49

CLINICAL RESULTS OF FARLUTAL APPLICATION IN CASES OF ADVANCED PROSTATE CARCINOMA

H. Koumanov, M. Tzvetkov, D. Mladenov, A. Filev
Medical Academy, NINUHT, Sofia, Bulgaria

In recent years we have applied Farlutal (produced by Farmitalia) to cases of advanced prostate carcinoma. We have divided the cases into two groups: cases treated with Farlutal only, and cases treated first by other drugs which had no particular effects. Treatment was carried out according to three schemes: parenteral administration only, per os administration only, parenteral administration follow-by per os administration. Patients should not suffer from thrombophlebitis, thromboembolitic disturbances or acute liver insufficiencies. To evaluate the responses to treatment, we performed subjective and objective investigations. We compared these results to results for a group of control patients treated with other cytostatics. Our clinical investigations of Farlutal show very good patient tolerance. Improvement of the general condition of patients and the local status of the prostate have been proved objectively.

50

MORPHOLOGICAL INVESTIGATION AS AN OBJECTIVE CRITERION FOR EVALUATING THE EFFECT OF TREATMENT FOR ADVANCED PROSTATE CANCER

H. Koumanov, M. Tzvetkov, Y. Topov,
D. Mladenov
Medical Academy, Sofia, Bulgaria

Treatment of advanced prostate carcinoma is exclusively conservative. There are a number of clinical, laboratory, x-ray and immunological methods available to ascertain the effect of the applied treatment. We consider morphological investigation to be the most accurate criterion for demonstrating successful treatment of such serious cases. At the beginning of our investigation, in 1976, we studied the morphological changes in malignant prostate tissue by cytological and histological methods. These investigations were performed the 1st, 3rd and 6th month after the beginning of treatment and every 6 months thereafter. We found that effective treatment causes changes in the tissue, cells and nuclei after 6 months, at the earliest. Our results with simultaneous use of histologic and cytologic methods justify our reliance on cytologic control completely.

51

COMBINING THE ANTIANDROGEN ANANDRON® WITH LHRH AGONIST: SEQUENTIAL ASSAYS OF HORMONES AND PROSTATE MARKERS DURING A DOUBLE-BLIND STUDY.

J.M.Kuhn, C.Bertagna, T.Billebaud, P.Costa, R.Dahan, R.Edelstein, J.Fiet, P.Grise, J.L.Louis, A.Moulonguet, H.Nevratil.
Univ.Rouen; Roussel-Uclaf, Romainville; C.H.Montfermeil; Lab.Cassenne, Paris; Hôp.St -Louis, Paris; CHU Bichat, Paris; CHR Nîmes, France

To evaluate if the antiandrogen Anandron (Nilutamide) can block the unwanted effects of the increase in testosterone (T) observed during the first days of treatment with an LHRH agonist, a multicenter double-blind study was performed. 36 patients with metastatic prostate cancer and elevated prostatic acid phosphatases (PAP) were randomized into two groups: the 1st group (G1, n=17) received buserelin, 500 µg/day sc and Anandron 300 mg/day orally; the 2nd group (G2,n=19) received buserelin and placebo. Symptoms were assessed and plasma was collected before treatment, every day for 2 weeks and after 3 and 4 weeks of treatment. Increase in pain, assessed on a visual analog scale, occurred more frequently in G2 than in G1) and 1 pt in G2 had to be withdrawn from the study on day (d) 9 because of renal insufficiency and hydronephrosis. Although a similar early (d 3-4) peak in T occurred in the 2 groups, PAP variations in G1 were significantly different from those in G2 ($p < 0.05$ from d7 to d10): in G1 there was a marked fall from d4 on (median PAP change from baseline: -44% on d4) while in G2 there was first an increase (+25% on d10) followed by a fall (-49% on d22). Results on prostate specific antigen and hormones other than T will also be presented. This data confirms that combining Anandron with buserelin can block the unwanted biological and clinical effects of the early increase in T induced by the LHRH agonist.

52

ANDROGEN RECEPTORS AND MOLECULAR MARKERS FOR GENE EXPRESSION AND REPRESSION IN THE PROSTATE

S.Liao, R.A.Hiipakka and C.Chang
Ben May Institute and the Dept. of Biochem. and Molecular Biology, Univ.Chicago, Chicago, Illinois, USA

In the rat ventral prostate, androgen receptors can recycle between free and nucleus-bound forms and can be present as forms which do not bind androgens, but can be activated to an androgen binding state. Therefore, it is important to consider the dynamic status of the receptors and their modulators when the androgen sensitivity of prostate cells is evaluated. A well-studied protein marker for androgen action in the rat ventral prostate is α-protein which binds cholesterol, in vivo, and is the most abundant protein in prostate fluid. Another protein marker is spermine-binding protein (SBP) which is also present in prostate fluid.SBP is a glycoprotein rich in aspartic acid. Specific spermine binding may be dependent on androgen-regulated SBP phosphorylation. cDNA dot hybridization analysis has shown that the levels of mRNAs for both α-protein and SBP decrease rapidly after castration but this effect is reversed by androgens. The expression of genes for several prostate proteins is negatively controlled by androgens. For example, the level of mRNA per unit DNA for a 27 kDa protein increases about 3-fold within 2 days after castration and this increase is rapidly reversed within 6 hours after androgen injection. The protein coded by this mRNA has been identified recently as an isozyme in the glutathione S-transferase (GST) family. GST isozymes function as detoxification enzymes in many organs. However, they may be involved in the control of androgen dependent cellular functions and castration induced involution of the prostate. (Supported by US NIH Grants DK-09461/DK-37694 and American Cancer Society Grant BC-528).