

## **The effects of changes in testosterone level on the development of cytokines among patients with prostate cancer**

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### Objectives

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.

### 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, 17 $\beta$ -estradiol, estrone, 5 $\alpha$ -dihydrotestosterone, insulin, 25-OHvitD<sub>3</sub>, main fibroblast growth factor (bFGF), epidermal growth factor (EGF), transforming growth factor- $\beta$ ( $\beta$ TGF), insulin-similar growth factor-1 (IGF-1), PSA, IL-1 $\beta$ , tumor necrosis factor  $\alpha$ (TNF $\alpha$ ), acid phosphatase, alkaline phosphatase, and Ca<sup>++</sup>.

### Results

Upon initial tests the average indicators of IL-1 $\beta$ , acid phosphatase, alkaline phosphatase, TNF $\alpha$ , and PSA had increased, while the indicators of testosterone and  $\beta$ TGF had decreased. A month after orchiectomy all patients showed a significant decrease in levels of testosterone ( $p < 0,005$ ), 5 $\alpha$ -dihydrotestosterone, 17 $\beta$ -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 5 $\alpha$ -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-I ( $p < 0.05$ ), bFGF ( $p < 0.01$ ), 25-OHvitD<sub>3</sub>, and Ca<sup>++</sup> ( $p < 0.05$ ) as well as by a reduction in the levels of  $\beta$ TGF, IL-1 $\beta$ , TNF $\alpha$  ( $p < 0.05$ ), 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 orchiectomy only intensifies the consequences of the age-related decrease of testosterone, and does not eliminate etiological and all pathogenetic factors of the development of the prostate cancer.