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## NEW DIAGNOSTIC OPPORTUNITIES FOR THE STUDY OF THE EXPRESSION OF PROSTATSPECIFIC GENES IN DEPOSIT AND URINE EXOSOMOX

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Evaluation of the expression of prostate-specific cancer 3 antigen (PCA3) by genetic methods in an organ tissue is a promising direction for determining the development of malignant processes in the prostate gland. This is due to the fact that overexpression of PCA3 in the prostate gland is markedly different in the presence of cancer. The same is true in the presence of metastases of this disease. At the same time, it does not manifest itself in the presence of benign processes in the prostate gland [1]. In 2007, exosomes were used in genetic studies as an object of study. This is due to the fact that exosomes include mRNA in their composition, and also take part in intercommunicative intercellular connections [2]. Tumor cells produce more exosomes than ordinary ones. Evidence was also obtained that exosomes are involved in the creation of predict, in which metastases will be located. They also affect the change in the tumor environment [3]. The study of new methods for assessing PCA3 expression will provide an opportunity to increase the success of diagnostics, as well as predict the development of diseases. The main objective of the work is to increase the success rate of predicting the recurrence of the disease in the early stages after radical treatment by studying the expression of PCA3 in microscopic extracellular vesicles and urine sediment of patients who have been diagnosed with localized prostate cancer.

**Materials and Methods.** The study involved 148 people with prostate cancer. For inclusion in the study, the patient had to meet several basic requirements. 1. Prostate cancer should be localized (T1c-T2c). 2. In surgical treatment, radical prostatectomy (RPE) should be performed. 3. The patient should not have distant metastases.

Every three months, blood samples for prostate-specific antigen (PSA) were taken from people studied after radical prostatectomy.

PCA3 expression in microscopic extracellular vesicles and urine sediment was assessed using a polymerase chain reaction, which was carried out under real-time conditions. After that, comparison of threshold cycles for the studied and reference gene (designated as Ct) was performed. In this case, the reference gene was the gene for kallikrein KLK3. It is characterized by prostate-specific expression. At the first stage of the sample preparation, genetic studies were carried out. For this, the urine of the studied person was taken in a volume of 70 ml after the massage of the prostate gland.

It was carried out in the form of three-time mechanical stimulation of each lobe of the gland. To obtain a sample of the precipitate, immediately after collecting the material for analysis, 20 ml of urine was centrifuged. This happened for 15 minutes at a speed of three thousand revolutions per minute. After that, the supernatant was eliminated. The next step was to resuspend the precipitate. It was transferred to a 1.5 ml "eppendorf" tube, adding 1 ml of "RNA Medium", the material was preserved. When microscopic intracellular vesicles were isolated, 50 ml of urine was taken for centrifugation, which was also carried out for 15 minutes, but at a speed of 10 thousand revolutions per minute. Then the supernatant was centrifuged for three hours at the same speed. For washing the precipitate used 3 ml of PBS. The precipitate was obtained using short-term centrifugation. After that, microscopic intracellular vesicles were resuspended in PBS buffer. For this, 200  $\mu$ l of material was taken.

**Results.** A recurrence of prostate cancer may occur within a few months or years after radical surgery. Allocate biochemical, systemic and local recurrence. With biochemical, PSA only increases in blood. It occurred in 20.3% of the studied patients during the first two years. Given this information, an analysis of pre-operative genetic studies was carried out (Table 1).

**Table 1.** The content of PCA in the blood and the expression level of the PCA3 gene in exosomes and urine sediment in patients with and without biochemical relapse

Indicator	Biochemical relapse is (n=30)	There is no biochemical relapse (n=118)	For the whole group (n=148)	p
PSA blood, ng/ml. Median [25-75%]	14,2 [9,9; 18,8]	12,0 [8,8; 16,7]	12,8 [9,2; 17,1]	0,19
$\Delta$ Ct PCA3–KLK3in urine exosomes. Median [25-75%]	-2,37 [-3,49; 0,55]	-0,95 [-1,93; 0,98]	-2,01 [-2,42; 0,87]	0,04
$\Delta$ Ct PCA3–KLK3in urine sediment. Median [25-75%]	-0,44 [-0,56; 0,57]	0,06 [-0,55; 0,90]	-0,35 [-0,54; 0,75]	0,75

In people with prostate cancer, the interquartile range of PSA and median were equal both before and after surgery ( $p=0,19$ ) (table 1).

These values of  $\Delta$ Ct of the PCA3 gene, when compared with the KLK3 gene that was present in the sediment, were also very similar in all subgroups ( $p=0,75$ ) (table 1). The presence of a negative  $\Delta$ Ct PCA3 value relative to the reference one indicated an increase in the expression of the gene under study. At the same time, in urine exomes in patients with an unfavorable course of the disease, an increased level of mRNA of the studied gene was found ( $p=0,04$ ). The median  $\Delta$ Ct PCA3 – KLK3 in microscopic intracellular vesicles at a biochemical recurrence reached -2,37. In people without biochemical recurrence, this figure was -0,95 (Table 1). With a lower  $\Delta$ Ct indicator, a higher PCA3 mRNA index can be noted if we compare it with the KLK3 gene in microscopic intracellular urine vesicles.

Increased PCA3 expression in microscopic intracellular vesicles was associated with biochemical recurrence.

**Conclusions.** Thus, we determined that the analysis of PCA3 gene expression in the sediment and microscopic intracellular urine vesicles, despite some limitations, provides a sufficient amount of data to predict the development of disease recurrence in the first 2 years. Assessment of PCA3 expression in microscopic intracellular vesicles and urine

sediment after prostate massage allows to predict the appearance of biochemical recurrence after RPE in patients with localized prostate cancer is higher than the determination of prostate specific antigen in the serum. Increase in PCA3 expression in microscopic intracellular vesicles and urine sediment after prostate massage in patients with localized prostate cancer suggests that the likelihood of recurrence of the biochemical type in the first 2 years is increased.

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**Key words:** prostate cancer, exosomes, sediment, urine, prostate-specific antigen 3.

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## DYNAMICS OF THE CHANGE OF LEUKOTRIENES SYNTHESIS AND LIPOPEROXIDATION ACTIVITY DURING THE EARLY PERIOD OF THE TREATMENT OF THE PATIENTS WITH DUODENAL PEPTIC ULCER IN COMBINATION WITH ESSENTIAL HYPERTENSION

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It is known that leukotrienes (LT) are considered not only as mediators of formation of the gastric and duodenal lesions but also as mediators of the constant inflammation in the periulcerous zone [1, 3, 4, 7, 8]. Local and systemic modulating effects of LT, their influence upon the initiation of production of the platelet activating factors and neutrophils binding factors [6, 10], the formation of superoxide anions, the release of lysosomal enzymes [2, 5, 9] and their direct participation in the inflammatory process let us suggest that the level and the character of dynamics of LT change are some of the possible indicators of the inflammatory process' treatment efficiency and prognosis of the course of the disease. We did not exclude the possibility of the comorbid pathology influences upon the quantitative and qualitative changes of biologically active substances and metabolic indices. It was the ground for carrying out the present study. The aim of the research was to study the dynamics of lipoxygenase metabolites of the arachidonic acid content and lipoperoxidation activity before treatment and during the early period after carrying out the basic therapeutic course in the patients with duodenal peptic ulcer and comorbid essential hypertension.

**Materials an Methods.** The group of the examined individuals included 54 patients with duodenal peptic ulcer aged 38-49 years, among whom 33 patients had the comorbid essential hypertension. The determination of  $LTB_4$  and  $LTC_4$  content in the blood serum was carried out by the radioimmune method (an assay kit « $LTB_4$ », « $LTC_4/B_4/D_4$ », Amersham, Great Britain), the level of malondialdehyde (MDA) in the blood serum was studied by means of spectrophotometry. The reference indices were obtained in 21 practically healthy individuals (the control group). They and the examined patients were of the same sex and age. Mathematical processing of the results was carried out by means of variation statistics methods using the application programs package Statistika 6.0.