that other factors than endogenous steroids may be more important in the physiological regulation of these proteins. Besides reducing T levels to orchidectomy values and further reducing free T by increasing SHBG levels, estrogen treatment also reduces adrenal DHA and DHAS levels, thus further decreasing the total amount of circulating androgen. A minor part of the decrease in DHAS may be due to the reduced albumin level, since albumin binds steroid sulfates with a higher affinity than it binds the corresponding unconjugated steroids.

54

Title : EFFECT OF SYNTHETIC ANTIPROGESTINS ON OVARIAN ESTRADIOL PRODUCTION

Authors : KHARBANDA S.M. and FAROOQ A

Address : Department of Reproductive Biology, All India Institute of Medical Sciences, New Delhi-110029, INDIA

Abstract: The effect of synthetic antiprogestins RMI - 14156 and STS 557 on gonadotrophin stimulated estradiol production in human ovarian Granulosa Cells has been tested in vitro . Granulosa cells from human ovaries were cultured in Eagles Minimum essential Medium with or without Luteinising Hormone (10 ng/ml), Follicle Stimulating Hormone (100 ng/ml), Androstenedione (10^{-7}M), RMI-14156 (10^{-9}M to 10^{-5}M) and STS 557 (10^{-9}M to 10^{-5}M) in a humidified 95% air, 5% CO_2 incubator at 37°C for 48 hours. Antiprogestins RMI-14156 and STS 557 were found to stimulate the production of estradiol by cultured human granulosa cells in a dose dependent manner. Significant stimulation (p o.oo1 - p o.o1) was observed at higher doses viz. 10^{-6}M and 10^{-5}M of RMI - 14156 and STS 557. The two antiprogestins also stimulated the gonadotrophin induced estradiol production significantly. Biotransformation studies of RMI-14156 suggested that this antiprogestin was firstly converted to its isomer 40 mts. after its addition to the cultures and this isomer further metabolised to an estrogen.