8

INTRATISSULAR ANDROGENS IN BPH AND PROSTATIC CANCER.

K.D.Voigt, W.Bartsch and M.Krieg. Dept. of Clinical Chemistry, Medical University Clinic, Martinistraße 52, D-2000 Hamburg 20, Fed.Rep.Germany.

The wellknown hormone dependency of the normal human prostate and of BPH and prostatic carcinoma stimulated the study of cellular events which would possibly lead to specific steroid hormone patterns under the respective prevailing condition. In extending earlier observations on a significant DHT and E_2 accumulation especially in stromal nuclei of BPH recent data on the uptake and metabolism of adrenal androgens clearly underline the important differential role of either stromal or epithelial cells. Epithelium and stroma of BPH contained a quantitatively different pattern of steroid metabolizing enzymes. This dualism of enzyme activity favours the conversion of testosterone to DHT in the stroma while androgens of adrenal origin are metabolized mainly in BPH epithelium. Further to quantitative data on the intracellular distribution of the three sex steroid classes (estrogens, androgens, adrenal androgens) and to k_m and V_{max} values of the respective steroid metabolizing enzymes in question (5α-reductase, 3α/ß-HSDH, 17ß-HSDH, sulfatase, aromatase) the impact of antihormones (cyproterone acetate) on the intratissular distribution and on the in vivo cytosolic and nuclear binding of DHT as well as on its biological implications will be discussed.

9

HORMONAL REGULATION OF EPITHELIAL AND STROMAL CELL GROWTH IN THE HUMAN PROSTATE

Jack Geller, M.D., Jerry D. Albert, Ph.D. and Junda Liu, M.D.
Mercy Hospital and Medical Center, San Diego CA 92103 U.S.A.

The normal human prostate contains both epithelial and stromal cells. This study addresses the important question of the biological effects of androgen and estrogen on growth of epithelial and stromal cells. To study androgen effects on epithelial and stromal growth, we treated patients with either 160 mg/day of Megace® (M) an anti-androgen or a combination of M 160 mg/day plus 1200 mg/day of ketoconazole (KC) an inhibitor of steroid synthesis. To study estradiol effects on stromal growth we gave tamoxifen (Tam), an anti-estrogen 40 mg/day for one week prior to TURP. Epithelial and stromal cells were separated with collagenase. The epithelial cells were incubated with either ^{3}H-leucine or L-^{35}S-methionine; ^{3}H-proline was used for labelling stromal protein and incorporation into protein was expressed as cpm/mg protein. Total prostate DHT concentration was also measured in each tissue. M alone and M + KC significantly decreased incorporation of either ^{3}H-leucine or L-^{35}S-methionine into protein. Tissue DHT levels were significantly suppressed by both protocols. Combining all the data for the epithelial cell studies gave a significant correlation of DHT with protein synthesis ($p < 0.001$) over a very wide range of DHT. A significant correlation was also noted between stromal growth and DHT. Estrogen also appeared to be an important growth factor for stromal cells since Tamoxifen significantly decreased stromal protein synthesis.

CONCLUSIONS: In hormone-dependent prostate cancer (epithelial cell disease), even small amounts of prostate DHT would have significant and almost exclusive effects on tumor cell growth. In BPH where the stromal cells are the dominant tissue component, both estrogen and DHT have significant growth-regulating effects.