
THE ROLE OF PSA IN PROSTATE CANCER DIAGNOSIS AND SCREENING

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Abstract: Most tumor markers are specific biomolecules present in higher concentrations than normal reference values in the serum of patients with a certain type of cancer. These molecules are produced by the cancer itself or the patient's body, which results in a metabolic or immune response of healthy cells due to the presence of cancer cells in the patient. According to the chemical structure, tumor markers can be enzymes, specific proteins, glycoproteins, various antigens, hormones, specific receptors, etc. PSA is a specific glycoprotein by chemical structure and is secreted by the acini and ducts of the prostate gland. Healthy prostate cells secrete it in normal concentrations from 0 to 4 ng/ml, while cancerous prostate cells secrete it in much higher concentrations. The tumor marker PSA is tissue-specific, that is, it is specific only for prostate diseases when its concentration increases many times. The concentration of tumor markers is determined to precisely monitor the success of the applied therapy in conditions of an already established diagnosis of the disease. Certain elevated PSA values may indicate progression of prostate disease or recurrence, or an inadequate response to prescribed therapy, while decreased PSA values indicate successful treatment for the disease and an adequate response of the body to it. The prostate is an important part of the male reproductive system whose role is to produce prostatic secretion that participates in the production of sperm, by mixing it with seminal fluid from the testicles. Prostatic secretion has a nutritional and protective role for sperm on their way to the egg in the uterus, so it facilitates the movement of sperm, creates an ideal acidic environment for their survival and contains substances with nutritional and energy value such as immunoglobulins, prostaglandins, fructose, citric acid, various enzymes. The prostate is responsible for the production of the male sex hormone testosterone, or dihydroxytestosterone (DHT), which is converted into testosterone under the action of the enzyme 5-alpha-reductase in the prostate. The prostate surrounds the ureter, and therefore any disease of it such as prostate cancer causes obstruction, i.e., urinary retention. Prevention of the disease is timely care for the general health of a man. The level of concentration of total PSA was examined in healthy male patients aged 40-80 years with diagnosed prostate cancer. The level of total PSA was also monitored in the same patients treated with appropriate anticancer therapy (Flutamid), and the effectiveness of the prescribed therapy was determined. The results obtained showed that in the control group of patients, the levels of total PSA were within normal reference values, while in patients with diagnosed prostate cancer, the values of total PSA significantly increased. In patients treated with appropriate anticancer therapy with Flutamid, a decrease in the concentration levels of total PSA was recorded, which indicates a successfully administered therapy and an appropriate response of the organism to it.

Keywords: total PSA, glycoprotein, prostate, prostatic secretion, carcinoma prostatae.

1. INTRODUCTION

In terms of frequency of occurrence, prostate cancer is the most common health problem and cause of death in men. In the early stages, the disease is difficult to notice because no symptoms or complaints appear, and when the first symptoms appear, it is a sign that the cancer is in an advanced stage. Therefore, urologists emphasize the importance of preventive prostate examinations as the only way to detect the disease early. The average age of men diagnosed with prostate cancer is about 66 years. The causes of cancer are not fully understood, but it is believed that certain risk factors increase the likelihood of the disease, such as: age, genetic predisposition, obesity, ethnicity, exposure to carcinogenic chemicals, heavy metals, herbicides, pesticides, excessive alcohol use, smoking. Symptoms that occur with prostate cancer are: difficulty urinating, feeling of incomplete emptying of the bladder, slow urine stream, urine leakage after urination, blood in the urine, blood in the semen, pain and tenderness in the lower back and pelvis (due to the spread of the cancer), swelling and pain in the legs (due to obstruction of venous or lymphatic vessels), weight loss, anemia, impotence. These symptoms are a sign that it is necessary to conduct a digital rectal examination of the prostate, an ultrasound examination and laboratory tests along with determining the concentration of PSA. Prostate cancer begins when changes in DNA occur in its cells, i.e. mutations. Mutations cause increased abnormal growth of prostate cells and they divide faster, forming a tumor due to their accumulation. Most often, prostate cancers are adenocarcinomas that develop from glandular cells of the prostate. Flutamid belongs to the group of drugs that

prevent testosterone from contacting cancer cells. It acts as a selective androgen receptor (AR) antagonist, competing with androgen hormones such as testosterone and dihydroxytestosterone (DHT) for binding to androgen receptors in the glandular tissue of the prostate. The objectives of the study were to determine the concentration of the tumor marker total PSA, in diagnosed prostate cancer. The role in determining the concentration of total PSA is to monitor its level after a diagnosis of prostate cancer is made, when treatment of the disease with anticancer therapy is started in order to see the effect of its application.

2. MATERIAL AND METHODS

The studies were conducted in male patients aged 40 to 80 years with a diagnosis of prostate cancer. The patients were divided into three groups:

- control group of patients with normal circulating PSA levels (n=55)
- group of patients with diagnosed prostate cancer (n=55)
- group of patients treated with anticancer therapy (Flutamide) which acts as a selective antagonist of androgen receptors (AR) (n=55).

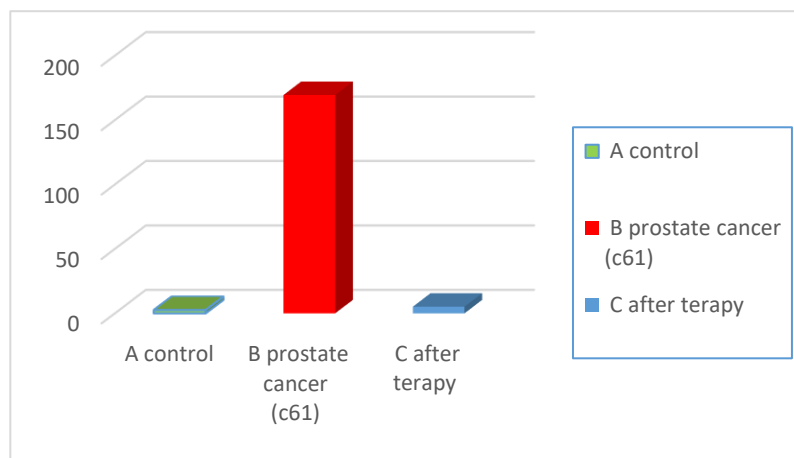
In these groups of patients, the level of total PSA concentration in the circulation was examined.

Principle of the method: The method for determining the concentration of total PSA is a chemiluminescent, immunometric "sandwich" method (ELISA) that uses two different antibodies specific for different epitope antigens. The solid phase of the PSA reagent is a microtiter plate coated with monoclonal anti-PSA antibodies from rat directed to an epitope of the PSA molecule as an antigen. The liquid phase of the reagent contains alkaline phosphatase derived from bovine intestine conjugated to a second polyclonal anti-PSA antibody (E-Ab). The light generated by the reaction is measured with a luminometer. The light produced is directly proportional to the PSA concentration in the sample. The normal reference values for the level of PSA concentration in serum are PSA < 4.0 ng/ml.

3. RESULTS

The results obtained in patients diagnosed with Carcinoma prostatae, diagnosis code C 61, show clearly significantly higher values for PSA concentration compared to the control group of patients. These patients with Carcinoma prostatae after treatment with anticancer therapy to reduce the PSA level have visibly reduced results for total PSA to levels close to the control group of patients. The graph clearly shows the effect of anticancer therapy with Flutamide in reducing PSA concentration, which acts as a selective antagonist of androgen receptors (AR), competing with androgen hormones such as testosterone and dihydroxytestosterone (DHT) for binding to androgen receptors in the prostate.

Graph: Serum PSA level in prostate carcinoma



Legend:

- group A, patients with normal serum PSA level (control group)
- group B, patients diagnosed with prostate carcinoma (increased serum PSA level)
- group C, patients treated with therapy to reduce serum PSA level (Flutamid)

Source: authors' research

4. DISCUSSION

The studies were conducted in patients with a definitive diagnosis of prostate cancer, some with surgical intervention, and others without surgical intervention on the prostate when surgical intervention is not possible due to metastasis of the cancer to other organs, most often the colon. In both cases, drug therapy is prescribed with regular biochemical tests for PSA concentration as an indicator of the course of the disease and the effectiveness of the applied anticancer therapy. The results shown in the graph for PSA concentration in patients with prostate cancer show that with the use of anticancer therapy with Flutamide, PSA concentration is evidently reduced, but it does not return to normal reference values, i.e. they are slightly elevated above these limits. However, any reduction in the enormously elevated PSA values in invasive prostate cancers is considered a success. The drug Flutamide works by preventing the hormone testosterone from contacting cancer cells and acts as a selective androgen receptor (AR) antagonist, competing with androgen hormones such as testosterone and dihydroxytestosterone (DHT) for binding to androgen receptors in the cells of the prostate glandular tissue. Since testosterone has the effect of stimulating prostate cancer cells to grow and multiply, this prevents its contact with its receptors that are already busy binding to the drug, and thus prevents its effect in stimulating the growth of cancerous prostate cells. The graph clearly shows the effectiveness of the applied anticancer therapy in patients with diagnosed prostate cancer by reducing the concentration of PSA in the treated group of patients with Flutamide.

5. CONCLUSIONS

From the studies conducted on the level of total PSA in serum in conditions of prostate cancer in men, we draw the following conclusions:

- reduced quality of life in patients with prostate cancer due to symptoms that occur in this disease such as difficulty urinating, incomplete emptying of the bladder, bloody urine and semen, pain and sensitivity in the lower back and pelvis, swelling and pain in the legs, anemia, impotence.
- it is evident that with the use of appropriate anticancer therapy (Flutamid), the negative effect of the disease is removed.
- in conditions of prostate cancer, the concentration of total PSA in patients significantly increases compared to the concentration in the control group of patients.
- with the use of drug therapy (Flutamid) in the treated group of patients, the level of PSA is evidently reduced to concentrations slightly higher than those in the control group.
- Once the problem is identified, appropriate therapy is initiated to reduce serum PSA levels using anticancer therapy that acts as a selective androgen receptor (AR) antagonist, competing with the androgen hormones, testosterone and dihydroxytestosterone (DHT), for binding to androgen receptors in prostate cells. This prevents the stimulation of the growth of cancerous prostate cells.

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