THE EFFECTS OF CHANGES IN TESTOSTERONE LEVEL ON THE DEVELOPMENT OF THE PROSTATE CANCER

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Introduction: The androgen blockade method has been widely used during treatment of prostate cancer for more than 60 years. However, a few years after the start of hormonal therapy the majority of patients show the development of low-differentiated androgen-resistant prostate cancer. The purpose of the work is to study the influence in changes in the testosterone level on the levels of hormones and on cell growth factors in men. The study was done in order to prove the hypothesis that a significant reduction in the level of testosterone has a strong influence on the development of cancer of the prostate, including it-s low-differentiated hormonal-resistant form.

Methods: 14 patients with cancer of the prostate of the 3-4 stage were held under examination. The ages of the patients ranged from 60-79. In all patients 1 month after an orchiectomy the levels of the following were measured in the serum of the blood: LH, FSH, prolactin, STH, testosterone, 17β-estradiol, estrone, 5α-dihydrotestosterone, insulin, 25-OHVitD3, main fibroblast growth factor (bFGF), epidermal growth factor (EGF), transforming growth factor-β(βTGF), insulin-similar growth factor-1 (IGF-1), PSA, IL-lβ, tumor necrosis factor α(TNFα), acid phosphatase, alkaline phosphatase, and Ca++.

Results: Upon initial tests the average indicators of IL-lβ, acid phosphatase, alkaline phosphatase, TNFa, and PSA had increased, while the indicators of testosterone and βTGF had decreased. A month after orchiectomy all patients showed a significant decrease in levels of testosterone($p<0.005$), 5α-dihydrotestosterone, 17β-estradiol ($p<0.05$) in comparison to initial indicators, while levels of LH and FSH had increased($p<0.001$). The reduction of testosterone was accompanied by a statistically meaningful increase of prolactin, STH, and estrone($p<0.05$). The reduction of 5α-dihydrotestosterone determined the reduction of EGF($p<0.05$). The decrease in the level of testosterone was accompanied by a statistically significant increase in the levels of insulin, IGF-l($p<0.05$), bFGF($p<0.01$), 25-OHVitD3, and Ca++($p<0.05$) as well as by a reduction in the levels of βTGF, IL-lβ, TNFα($p<0.05$), acid phosphatase($p<0.01$), alkaline phosphatase($p<0.05$) and PSA($p<0.005$).

Conclusions: The increase in aromatase activity and the levels of the majority of growth factors after orchiectomy indicates that compensatory-adaptation reactions which develop when the level of testosterone goes down are

directed towards an increase in the activity of the cells. Their expression is proportional to the degree of reduction of the testosterone level.

The reduction of the level of testosterone causes the breach of regulation of the cell-cycle and the start of apoptosis. Furthermore, a decrease in the indicators of anti-tumor cell immunity was observed (when the reduction of the level is significant).

Thus the orhchiectomy only intensifies the consecquences of the age-related decrease of testosterone and doesn't eliminate ethiological and all pathogenetic factors of the development of prostate cancer.