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Plastic orchiectomy and some indicators of improvement of vital parameters and general condition of the organism in blood of the men with prostate cancer

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Prostate cancer (PCa) is the most common malignancy affecting men in developed countries. Prostate gland cells, normal or cancerous, are dependent upon androgens for survival and growth. Consequently, androgen deprivation therapy (ADT) is still the mainstay for PCa treatment. Recent studies revealed that in comparison with pharmaceutical approaches, surgical castration may be associated with significantly lower risks of peripheral arterial disease and cardiac-related complications compared to chemical castration. Thus, our present research work aimed to investigate potential alterations in lipid components, in particular the amount of phospholipids, cholesterol and free fatty acids in the blood of the men with prostate adenocarcinoma before and after plastic orchiectomy in order to demonstrate the contribution of these changes in PCa progression. We also studied the activities of antioxidant enzyme - superoxide dismutase (SOD) and prostatic acid phosphatase (PAP) to estimate general condition of an organism. Revealed alterations in lipid spectrum components (quantitative changes in the amounts of phospholipids, cholesterol, and fatty acids) before and after plastic orchiectomy indicates on remodeling of lipid metabolism after plastic orchiectomy. Approximation of total cholesterol and phospholipids levels to control group indices together with the reduced amounts of fatty acids indicates on the regression of the pathology for a certain period of time (~6-18 months). Furthermore, increased activity of SOD and sharply reduced activity of acid phosphatase after plastic orchiectomy must be the indicators for improvement of general condition of the body.

Keywords: Androgen deprivation therapy, Antioxidant enzymes, Fatty acids, Lipid reprogramming, Phospholipids, Plastic orchiectomy, Prostate cancer

Prostate cancer (PCa) is the most common malignancy affecting men in the developed countries[1]. Prostate cells (normal or cancerous) are dependent upon androgens for survival and growth. Consequently, androgen deprivation therapy (ADT) (also known as hormone therapy) is still the mainstay of PCa treatment[2]. Surgical (bilateral orchiectomy) or chemical (pharmaceutical) interventions resulting in the reduction of serum testosterone or blockade of the androgen receptor are referred to as ADT[2]. While ADT remains the therapeutic choice for metastatic PCa, other modern therapies, particularly immunotherapies are improving the clinical outcomes in combatting the androgen-resistant state. Additionally, antibody-based vaccination strategies with such combinations as radiotherapy, hormone therapy, chemotherapy, and/or anti-angiogenic therapy are evolving rapidly. Targeted immunotherapy is promising because it enhances tumor-specific T-cell responses in PCa. Specifically, PCa cells with stemness and mesenchymal signatures may act together in metastatic progression and the inhibition of stemness genes, thereby overexpression of hormone receptors decreases the rate of metastasis and sensitizes tumors to hormone therapy.

Surgical treatment, also known as bilateral or plastic orchiectomy, means removal of testicles, since they are responsible for production of ~90% of circulating testosterone in the body[3]. In case of pharmaceutical treatment, luteinizing hormone-releasing hormone (LHRH)/gonadotropin-releasing hormone (GnRH) agonists are the most commonly utilized forms of ADT in clinical practice, targeting the LHRH/GnRH receptor in the anterior pituitary gland. Nowadays, chemical castration has largely replaced plastic orchiectomy in clinical practice because of the ease in administration, reversibility, and the avoidance of disfiguring surgery with its associated aesthetic and psychological

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consequences for patients[2]. However, adverse effects of chemical treatment must also be taken into account, such as: hot flashes, fatigue, sexual/erectile dysfunction, testicular atrophy, cognitive decline, increased risk of diabetes and cardiovascular events, and decreased bone mineral density associated with joint disorders and/or osteoporosis[2,4].

Hence, prostate tumors belong to hormone-dependent tumors and pharmaceutical therapy includes using hormonal preparations during the therapy, that is why it is not practical to conduct fundamental research in this direction considering the wide spectrum of hormone action and a variety of adverse effects on the body. We support that the direct comparison studies on metabolic adverse effects should be performed in the future to compare therapeutic outcomes between the two options of ADT.

Recent studies demonstrated that in comparison with pharmaceutical approach, surgical castration may be associated with significantly lower risks of peripheral arterial disease and cardiac-related complications compared to chemical castration[2]. Therefore, plastic orchiectomy remains a classical "gold standard" for androgen deprivation[4]. In case of progressive prostatic cancer, it is important to select the proper form of ADT that will extend the patient's quality-of-life and survival outcomes.

It is well-known that steroid hormones significantly affect the growth and differentiation of prostate epithelium and its tumor transformation[5]. Moreover, malignant epithelial cells of the prostate are androgen-dependent[6]. In this case, the critical role is given to biologically most active androgen - testosterone (T)[7]. It is established that after plastic orchiectomy, only the adrenal gland supplies the tumor epithelium with T[2]. Besides, other hormones, such as progesterone (P) and estradiol (E2) are also necessary among the steroid hormones involved in the development of PCa.

The cancerous cells may alter the lipid profile in order to satisfy their metabolic requirements. Notably, by controlling the lipid metabolism it is possible to induce (as well as inhibit) the tumor progression. Lipids contribute also in the tumor cell proliferation and metastasis. Nowadays, the lipid alterations and reprogramming of the signaling pathways are considered as critical aspect for cancer biology[8].

Thus, in view of the primary objective of this study was to examine the quantitative alterations of T, P, and E_2 in the blood of men with progressive PCa before and after plastic orchiectomy to demonstrate as to how the hormonal status alterations affect the progression of the pathology. Additionally, our research aimed to investigate potential alterations in the amount of phospholipids, cholesterol, and free fatty acids in the blood of men with prostate adenocarcinoma before and after plastic orchiectomy in order to demonstrate the contribution of these changes in PCa progression and also to estimate general condition of the organism by assessing the activities of the antioxidant enzyme - superoxide dismutase (SOD) and prostate-specific enzyme - acid phosphatase (PAP).

Material and Methods

Samples

We collected blood samples from men with prostate adenocarcinoma before and after plastic orchiectomy (15 cases in each group). The age of all subjects ranged from 60-75 years in each group. Control group consisted of healthy men of the same age. The disease status and clinical stage of the subjects was determined based on rectal, histomorphological, and ultrasound examinations of the prostate gland at the A. Tsulukidze Urology National Center, Tbilisi, Georgia. The prostate specific antigen (PSA) test has been conducted prior to surgical operation for all patients at the A. Tsulukidze Urology National Center in order to make preliminary diagnosis. Later the final diagnosis was established after histomorphological analysis of the tumor tissues. The study was approved by the National Council on Bioethics of Georgia and written informed consent was obtained from all subjects.

Methods

Total amount of phospholipids, as well as amount of amino- and choline-containing phospholipids were determined by using the Kates method[9]. Analysis of fatty acids was performed using high-performance liquid chromatography (HPLC)[10]. We determined the lipid peroxidation levels according to the method described by Uchiyama & Mihara[11]. Total amount of cholesterol was assessed by using the colorimetric reagent kit from Human Diagnostics, Germany (Cholesterol liquicolor, complete kit, 10017). Spectrophotometric methods were used to assess the activities of the acid phosphatase and SOD in the blood of patients. Analysis of SOD activity was performed routinely as described by Dubinina et al[12] and expressed in U/μL. Activity of prostatic acid phosphatase (PAP) was assessed according to the method by Gianetto & De Duve[13].

The obtained data were analyzed using the statistical methods by MINITAB (Basic Statistic), and *p*-value of ≤ 0.05 was considered statistically significant.

Results and Discussion

Our studies revealed that steroid hormones (T, P and E2) levels were significantly elevated in men with prostate adenocarcinoma before orchiectomy compared to the control group (Table 1). It is probably due to the increased demand for these hormones by tumor tissues, together with enhanced production of the hormones by testes and the adrenal cortex**.**

The studies regarding plastic orchiectomy have shown that the level of steroid hormones (T, P, and E2) in the blood of the men with prostate adenocarcinoma after plastic orchiectomy is significantly reduced compared to the preoperative and control groups (Table 1).

Given that the maintenance of a minimal level of T in the blood after plastic orchiectomy is mainly due to the conversion of adrenal androgens [androstenedione and dehydroepiandrosterone (DHEA)] into T (conditionally I and II pathway)[14]. We hypothesize that production of T by the pregnenolone → DHEA → T pathway (conditionally "II pathway") is responsible for minimal amount of T in the blood[15]. On the background of a significant decrease in the levels of P, biosynthesis of T should also be decreased, eventually decreasing its blood level. We assume that the pregnenolone → P → T pathway (conditionally "I pathway") is less productive according to our data (Table 1). We presume that the minimum amount of T in the blood of these patients after plastic orchiectomy is mainly provided by pregnenolone → DHEA → T pathway (conditionally "II pathway").

In addition to the above (*i.e*., a significant decrease in T levels), our studies have shown that after surgery, the level of T in blood is sharply decreased (Table 1) even compared to the control group.

It is known that 30% of the estrogens within man's blood are produced and secreted by the testicles. The remaining estrogen (predominantly E2) is produced from adrenal C19 steroids (DHEA and androstenedione) by peripheral aromatization pathway[16]. Thus, after plastic orchiectomy, the estrogens (E2) in the patients' blood must entirely be of adrenal origin, which leads to a reduction in the portion of these hormones (as confirmed by our data) (see Table 1).

It is established that progesterone acts as an anti-estrogen, down-regulating estrogen receptors that eventually decreases the effectiveness of their activity[17]. We suggest that the anti-estrogenic action of progesterone together with sharply decreased level of P in the blood of these patients should be a reason for higher level of E2 compared to P after plastic orchiectomy. A significant decrease in P levels may also be due to the presence of cells with a high proliferative potential and higher requirement for P[18].

It is well-known that steroid hormones are actively involved in energy production and regulation of mitochondrial functions[18]. Furthermore, it is known that malignant transformation is accompanied by significant disturbance in lipid metabolism. It appears that lipids and their metabolites play an essential role in cell proliferation and tumorigenesis[19]. It is also known that lipid metabolism is significantly affected by lipid peroxidation processes in the body[8]. In view of these, the study of alterations in lipid composition, in particular total amount of phospholipids, amino-containing, and choline-containing phospholipids and total amount of cholesterol in the blood of patients with progressive PCa before and after plastic orchiectomy is an actual issue today.

According to our experimental results, there are elevated levels of total phospholipids as well as amino-containing and choline-containing phospholipids in the blood of patients with progressive PCa before plastic orchiectomy (Table 2 and Fig. 1). This fact can be explained by the mobilization of lipids during the development of malignant tumor[19]. As for plastic orchiectomy, it was found that there is a decrease in the total amount of phospholipids compared to the preoperative data, which is almost equal to the control group index (Table 2 and Fig. 1). Furthermore, amino-containing and choline-containing phospholipids are also reduced compared to preoperative and control group data (Table 2). All these changes in lipids

Table 1 — Quantitative alterations of the steroid hormones in the blood of men with prostate adenocarcinoma before and after plastic orchiectomy

Steroid hormones	Control group	Adenocarcinoma of the prostate before plastic orchiectomy	Adenocarcinoma of the prostate after plastic orchiectomy
Progesterone (nM/L)	0.53±0.01	4.6±0.9	0.053±0.01
Testosterone (ng/mL)	7.17±0.2	13.3±1.2	0.087±0.003
Estradiole (pg/mL)	16.7±3.4	36.5±0.0.3	12.48±0.75

n=15, number of patients in each study group; $P < 0.05$; The age range of the patients: 60-75 years

Table 2 — A comparative evaluation of the total amounts of phospholipids, cholesterol and change in the intensity of lipid peroxidation in the blood of men with prostate adenocarcinoma before and after plastic orchiectom

Study parameters	Control group		Adenocarcinoma of the prostate before plastic orchiectomy		Adenocarcinoma of the prostate after plastic orchiectomy	
	mg/mg	%	mg/mg	%	mg/mg	%
Total amounts of phospholipids (dry weight in mg/mg lipids)	0.28±0.07	100	0.48±0.12	100	0.24±0.02	100
Amino-containing phospholipids (dry weight in mg/mg lipids)	0.09±0.02	32.1	0.18±0.06	37.5	0.04±0.007	16.6
Choline-containing phospholipids (dry weight in mg/mg lipids)	0.14±0.04	50.0	0.28±0.1	58.3	0.13±0.019	54.2
Un-identified phospholipids (dry weight in mg/mg lipids)		17.9		4.2		29.2
Total cholesterol (mM/L)	0.99±0.08		4.95±0.2		0.67±0.015	
Lipid peroxidation (μM/mL, per 1 mg protein)	0.80±0.07		5.35 ±0.45		3.4±0.2	

n=15, number of patients in each study group; P <0.05; The age range of the patients 60-75 years

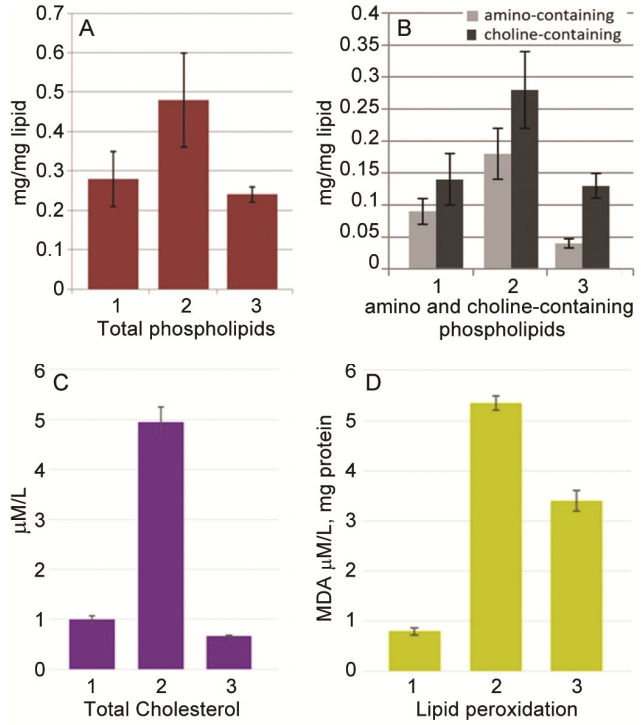

Fig 1 — A comparative representation of the total amount of (A) phospholipids, (B) total amount of cholesterol, (C) amounts of amino and choline-containing phospholipids; and (D) intensity of lipid peroxidation in the blood of the men with prostate cancer. 1. control group; 2. adenocarcinoma of the prostate before orchiectomy; and 3. adenocarcinoma of the prostate after orchiectomy

composition are accompanied by reduced intensity of lipid peroxidation after plastic orchiectomy (Table 2).

Significant decrease in total amount of phospholipids must be conditioned by the following possible mechanism(s). It has been suggested that the decrease in total phospholipid levels may be due to increased amount of high-density lipoproteins in patients' blood after plastic orchiectomy[21]. It is known that steroid hormones, especially estrogens, affect the level of high-density lipoproteins[21]. It is also known that estrogen decreases activity of lipoprotein lipase by a post-transcriptional modification of the protein levels. Lipoprotein lipase regulates the plasma concentrations of triglycerides and high-density lipoprotein (HDL). Therefore, a decrease in estrogen levels after orchiectomy must lead to an increase in the enzymatic activity of lipoprotein lipase and enhancement of high-density lipoproteins production from triacylglycerols[22].

In addition, HDLs, both under physiological conditions and in case of large quantities (during pathogenesis), can remove and exchange oxidized forms of phospholipids from the plasma membrane. It has been suggested that this is one of the mechanisms by which phospholipid bilayer of the membrane is renewed, thereby exchanging places between oxidized phospholipids of the membrane and non-oxidized phospholipids in the fraction of HDLs[23].

Thus, we assume that in our case, the sharp reduction of steroid hormones (estrogens) in the blood after plastic orchiectomy should lead to an increased amount of HDLs in the blood according to the mechanism described above. As a result, inclusion of blood phospholipids in the processes of renewal of membrane structures should occur, which may lead to decreased levels of phospholipids in the blood (as observed during our investigations) (Table 2).

As for the sharp decrease in the concentration of amino-containing phospholipids (compared to the control group), this may be conditioned by: i) increased requirement for choline-containing phospholipids (as for the major component of the plasma membrane), and ii) enhanced production of choline-containing *phospholipids from amino-containing phospholipids* (phosphatidylserine → phosphatidyl-ethanolamine → phosphatidyl-choline**)** at the same time[24]. The

significant decrease in the level of amino-containing phospholipids may also be due partly to the involvement of the latter (as easily oxidizing substrates) in lipid peroxidation processes[25].

In the next stage of our investigation, a quantitative change in cholesterol (one of the representatives of the lipid spectrum of the biological membrane), was studied. Cholesterol is a precursor for the production of steroid hormones (T, P, and E2), so alterations in the levels of the mentioned hormones in the blood plasma is closely associated with the changes in cholesterol levels[20].

We found that before plastic orchiectomy cholesterol level was sharply increased (~5-times) compared to the control (Table 2; Figure 1). Recent studies indicated that this change can be conditioned by the impaired regulation of lipid biosynthesis and avoiding any negative feedback mechanism(s) by cancer cells that regulates cholesterol production rate in normal cells[20].

A significant decrease in cholesterol level (due to a reduction of steroid hormones) was observed after plastic orchiectomy (Table 2 and Fig. 1). Notably, compared to preoperative results, significant decrease in cholesterol levels is likely due to increased HDLs and enhanced cholesterol esterification in patients' blood after plastic orchiectomy[21]. Besides, it is also known that HDLs containing esterified cholesterol are eliminated more rapidly from the bloodstream through the liver[26], which may decrease cholesterol levels in the blood as compared to the control group. On the other hand, significant decrease in cholesterol levels in the blood after plastic orchiectomy compared to preoperative levels may also be due to a reduction in the requirement for cholesterol as a primary source of steroid hormones' production.

Besides above, disturbance of lipid metabolism in blood plasma are known to cause a change in the levels of fatty acids[8,27]. Furthermore, the ratio between saturated and unsaturated fatty acids indicates the ongoing tumorigenesis process in the body[28]. Thus, it was interesting to study the quantitative changes of saturated acids [palmitic acid (C16:0), stearic acid (18:0)], as well as unsaturated fatty acids [oleic acid (18:1), linoleic acid (C18:2), linolenic acid (18:3) and arachidonic acid (20:4)] in case of progressive PCa.

The following changes have been observed during our investigations before plastic orchiectomy: amount of stearic acid was slightly increased, while the amount of palmitic acid did not reveal any sharp changes. In case of unsaturated fatty acids, we observed sharp decrease in the amount of oleic acid, but linoleic acid concentrations remain unchanged. As for arachidonic and linolenic acids, their levels were slightly increased before plastic orchiectomy (Table 3 and Fig. 2).

In the blood of patients with progressive PCa after plastic orchiectomy, levels of saturated fatty acids (amounts of palmitic and stearic acids) were increased, but the levels of polyunsaturated fatty acids (linoleic, linolenic, and arachidonic acids) were decreased. However, concentration of monounsaturated oleic acid was increased after plastic orchiectomy compared to the same index before surgery (Table 3 and Fig. 2).

In addition, after plastic orchiectomy, the ratio of saturated and unsaturated fatty acids was increased up to ~ 0.7 compared to the preoperative data index (~ 0.4), which indicates inhibition in the tumor growth process in the body as it is also confirmed by the clinical data[28]. As for the reduction of polyunsaturated fatty acids (linoleic, linolenic, and arachidonic acids) compared to preoperative data, we suggest that this phenomenon could be due to the inhibition of phospholipids' hydrolysis in these patients, and consequently resulting in the limited production of polyunsaturated fatty acids as the products of this reaction[29], that is also confirmed by our data.

It is established that polyunsaturated fatty acids (especially linoleic and arachidonic acids) are involved

Table 3 — A comparative evaluation of individual fatty acids in the blood of men with prostate adenocarcinoma before and after plastic orchiectomy (in mg/%)

Fatty acids (mg/%)	Control group	Adenocarcinoma of the prostate before plastic orchiectomy	Adenocarcinoma of the prostate after plastic orchiectomy
Palmitic acid C16:0)	675.0±7.5 (22%)	625.0±3.6 (21%)	650.73±3.2 (28%)
Stearic acid (C18:0)	208.7±5.6 (6.8%)	249.0±4.1(8.7%)	533.83±3.5 (23%)
Oleic acid (C18:1)	1057.3±18.5 (34.5%)	660.0±7.0 (23%)	769.04±4.4 (29%)
Linoleic acid (C18:2)	251.8±5.0 (8.2%)	247.8±4.4 (8.6%)	181.15±2.8 (7.8%)
Linolenic acid (C18:3)	516.6±3.4 (17%)	693.0±4.4 (24%)	562.6±3.0 (22%)
Arachidonic Acid (C20:4)	351.2±1.2 (11%)	383.8±0.9 (13%)	292.45±3.4 (9%)

n=15, number of patients in each study group; $P < 0.05$; The age range of the patients 60-75 years

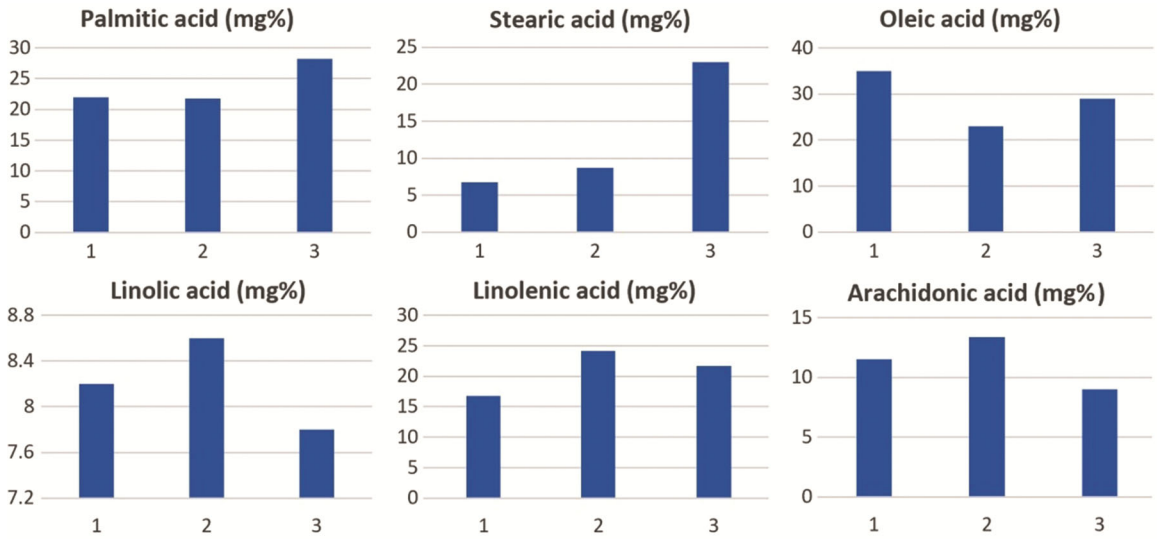

Fig. 2 — A comparative representation of the total amount of *"individual"* free saturated fatty acids (palmitic acid and stearic acid) and unsaturated fatty acids (oleic acid, linoleic acid, linolenic acid, and arachidonic acid) in the blood of the men with prostate cancer (mg/%). 1. control group; 2. adenocarcinoma of the prostate before orchiectomy; and 3. adenocarcinoma of the prostate after orchiectomy

Table 4 — The alterations in the activities of acid phosphatase and superoxide dismutase in the blood of men with prostate adenocarcinoma before and after plastic orchiectomy

Activity of the enzyme	Control group	Adenocarcinoma of the prostate before plastic orchiectomy	Adenocarcinoma of the prostate after plastic orchiectomy
Prostatic acid phosphatase (PAP) (IU, per mg protein)	1.105±0.03	1.604±0.02	0.093±0.05
Superoxide dismutase (SOD) (IU/µL, per mg protein)	1.0±0.02	0.47±0.003	0.67±0.05

n=15, number of patients in each study group; The age range of the patients: 60-75 years. $P < 0.05$

in cholesterol esterification process[20,30]. It has been suggested that the reduction in the amount of linoleic and arachidonic acids should be due to the active participation of these fatty acids in the esterification of cholesterol[30]. Our study revealed that, in contrast to polyunsaturated fatty acids, a significant increase in the level of monounsaturated oleic acid was observed as compared to preoperative data (Table 3 and Fig. 2). It is known that the accumulation of oleic acid by cancer cells greatly contributes primarily to the maintenance and fluidity of the membranes of these cells as well as for resistance to free-radical processes[31].

It is known that the normal functioning of the enzymes determines the physiological course of vital processes in the cell, therefore, the general condition of the organism. Besides, it should be noted that enzymes also actively contribute to initiating the pathological processes, or they result from the altered processes[32]. Given that, it was interesting to study the alteration in the activity of main antioxidant enzyme in the blood (SOD), to reveal the body's protective function in case of progressive prostatic cancer before and after plastic orchiectomy. Furthermore, the degree of regression of the tumor growth process was evaluated according to the alteration of the prostate-specific tumor marker, prostatic acid phosphatase (PAP).

It is known that there are two forms of acid phosphatase (*i.e.*, lysosomal and secretory). The prostate epithelial cells are known to secrete both forms of this enzyme. Secretory acid phosphatase secretion is an exocrine function for normal prostate epithelium. However, during malignant transformation, direct and positive relationship is observed between the progression of the pathology and the change in the activity of acid phosphatase in the blood of patients[33].

Our studies have shown that in case of progressive PCa before plastic orchiectomy, activity of acid phosphatase was substantially increased (~1.5 times) compared to the control group. The activity of the given enzyme after plastic orchiectomy is significantly reduced not only compared to the preoperative (~17 times) but also compared to the control group (~12 times) indices (Table 4 and Fig. 3).

It is confirmed that the steroid hormones regulate the secretion of secretory acid phosphatase by the prostate tumor epithelium[34]. It is also known that steroid

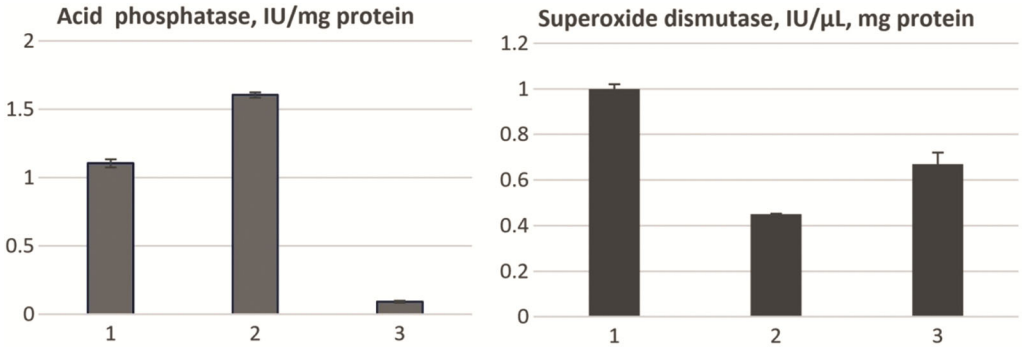

Fig. 3 — Alterations in the activities of (A) prostatic acid phosphatase (PAP); and (B) superoxide dismutase (SOD) in the blood of men with prostate cancer. 1. control group; 2. adenocarcinoma of the prostate before orchiectomy; and 3. adenocarcinoma of the prostate after orchiectomy

hormones (T and P) regulate the body's secretory as well as lysosomal acid phosphatase levels[35]. Furthermore, testosterone and progesterone increases the degree of lysosomal membrane lability, increasing membrane permeability, and releasing acid phosphatase (along with another hydrolases) from lysosomes[32]. According to our results, alterations in the steroid hormones' levels are in accordance with the alteration in the activity of acid phosphatase before and after plastic orchiectomy. We presume that a significant reduction in steroid hormones' levels after plastic orchiectomy (Table 1) caused a decrease in the amount of both (secretory as well as lysosomal) forms of acid phosphatase, decreasing consequently their enzymatic activities.

The study of the activity of SOD, as one of the body's main antioxidant enzymes, before plastic orchiectomy revealed about 2-fold decrease in the activity of this enzyme compared to the control group. After plastic orchiectomy, the activity of the enzyme was increased compared to preoperative data (~1.5-fold increase) but decreased compared to the control group (~1.5-fold decrease) (Table 4 and Fig. 3). It is noteworthy, that on the background of increased SOD activity (after plastic orchiectomy, compared to preoperative data) superoxide and hydroxyl radicals can no longer effectively interact with nitric oxide to produce peroxynitrite ($ONOO^-$), which is a powerful stimulator of lipid peroxidation[36]. This process may lead to a reduction of lipid peroxidation intensification, which is confirmed by our results as well (Table 2). It should be noted that at the same time, based on our previous results, there is a decrease in the level of MetHb and Mn^{2+}-containing complexes in the blood after orchiectomy[37], which is directly related to the reduction of the lipid peroxidation intensification. It is noteworthy that these processes take place on the background of an increased (Fe^{3+})-transferrin in the blood as one of the antioxidant components of the body[37-39].

On the background of activation of SOD after plastic orchiectomy, that indicates on the enhancement of the body's antioxidant properties, the possibility of the production of $ONOO^-$ from nitric oxide decreases (which is a strong damaging agent for proteins, nucleic acids, and lipids) delaying the damage of the proteins involved in distinct signal transduction pathways. It was also suggested that inhibition of SOD does not occur due to the reduction in the intensity of lipid peroxidation and decreased levels of paramagnetic metals and other damaging agents (*e.g.*, OH^-, $ONOO^-$, $O2^-$) in the blood[40].

We suppose that activation of SOD after plastic orchiectomy should result from the partial reversal of the tumor growth process. In addition, the activation of SOD should help inhibit peroxidation processes (as one of the indicators of pathology) and improve the overall antioxidant status of the patients' body.

Sharply decreased activity of prostatic acid phosphatase after plastic orchiectomy, as one of the prostate-specific tumor markers, is another indicator that points at inhibition of the progression of the pathology. Collectively, these alterations should lead to an improvement in the general condition of the patients after plastic orchiectomy.

Thus, improvement in some vital parameters and general condition of the body of patients with progressive PCa were revealed after plastic orchiectomy. This is also confirmed by the anamnesis of these patients, in particular the absence of pain and intoxication, delay in metastasis, and consequently, extension of life for a certain period (~18 months). However, it should be noted that the improvement in vital parameters of the body is not permanent (it lasts about 18 months only), because over time, most

prostate cancers eventually stop responding to hormone therapy and become hormone resistant or castration resistant.

Conclusion

Reduction in the levels of all three steroid hormones (T, P, and E2) in the blood of men with prostate adenocarcinoma after plastic orchiectomy should indicate the regression of tumor growth process, which is also confirmed by the clinical data. This fact should be mainly due to plastic orchiectomy and adrenal gland must be responsible for the production of minimum quantities of these hormones in the blood of the patients.

Revealed alterations in lipid spectrum components (quantitative changes in the amounts of phospholipids, cholesterol, and fatty acids) before and after plastic orchiectomy indicates on remodeling of lipid metabolism after plastic orchiectomy. Inhibition of lipid peroxidation, approximation of total cholesterol, and phospholipids levels to the control group indices resulted in reduced amounts of fatty acids (as products of the hydrolysis) and increasement of the ratio between saturated and unsaturated fatty acids after plastic orchiectomy. All these alterations indicate on the regression of the pathology for a certain period (~ 6-18 months).

We implicate that the increased activity of superoxide dismutase (as one of the major antioxidant enzymes) should be the indicator for strengthening the body's defense system after surgery. Furthermore, approximation of the activity of prostatic acid phosphatase to the control group after plastic orchiectomy must be the indicator for improvement in general condition of the body of patients with progressive prostatic cancer.

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Conflict of interests

All authors declare no conflicts of interest.

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