FEATURES OF BIOCHEMICAL PARAMETERS AND NON-SPECIFIC RESISTANCE FACTORS OF VAGINAL CONTENTS IN WOMEN WITH UROGENITAL TRICHOMONIASIS AND CERVICAL INTRAEPITHELIAL NEOPLASIA AGAINST THE BACKGROUND OF PAPILLOMAVIRUS INFECTION

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INTRODUCTION

Recently, the growth of cervical diseases associated with human papillomavirus (HPV) has attracted special attention due to the significant contagiousness and high oncogenic potential of this pathogen. The frequency of pathology of the cervical epithelium among women of reproductive age is 15–20% [1–3]. Sufficient biological potential of the human microbiome is able to resist the potential negative effects of pathological microflora for a long time, and only a significant loss of physiological endogenous microbiota leads to the development of diseases and their complications [4–6].

According to modern concepts, an important role in the functioning of the female reproductive system is played by the vaginal microflora, which is a balanced ecosystem, the species and quantitative composition of which is regulated by the endocrine and immune systems of the female body. The vaginal biotope, as an integral biological environment, directly or indirectly reflects the state of all parts of the female reproductive system [7, 8]. The vaginal contents consist of microorganisms, epithelial cells and a liquid phase containing substances that quantitatively and qualitatively reflect the state of the vaginal microecosystem as a whole. The dynamics of the waste products of vaginal microorganisms allows us to characterize the state of the biocenosis, the ability to predict the development and consequences of inflammatory diseases, and analyse the patterns of formation of pathological processes. In various pathological conditions, including trichomoniasis, the content of metabolites can vary, which has diagnostic and prognostic value [9–11].

An important role in biological fluids is played by proteins that affect the regulation of metabolic processes, provide immune protection, are part of cellular structures, and maintain oncotic pressure. The protein content in the vaginal fluid correlates with the composition of the microflora. Urea is the end product of protein and nucleic acid metabolism, which significantly determines the water and electrolyte balance of biological fluid [12].

The exchange of trace elements is an integral part of the homeostasis of internal environment of the body, since it ensures the optimal course of enzymatic reactions in the implementation of metabolism. Thus, copper in the cells of the human body takes part in providing biochemical processes associated with the transport of electrons in the respiratory chain, is part of the active receptors of certain enzymes. Iron in the body's cells provides redox reactions, forms active centres of enzymes, and determines the degree of immunological protection. In biological fluids, the concentration of calcium is a relatively constant value. Calcium is distributed in three fractions: ionized, bound by a complex bond with inorganic acids, bound to proteins, mainly with albumin. When the biological fluid is alkalized, the proportion of bound calcium increases, while when it is acidified, the content of its ionized biologically active form increases. Calcium affects the permeability of biological membranes and is necessary for the activation of polymorphonuclear leukocytes in all forms of their functional activity. Ionized magnesium also affects the permeability of biological membranes, is a cofactor of many enzymes associated with cell energy supply, and has an immunotropic effect [13, 14]. Phosphates are found in body fluids mainly in the form of free anions. A small part of them is bound to proteins. They act as a component of phosphoproteins, nucleic acids, phospholipids of cell membranes, coenzymes, phosphorylate carbohydrates, which ensures their availability for metabolic processes, as well as for binding inorganic phosphorus to the formation of macroergic molecules [15, 16].

Enzymes of the vaginal biotope, as well as other biological fluids, can be divided into bacterial and cellular enzymes that enter the vaginal contents due to cytolysis processes from epithelial cells. Normally, the activity of cellular enzymes is insignificant, which is determined by the physiological renewal of epithelial layers with the corresponding destruction of desquamated cells. The pathological process is usually accompanied by increased cellular degradation

due to the presence of microorganisms that change the enzymatic spectrum as a result of metabolism. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are known to be cytosolic transaminases. The optimum of their catalytic activity is in the neutral range. Normally, the process of physiological desquamation occurs in vagina with certain intensity, followed by cytolysis [17].

Chronic infectious and viral diseases of vagina and cervix are most often caused by inhibition of the activity of local immune factors, primarily due to a decrease in the synthesis of secretory immunoglobulin A (sIgA), the main functional property of which is to protect the mucous membranes from microbial aggression. This is due to the high resistance of sIgA to proteases, which ensures its functioning in the secretions of the mucous membranes, prevents the binding of complement components and the harmful effect of the antigen–antibody complex on the mucous membranes, as well as the ability to prevent the attachment (adhesion) of microorganisms and their toxins to the epithelium of the mucous membranes, which makes it difficult for them to penetrate into the internal environment of the body. The anti-adhesive properties of sIgA ensure its antibacterial, antiprotozoal and antiviral properties. A decrease in the concentration of sIgA in vagina and cervical canal causes an increase in the resistance of the woman's body to bacterial, protozoan and viral infectious agents. Humoral and cellular components of the immune complex play a special role in maintaining the vaginal microbiocenosis. The activity of the immune complex is determined by both antigenic stimulation and the state of hormonal homeostasis. The peculiarity of the immunity of the lower reproductive tract is that in response to the intrusion of a foreign antigen, the humoral link of local immunity is sensitized. *Trichomonas* invasion is caused damage of the epithelial layers which leads to impaired functional activity of sIgA-producing plasma cells [18, 19].

Trichomonas vaginalis as a causative agent of urogenital trichomoniasis is currently undergoing a number of pathomorphosis, which are characterized by a low-symptom and erased clinical course, detection of atypical morphological forms of the pathogen, contradictory interpretation of the results of clinical and laboratory studies, as well as the formation of strains resistant to etiotropic treatment. This phenomenon contributes to the development of chronic forms of the disease, difficulties in diagnosis and treatment, as well as persistent violations of the vaginal biocenosis [20–22]. In the modern literature there is practically no information about the features of the functioning of the vaginal microecosystem in *Trichomonas* invasion in women with atypical squamous cells of undetermined significance/cervical intraepithelial neoplasia (ASCUS/CIN) of the cervix against the background of papillomavirus infection (PVI), the role of the inflammatory process in the mechanisms of penetration of HPV into the basal layer, with subsequent violation of stratification of the multilayer epithelium of the cervix is not determined [23–25], the influence of the inflammatory process caused by *Trichomonas* infection, on the persistence of HPV and the state of local immunity and, as a result, the progression of intraepithelial lesions of the cervix is not studied enough, there is no consensus on the tactics of managing women with ASCUS/CIN of the cervix against the background of HPV infection in combination with *Trichomonas* infection, which, in turn, plays a significant role in the formation of cervical ectopia [26–30].

Research objective: to improve the effectiveness of diagnosis and prognosis of complications in women of reproductive age with ASCUS/CIN of the cervix in *Trichomonas* and papillomavirus infection by studying the main biochemical and immunological parameters of vaginal contents.

MATERIALS AND METHODS

Under our observation there were 200 women of reproductive age (mean age 32.04 ± 0.95 years) with ASCUS/CIN of the cervix on the background of PVI associated with trichomoniasis, who were divided into three main groups according to the results of the PAP test (liquid cytology):

- group I included 50 (25%) patients with ASCUS;
- group II included 118 women (59%) with low grade squamous intraepithelial lesions (LSIL) (CIN I);
- group III included 32 (16%) respondents with high-grade squamous intraepithelial lesion (HSIL) (CIN II).

The control group included 50 healthy nonpregnant women.

Inclusion criteria: reproductive age, ASCUS, LSIL (CIN I), HSIL (CIN II) as a result of the Pap-test, HPV, *Trichomonas vaginalis* detected by InPouch test.

Exclusion criteria: age younger than 18 and older than 45 years, HSIL (CIN III, according to the WHO classification, 1995), malignant disease based on the results of histological examination, the period of pregnancy or lactation, mental disorders.

All groups were representative by age, medical history and concomitant gynaecological pathology and were examined at the clinical bases of the Obstetrics and Gynaecology Department No. 3 of the Bogomolets National Medical University and at the ProfiMed clinic (Kyiv, Ukraine). The study was approved by the Commission on bioethical expertise and ethics of scientific research at the Bogomolets National Medical University, Protocol No. 127 of 02.12.2019. All participants signed an informed consent.

The collection of anamnesis, study of complaints, clinical and instrumental examination of patients ensured the effectiveness of clinical diagnostics, which in turn determined the feasibility of conducting laboratory tests within the framework of the presented scientific work. In the course of gynaecological examination standardized techniques and manipulations were used [31–33].

Determination of the acidity and pH of vaginal contents was carried out using a universal indicator paper (Lachema, Czech Republic) directly during speculum examination and using a pH meter "LKB" (Pharmacia, Sweden) with a solid electrode, which made it possible to make measurements with an accuracy of 0.01 units with a delayed examination of the obtained discharges from the walls of the vagina. The results of the amine test were evaluated using the semi-quantitative method (E.F. Kira, 1995). A vertical beam path spectrophotometer "Sumal PE-2" (Germany) and an automatic biochemical analyzer Hitachi 917 (Japan) were used for biochemical studies. Preparations for microscopy were prepared by mixing a drop of vaginal contents with a drop of 0.9% saline sodium chloride solution, studied in several fields at 400-fold magnification [34].

Biochemical studies of vaginal contents consisted in determining the concentration of total protein, urea, hydrogen peroxide, mineral metabolism (copper, iron, calcium, magnesium, inorganic phosphorus), glucose, lipid metabolism (cholesterol, triglycerides), enzyme activity (creatine phosphokinase, lactate dehydrogenase, alkaline phosphatase, α-amylase, γ-glutamyltransferase, AST, ALT. From the factors of non-specific resistance in the vaginal contents, the sIgA and hydrogen peroxide concentrations were determined.

Statistical processing of the obtained data was carried out with standard statistical analysis programs (GraphPad InStat, Stastica for Windows 7.0, Microsoft Excel).

RESULTS

In patients of the control group vaginal discharge was a mucous substance in moderate or insignificant amounts, odorless (Table 1). In the case of trichomoniasis respondents with ASCUS/CIN on the background of HPV had abnormal discharge from the genital tract, usually of a liquid homogeneous consistency, white or yellowish in colour. They were evenly distributed along the walls of the vagina and stood out.

Analysis of the results shows that women with ASCUS/CIN on the background of PVI in the case of *Trichomonas* invasion are characterized by an increase in the amount and changes in the qualitative composition of vaginal secretions. Patients of the main groups noted foamy, with an unpleasant characteristic putrid smell discharges, colored yellow. In terms of the number and nature of secretions, there were no significant differences between groups I, II and III of women ($p > 0.05$), but there was a statistically significant difference in all studied parameters with patients in the control group ($p < 0.01$).

During our gravimetric studies it was found that the average amount of discharge per day in healthy nonpregnant women was 1.34 ± 0.08 g/day. In patients with ASCUS/CIN on the background of PVI with trichomoniasis this indicator was 2.6 times higher ($p < 0.01$) in all the main three follow-up groups (Table 2).

The acidity of vaginal contents in women of the control group was 3.99 ± 0.04 units, while in patients of the main groups it was 1.2 times higher ($p < 0.05$). The results of the study of the amine test of vaginal contents indicate that in the control group the indicator was 0.21 ± 0.11 units, while in the main groups it was almost 13 times higher ($p < 0.01$).

The protein content in the vaginal contents of women in the control group was 1.92 ± 0.05 g/l, compared with patients with

Table 1. Characteristics of discharge from the genital tract in the examined patients (n, %)

Quantitative and qualitative characteristics of secretions	Group I (n = 50)		Group I (n = 118)		Group III (n = 32)		Control group (n = 50)	
	n	%	n	%	n	%	n	%
Plentiful	47	94*	106	89.8*	29	90.6*	3	6
Moderate	3	6*	12	10.2*	3	9.4*	47	94
Frothy	39	78*	95	80.5*	26	81.3*	2	4
Mucous	3	6*	9	7.6*	2	6.3*	48	96
Liquid	8	16*	18	15.3*	5	15.6*	4	8
Smell	46	92*	110	93.2*	30	93.8*	2	4
Colored	37	74	94	79.7	26	81.3	–	–

* the difference is statistically significant compared to the control ($p < 0.01$)

Table 2. Biochemical parameters of vaginal contents of the examined women (M ± m)

Indicator	Group I (n = 50)	Group I (n = 118)	Group III (n = 32)	Control group (n = 50)
Weight of vaginal contents (g/day)	3.43 ± 0.09**	3.67 ± 0.12**	3.52 ± 0.11**	1.34 ± 0.08
pH (units)	4.96 ± 0.08*	4.82 ± 0.07*	5.01 ± 0.12*	3.99 ± 0.04
Amine test (units)	2.68 ± 0.06**	2.71 ± 0.08**	2.76 ± 0.13**	0.21 ± 0.11
Urea (mol/l)	20.84 ± 1.91	21.41 ± 1.83	22.05 ± 1.74	21.36 ± 1.71
Total protein (g /l)	4.43 ± 0.17**	4.37 ± 0.16**	4.52 ± 0.18**	1.92 ± 0.05
Glucose (g/l)	4.23 ± 0.51	4.18 ± 0.33	4.39 ± 0.52	4.05 ± 0.61
Cholesterol (mmol/l)	6.63 ± 0.22	6.55 ± 0.34	6.81 ± 0.78	6.75 ± 0.72
Triglycerides (mmol/l)	5.39 ± 0.25	5.81 ± 0.42	5.73 ± 0.36	5.42 ± 0.21
Iron (μmol/l)	205.53 ± 11.32**	212.65 ± 12.21**	203.71 ± 13.15**	390.19 ± 31.18
Copper (μmol/l)	16.27 ± 3.08*	16.12 ± 3.17*	15.96 ± 3.12*	27.01 ± 4.09
Magnesium (mmol/l)	0.41 ± 0.02	0.39 ± 0.04	0.42 ± 0.05	0.37 ± 0.03
Zinc (mmol/l)	71.96 ± 3.36	72.65 ± 3.68	71.49 ± 3.27	73.85 ± 4.01
Calcium (mmol/l)	6.10 ± 0.33*	6.16 ± 0.34*	6.01 ± 0.31*	9.21 ± 0.56
Phosphates(mmol/l)	6.02 ± 0.53	5.93 ± 0.61	5.81 ± 0.55	6.12 ± 0.51

* the difference is statistically significant compared to the control ($p < 0.05$)
** the difference is statistically significant compared to the control ($p < 0.01$)

ASCUS/CIN on the background of HPV and trichomoniasis, the concentration of which was 2.3 times higher ($p < 0.01$).

The concentration of copper ions in the vaginal contents of women of the control group was 27.01 ± 4.09 mmol/l, which is 1.7 times higher than in the main three groups of patients ($p < 0.01$). The iron content in the vaginal fluid of women in the control group was 390.19 ± 31.18 μmol/l, while this indicator in women in the main groups was 1.9 times lower ($p < 0.01$). The calcium content in the control group of patients was 9.21 ± 0.56 mmol/l, while in women with ASCUS/CIN on the background of HPV and trichomoniasis it was 1.6 times lower ($p < 0.05$).

The level of urea, concentration of zinc, magnesium, phosphorus, glucose, cholesterol and triglycerides in the vaginal contents of women with ASCUS/CIN on the background of HPV and trichomoniasis was not significantly differ from similar indicators of the control group of women, corresponding to the level of reference values ($p > 0.05$).

The level of alkaline phosphatase was not significantly differ in the groups of women with ASCUS/CIN on the background of HPV and trichomoniasis ($p > 0.05$), but was 3.7 times higher than in the control group of patients ($p < 0.05$) (Table 3). The creatine phosphokinase content was 10.6 times higher in the main groups of women than in patients in the control group ($p < 0.01$). At the same time, it was not differ significantly between women in the main groups ($p > 0.05$).

The activity of AST in the vaginal fluid of women with ASCUS/CIN on the background of HPV and trichomoniasis exceeds the indicator of women in the control group by 6.5 times ($p < 0.01$), ALT by 9.1 times, compared with patients in the control group ($p < 0.01$). The concentration of lactate dehydrogenase in women with ASCUS/CIN on the background of HPV and trichomoniasis was 5.4 times higher than in the control group ($p < 0.05$). According to our data, the activity of α-amylase in the control group was 56.49 ± 13.92 units/l, which is 3.3 times less than in women of the main follow-up groups ($p < 0.05$). The content of γ-glutamyltransferase had no significant differences between patients in the main and control groups ($p > 0.05$).

According to our data, the level of hydrogen peroxide in women with ASCUS/CIN on the background of HPV in the case of *Trichomonas* invasion did not significantly differ from the indicators of women in the control group ($p > 0.05$) (Table 4).

The indicator of sIgA in the vaginal contents of the examined patients in the control group was 62.5 ± 11.2 ng/ml. Studying the sIgA content in patients with ASCUS/CIN on the background of HPV and *Trichomonas* invasion shows that its value was in a fairly wide range — from 19.2 to 69.4 ng/ml. However, the average values were lower than those of women in the control group of 1.7; 1.9 and 2 times in I, II and III main groups respectively ($p < 0.05$).

Thus, it was found that women with ASCUS/CIN on the background of HPV and trichomoniasis have significant changes in biochemical parameters and non-specific resistance of vaginal contents, which can be used to conclude that the main types of cellular metabolism are disrupted. Changes in the composition of the vaginal fluid determine the corresponding features of the functional activity of the vaginal epithelium and composition of the vaginal biotope. Vaginal dysbiosis, in turn, is the basis for the development of persistence of the human papillomavirus with a tendency to form severe forms of intraepithelial neoplasia and cervical cancer.

DISCUSSION

It is known that normally healthy nonpregnant women have a certain amount of discharge from the genital tract, which characterizes the physiological secretory function of the genital tract. In the case of inflammatory and dysbiotic processes, the amount of discharge can significantly increase. Therefore, the reason for the increase in the amount and change in the nature of secretions in the case of *Trichomonas* invasion in women with ASCUS/CIN on the background of HPV is obvious, which can be explained by the presence of an inflammatory reaction from the vaginal mucosa in response to the invasion of pathogenic microorganisms. At the same time, the formation of a putrid smell in trichomoniasis is determined by the factor of tissue

Table 3. Level of enzyme activity in the vaginal fluid of the examined women (M ± m)

Indicator	Group I (n = 50)	Group I (n = 118)	Group III (n = 32)	Control group (n = 50)
ALT (units/l)	39.34 ± 3.79**	43.07 ± 4.16**	38.41 ± 3.28**	4.45 ± 0.89
AST (units/l)	446.29 ± 82.17*	435.31 ± 89.13*	441.48 ± 91.04*	68.15 ± 12.54
γ- glutamyltransferase (units/l)	29.12 ± 4.06	21.93 ± 3.48	24.32 ± 3.18	20.11 ± 2.75
α-amylase (units/l)	179.52 ± 48.76*	195.61 ± 51.43*	185.16 ± 49.32*	56.49 ± 13.92
Lactate dehydrogenase (units/l)	771.29 ± 99.85*	756.63 ± 101.30*	762.03 ± 102.58*	142.23 ± 21.35
Alkaline phosphatase (units/l)	345.16 ± 46.65*	314.18 ± 39.38*	324.09 ± 42.56*	87.98 ± 29.51
Creatine kinase (units/l)	301.66 ± 12.27*	304.79 ± 12.15*	299.92 ± 13.37*	28.44 ± 8.12

* the difference is statistically significant compared to the control ($p < 0.05$)
** the difference is statistically significant compared to the control ($p < 0.01$)

Table 4. Factors of non-specific resistance of vaginal contents in the examined women (M ± m)

Indicator	Group I (n = 50)	Group I (n = 118)	Group III (n = 32)	Control group (n = 50)
sIgA (ng/ml)	36.9 ± 11.4*	32.7 ± 10.7*	31.6 ± 10.3*	62.5 ± 11.2
Hydrogen peroxide (μmol/l)	193.11 ± 9.06	198.05 ± 10.13	195.13 ± 11.09	236.41 ± 14.12

* the difference is statistically significant compared to the control ($p < 0.05$)

inflammatory destruction, the actual products of *Trichomonas* metabolism and concomitant microflora.

An increase in the acidity of vaginal contents in women with trichomoniasis and ASCUS/CIN on the background of HPV indicates a relative alkalinization of the environment and is explained by the disintegrating and epitheliotoxic effects of *Trichomonas vaginalis*, as a result of which there is a violation of the functional activity of the vaginal epithelium and mechanisms responsible for regulating the acidity of vaginal secretions. In addition, *Trichomonas vaginalis* and their symbiotic anaerobic microflora in the process of vital activity produce and secrete biogenic amines into the vaginal fluid, the presence of which causes a significant increase in the pH of the vaginal contents, which creates optimal conditions for the further development of pathogenic microflora. The results of an amine test of vaginal contents strongly indicate the initiation of bacterial vaginosis in patients of the main follow-up groups.

The increase in protein rate in the vaginal contents, in our opinion, is primarily associated with leukorrhea, which occurs in women with cervical ectopia/intraepithelial neoplasia with a concomitant inflammatory process.

The decrease in the concentration of copper ions in the vaginal contents of the main three groups' patients is likely due to hypercolonization of the vagina by microorganisms that actively use copper to meet their metabolic needs. Iron is essential for most bacteria, especially *Trichomonas* and anaerobes, providing plastic and energy processes. A decrease in the concentration of iron ions in the vaginal fluid of the main groups of patients could occur due to increased consumption by *Trichomonas* and hypercolonization by anaerobic microorganisms. The decrease in the level of calcium is probably due to the fact that when the biological fluid is alkalized, its ionized form passes into a state associated with protein macromolecules. In turn, a decrease in the calcium content in women with ASCUS/CIN on the background of HPV and trichomoniasis in the vaginal fluid can lead to disintegration of epithelial cell layers, which is manifested by increased desquamation and impaired functional activity of the vaginal epithelium as a whole.

Obviously, an increase in the activity of the creatine phosphokinase enzyme in women with ASCUS/CIN on the background of HPV and trichomoniasis is associated with concomitant deep erosive lesions of the cervix. It is known that creatine phosphokinase catalyzes the reaction of formation of a macroergic compound of creatine phosphate with creatine in muscle tissue. In particular, the involvement of myometrial cells in the process of pathological cytolysis provides similar dynamics. An increase in the activity of cytosolic enzymes AST and ALT in patients of the main observation groups is caused by activation of cytological processes and an increase in the pH of vaginal fluid, that is, the creation of favourable conditions for the release of the enzyme from the cell into the biological fluid. An increase in lactate dehydrogenase activity indicates acute or chronic cell damage that occurs in women with ASCUS/CIN on the background of HPV and *Trichomonas* invasion. An increase in the level of the calcium-dependent enzyme α-amylase in women of the main observation groups can be explained by the presence of an inflammatory process and, as a result, the destruction of cervical and vaginal tissues due to the action of pathogenic microorganisms.

Hydrogen peroxide is one of the main factors that ensures the bactericidal and virility of vaginal contents. In patients with ASCUS/CIN on the background of HPV in the case of trichomoniasis, this indicator was identical to that of women in the control group. It can be assumed that the development of an acute process in trichomoniasis is not able to significantly disrupt the pool of acidophilic lactobacilli producing hydrogen peroxide in a short period of time after infection. However, the destruction of epithelial layers and changes in the composition of vaginal contents can modify the vaginal microbiological spectrum.

The level of sIgA in the vaginal contents of the examined patients with ASCUS/CIN on the background of HPV and *Trichomonas* invasion was reduced. On the one hand, a decrease in the concentration of sIgA in the vaginal contents leads to an increase in the resistance of the woman's body to infections. On the other hand, damage to the epithelial layers and the inflammatory process associated with trichomoniasis and associated microorganisms lead to violations of the functional activity of plasma cells producing sIgA.

CONCLUSIONS

1. The results of gravimetric studies revealed a 2.6-fold increase in the amount of discharge from the genital tract and their pathological nature with ASCUS/CIN against the background of PVI and trichomoniasis ($p < 0.01$) due to tissue destruction of the vaginal mucosa under the influence of vaginal pathogens. The acidity of the vaginal contents was 1.2 times higher ($p < 0.05$), the amine test index was 13 times higher ($p < 0.01$), the protein concentration was 2.3 times higher ($p < 0.01$) than in healthy women, which indicated the presence of an inflammatory process and the development of vaginal dysbiosis and did not depend on the degree of cervical damage ($p > 0.05$).

2. Analysis of the mineral metabolism of vaginal contents in patients with ASCUS/CIN on the background of PVI in the case of Trichomonas invasion revealed a decrease in the concentration of copper ions by 1.7 times ($p < 0.01$), iron by 1.9 times ($p < 0.01$), calcium by 1.6 times ($p < 0.05$) than in the control group of women, which is associated with hypercolonization by anaerobic microorganisms and providing plastic and energy needs for *Trichomonas vaginalis*.

3. When evaluating the activity of enzymes, an increase in the level of alkaline phosphatase was detected by 3.7 times ($p < 0.05$), creatine phosphokinase by 10.6 times ($p < 0.01$), ASAT by 6.5 times ($p < 0.01$), ALT by 9.1 times ($p < 0.01$), lactate dehydrogenase by 5.4 times ($p < 0.05$), α-amylase by 3.3 times ($p < 0.05$) in groups of women with ASCUS/CIN on the background of HPV and trichomoniasis compared to those of healthy women, which is associated with erosive lesions of the cervix caused by activation of cytological processes and an increase in the pH of vaginal fluid in the case of acute or chronic inflammatory cell damage.

4. In the study of non-specific resistance in patients with ASCUS/CIN on the background of HPV and trichomoniasis, a decrease in the average value of sIgA content was found

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than in women of the control group by 1.7; 1.9 and 2 times in I, II and III main groups respectively, which is caused by a violation of the functional activity of plasma cells responsible for sIgA production, and can be considered as a prognostic indicator of the development of post-trichomonas vaginal dysbiosis. The level of hydrogen peroxide in patients with ASCUS/CIN on the background of HPV in the case of *Trichomonas* invasion did not significantly differ from the indicators of healthy women, which is associated with the impossibility of rapid destruction of saprophytic acidophilic flora in the case of acute inflammation.

Conflict of interest

The authors declare no conflict of interest regarding commercial or financial relations with organizations and/or individuals.

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ОСОБЛИВОСТІ БІОХІМІЧНИХ ПОКАЗНИКІВ І ФАКТОРІВ НЕСПЕЦИФІЧНОЇ РЕЗИСТЕНТНОСТІ ПІХВОВОГО ВМІСТУ ПРИ УРОГЕНІТАЛЬНОМУ ТРИХОМОНІАЗІ В ЖІНОК З ІНТРАЕПІТЕЛІАЛЬНОЮ НЕОПЛАЗІЄЮ ШИЙКИ МАТКИ НА ТЛІ ПАПІЛОМАВІРУСНОЇ ІНФЕКЦІЇ

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Мета дослідження: підвищення ефективності діагностики та прогнозування ускладнень у жінок репродуктивного віку з атиповими клітинами плоского епітелію невизначеного значення/ плоскоклітинною інтраепітеліальною неоплазією (ASCUS/CIN) шийки матки при трихомонадній і папіломавірусній інфекції шляхом вивчення основних біохімічних та імунологічних показників піхвового вмісту.

Матеріали і методи. Обстежено 200 жінок репродуктивного віку з ASCUS/CIN шийки матки на тлі папіломавірусної інфекції, асоційованої з трихомоніазом, яких за результатами PAP-тесту розподілено на три основні групи.

I групу становили 50 пацієнток з ASCUS, II – 118 жінок із плоскоклітинним інтраепітеліальним ураженням низького ступеня (LSIL), III – 32 пацієнтки з плоскоклітинним інтраепітеліальним ураженням високого ступеня (HSIL). До контрольної групи увійшло 50 здорових невагітних жінок. Проведено аналіз біохімічних показників піхвового вмісту, що включав визначення концентрації загального білка, сечовини, вивчення мінерального й ліпідного обміну, глюкози, активності ферментів, а також факторів неспецифічної резистентності – секреторного імуноглобуліну А та перекису водню.

Результати. Виявлено збільшення у 2,6 раза кількості виділень зі статевих шляхів та їхній патологічний характер у пацієнток з урогенітальним трихомоніазом та ASCUS/CIN на тлі папіломавірусної інфекції, підвищення кислотності в 1,2 раза, показника амінного тесту в 13 разів, концентрації білка у 2,3 раза, порівняно з аналогічними показниками у здорових жінок. У досліджуваного контингенту пацієнток виявлено підвищення концентрації іонів міді в 1,7 раза, заліза в 1,9 раза, кальцію в 1,6 раза, рівня лужної фосфатази у 3,7 раза, креатинфосфокінази в 10,6 разів, аспартатамінотрансферази в 6,5 раза, аланінамінотрансферази в 9,1 раза, лактатдегідрогенази у 5,4 раза, α-амілази у 3,3 раза порівняно з показниками групи контролю. Встановлено зниження середнього значення вмісту секреторного імуноглобуліну А в пацієнток з ASCUS/CIN при трихомонадній та папіломавірусній інфекції в 1,7; 1,9 і 2 рази відповідно у I, II та III групах, що може слугувати предиктором розвитку посттрихомонадного дисбіозу піхви.

Висновки. Аналіз результатів дослідження піхвового вмісту в жінок з ASCUS/CIN на тлі вірусу папіломи людини та трихомонадної інвазії виявив достовірні зміни біохімічних показників і факторів неспецифічної резистентності, що визначають відповідні патологічні зміни у функціональній активності піхвового епітелію та складі вагінального біотопу.

Ключові слова: урогенітальний трихомоніаз, інтраепітеліальна неоплазія, шийка матки, папіломавірусна інфекція, піхвовий вміст, біохімічні показники, фактори неспецифічної резистентності.

FEATURES OF BIOCHEMICAL PARAMETERS AND NON-SPECIFIC RESISTANCE FACTORS OF VAGINAL CONTENTS IN WOMEN WITH UROGENITAL TRICHOMONIASIS AND CERVICAL INTRAEPITHELIAL NEOPLASIA AGAINST THE BACKGROUND OF PAPILLOMAVIRUS INFECTION

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Research objective: to improve the effectiveness of diagnosis and prognosis of complications in women of reproductive age with atypical squamous cells of undetermined significance/cervical intraepithelial neoplasia (ASCUS/CIN) of the cervix in *Trichomonas* and papillomavirus infection by studying the main biochemical and immunological parameters of vaginal contents.

Materials and methods. 200 women of reproductive age with ASCUS/CIN of the cervix were examined against the background of papillomavirus infection associated with trichomoniasis, who were divided into three main groups according to the results of the PAP-test. Group I consisted of 50 patients with ASCUS, II – 118 women with LSiL, III – 32 patients with HSiL. The control group included 50 healthy non-pregnant women. The analysis of biochemical parameters of vaginal contents was carried out, which included determining the concentration of total protein, urea, studying mineral and lipid metabolism, glucose, enzyme activity, as well as factors of non-specific resistance – secretory immunoglobulin A and hydrogen peroxide.

Results. There was a 2.6-fold increase in the amount of discharge from the genital tract and their pathological nature in patients with urogenital trichomoniasis and ASCUS/CIN against the background of papillomavirus infection, an increase in acidity by 1.2 times, the indicator of the amine test by 13 times, protein concentration by 2.3 times, compared with similar indicators in healthy women. Analysis of mineral metabolism in this contingent of patients revealed a decrease in the concentration of copper ions by 1.7 times, iron by 1.9 times, and calcium by 1.6 times. Evaluation of the enzyme activity revealed an increase in the level of alkaline phosphatase by 3.7 times, creatine phosphokinase by 10.6 times, AST by 6.5 times, ALT by 9.1 times, lactate dehydrogenase by 5.4 times, and α-amylase by 3.3 times compared to women in the control group. A decrease in the average value of sIgA content in patients with ASCUS/CIN on the background of HPV and *Trichomonas* invasion was found than in healthy women by 1.7, 1.9 and 2 times, respectively, in the I, II and III main groups, which can serve as a predictor of the development of post-trichomonas vaginal dysbiosis.

Conclusions. Analysis of the results of studies of vaginal contents in women with ASCUS/CIN against the background of human papillomavirus and *Trichomonas* invasion revealed significant changes in biochemical parameters and factors of non-specific resistance, determining the corresponding pathological changes in the functional activity of the vaginal epithelium and the composition of the vaginal biotope.

Keywords: urogenital trichomoniasis, intraepithelial neoplasia, cervix, papillomavirus infection, vaginal contents, biochemical parameters, factors of non-specific resistance.