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Comparative characteristics of the effectiveness of complex therapy in the surgical treatment of acute condyloma of the anogenital region with the use of drugs - nitrogen donors

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Abstract

The paper presents comparative data on the effectiveness of complex treatment of acute condyloma of the anogenital region (n = 105). Destruction of genital warts was performed surgically, preceded by immunomodulatory and antiviral systemic therapy and local treatment with antiseptic measures and hyaluronic acid, which continued in the postoperative period. Patients of the first group (n = 70) were added to the complex therapy drug - nitrogen donor L - arginine. Efficacy control consisted of subjective assessment and patient complaints; objective determination of the clinical condition, the course of the postoperative period, assessment of the state of microcirculation; laboratory dynamics of interleukin levels; the presence of recurrence of the disease. The use of nitrogen donor (L-arginine) in complex therapy allows to eliminate subjective symptoms, signs of secondary bacterial contamination in the preoperative period, postoperative pain, post-traumatic stress and to provide a significantly higher rate of epithelization, which optimizes the patient's stay. prognosis for recurrence of AW. The obtained results showed a significantly higher efficiency

of complex treatment of acute genital warts of the anogenital region in the group of patients receiving a nitrogen donor L - arginine. In the group of patients receiving L-arginine (n = 70), there were 2 (2,86 %) relapses. In the control (n = 35) group – 3 (8,57 %) ($p < 0.05$).

Key words: acute condyloma of the aogenital region; arginine; interleukin profile; fluometry; microcirculation; L - arginine.

At the present hour, there is an increase in the incidence of human papillomavirus infection (HPV) worldwide. Its frequency continues to increase, becoming epidemic [7].

HPV induces a number of diseases of pre-tumor and tumor origin, has various forms and its own link of pathological influence [4]. HPV is highly contagious. According to the literature, the infection, even with one unprotected contact, ranges from 40 - 60%. [2]. In turn, there is evidence of a dissonance between infection and the implementation of clinical manifestations. Thus, according to current epidemiological data, 75,6 % of sexual partners of patients with anogenital warts do not have clinical manifestations of the disease. [1], which leads to an increase in infection and carrier [17].

Gender differences in the speed of HPV infection are now proven. According to the latest literature, the risk of transmission of any type of HPV from man to woman is lower than from woman to man, which explains the higher elimination of infection, faster reduction of viral load and low seroconversion in men compared to women [2].

According to the type of oncogenicity, the types of HPV, which affecte the anogenital link, are divided into three groups - low, medium and high oncogenic risk. High risk of oncogenicity (hrHPV) includes types 16, 18, 48, 56. Medium - 31, 33, 35, 51, 52, 58. Low risk of oncogenicity (lrHPV) includes types 6, 11, 42, 43, 44. In the future, the level of oncogenic risk of HPV affects the course of the pathological process [8]. More than 90% of acute warts (AW) caused by HPV types 6 and 11 are one of the most common sexually transmitted diseases, and account for 1% of the world's sexually active population [2, 8, 11]. The peculiarity of the pathogenesis of HPV is its high tropism and infection of only proliferating epitheliocytes. Intense replication and release of the virus occur in differentiated keratinocytes located in the upper layers of tissue [8].

There are a number of factors in the pathogenesis of HPV that allow long-term persistence of the virus in human cells. By infecting keratinocytes, HPV causes a minimal inflammatory response due to inhibition of the cellular and humoral response. Under the influence of the virus a decrease in interferon levels α-γ occurs, inhibition of

histocompatibility complex, changes in interleukin profile and qualitative composition of lymphocytes in the direction of increasing suppressors, inhibition of maturation of Langerhans cells (immunocompetent cells), which leads to impaired apoptosis of infected cells [11, 15].

In addition to known factors such as immunosuppression, concomitant somatic pathology, the use of cytostatics high infectious index, the presence of sexually transmitted infections [15], the course of the disease is affected by microtrauma, surgical trauma that accompanies the postoperative period.

In turn, there is currently no effective method of treatment other than surgical excision of genital warts [8, 10]. There is no data to indicate which treatment is most effective. There is no clear understanding of how modern treatments affect the spread or recurrence of the disease, and the physiological process of wound healing, which is based on the proliferation of cells of the basal layer of the epithelium, in itself can provoke recurrence of the disease [10, 18]. The method of treatment is determined taking into account the following factors: the size of the lesion, the number of lesions (single or multiple), the degree of lesion (intense or extensive), anatomical location (internal or external genitalia), patient preferences, ease of treatment, adverse effects of drugs and surgery, as well as the experience of the doctor, among others [18].

The aim of the study. Optimization of the results of treatment of acute genital warts of the anogenital region with different clinical forms of the disease through the determination of somatic and immune status of patients, and their timely correction.

Materials and methods. 105 patients with AW of the anogenital region were examined and treated, among which single AW – 36 (34,29 %); multiple AW – 66 (62,86 %); giant Bushke-Levenstein warts – 3 (2,86 %.). The control group consisted of 20 people. In terms of gender, the main group consisted of 63 (60 %) women and 42 (40%) men. In the control – 10 (50 %) women and 10 (50 %) men. The exclusion criteria from the main group were the presence of diabetes, pregnancy, HIV, syphilis, oncological pathology of the skin of the anogenital link, rectum, genitals.

The level of cytokines TNFa, IL-4 IL-6 IL-8 was determined using a solid-phase enzyme-linked immunosorbent assay with monoclonal and polyclonal antibodies.

The intensity of pain in the preoperative and postoperative period was determined by the Visual Analog Scale (VAS): 0 - absence, 1-2 - weak, 3-4 - insignificant, 5-6 - moderate, 7-8 - strong, 9-10 most pronounced, intolerable [14].

Assessment of local blood circulation was determined by laser Doppler flowmetry (LDF). The examination was performed on a Doppler laser fluometer LAKK-01 (NPP "LAZMA", Russia) with a single-channel sensor with a wavelength of 0.63 μm (in the red range) and three optical fibers using a surface sensor to measure the surface of the skin. for three minutes. The microcirculation index (M), which is the total capillary circulation in real time, was determined.

M is the arithmetic mean value of the microcirculation index, which is measured in perfusion units. This figure depends on the state of arteriolar vascular tone and / or decreased blood flow in the venules.

σ («flax») is the standard quadratic deviation (SCR) of the amplitude of blood flow oscillations from the mean value of M, which characterizes the temporal variability of microcirculation, which is provided by neurogenic and mitogenic tone. The decrease in σ indicates the suppression of active vasomotor mechanisms of blood flow modulation.

K_v - coefficient of variation - reflects the relationship between perfusion and its variability: $Kv = \sigma / M \times 100\ \%$ [3, 9, 12].

Mathematical processing of research results and comparative assessment of the significance of differences between the main and control groups was carried out using programs for calculating the indicators of the variational series and the Student's criterion. The reliability interval was obtained with a probability of 95% ($p < 0,05$) [6].

In designing the treatment, we were guided by modern scientific data on the epidemiology and pathogenesis of AW anogenital area, namely:

1). The main method of infection – contact (sexual, household, artificial), which is clinically realized under conditions of local changes in the skin and mucous membranes, in the form of microtrauma or inflammation on the background of microbial and fungal contamination. 2). The conditions for the manifestation of AW of the anogenital region in infected patients are changes in the immune system. 3). AW is a reservoir of vegetative forms HPV [4], so their surgical removal reduces the viral load. 4). At present, there are no evidence-based treatments for AW, including surgical removal, or other types of destruction [4, 8, 10].

Based on this, our proposed treatment design included antiviral / immunomodulatory therapy, local antibacterial and antifungal treatment, surgical treatment. Systemic antibiotic therapy was prescribed according to the indications. AW excision was performed by electrocoagulation using the BOWA device (Germany) with mandatory histological verification of the removed tissues.

For antiviral action, we used «Alokin-Alpha» (Aloferon). The standard course of treatment was 12 days and was administered in the preoperative and postoperative periods as subcutaneous injections at a dose of 1 mg every other day (for a total of 6 injections). Alloferon belongs to the group of oligopeptides, is an effective inducer of the synthesis of endogenous alpha- and gamma-interferons and an activator of the natural killer system. The drug stimulates the recognition and lysis of defective cells by cytotoxic lymphocytes and is highly effective against infections caused by influenza A and B viruses, hepatitis B, herpes, HPV [16].

In order to normalize the microcynosis and the functional state of the intestine, all patients were prescribed a biologically active supplement «Subalin-forte» (capsules) (FZ "Biopharma" Ltd., Ukraine), which is a source of active culture of Bacillus subtilis. Also live bacteria Bacillus subtilis have antiviral activity due to stimulation of α_2-interferon synthesis [13]. «Subalin-forte» was administered 4×10^9 live culture of Bacillus subtilis 3 times a day for 14 days before surgery and 7 days after.

In order to eliminate the inflammatory process as a local therapy on the location of HA before surgery and in the postoperative period, patients were prescribed the drug "Ginodek", which is a gel based on high molecular weight hyaluronic acid in the form of 1,5% sodium hyaluronate, antiseptic decamethoxine 20 % and lactate buffer pH 3,8 to 4,5. The pH level of the drug coincides with the indicators of healthy skin, which allows its use topically on the skin of the perineum. Lactate, which is part of the drug, stimulates the growth of connective tissue and collagen production, which is important in wound healing. Decamethoxine has a purely local effect, as it is not absorbed by mucous membranes, skin and wound surface, which eliminates the systemic effect on homeostasis. Its antimicrobial, fungicidal and antiviral effects are realized due to the effect on the phospholipids of the membrane of the pathological agent, which leads to a violation of their permeability and death. Decamethoxine has activity against microorganisms that are resistant to antibiotics. Sodium hyaluronate enhances angiogenesis, reduces cytokine levels, promotes wound healing and protects blood vessels from damage. In the postoperative period, sodium hyaluronate reproduces a protective film on the skin, which protects the postoperative wound from infection [19]. The drug was administered in the preoperative period at 2.0 ml per affected area 2 times a day for 10 days and 10 days after surgery. In women, according to the indications, in order to rehabilitate the vagina, the drug was also prescribed vaginally 5 ml 2 times a day.

Given the data we received during the examination of patients on the violation of microcirculation in the anogenital area in HA, one of the areas of treatment was the impact on

the normalization of blood circulation in the anogenital area. For this purpose, we proposed the drug «Tivortin aspartate» (L-arginine). Arginine is a nitrogen donor for the enzyme NO synthase, which is required for the synthesis of nitric oxide by endothelial cells, thereby having the effect of pronounced vasodilation by inhibiting the synthesis of endothelin-1. The latter is a powerful vasoconstrictor. Arginine reduces oxidative stress by inhibiting the synthesis of asymmetric dimethylarginine. Stimulates the activity of the thymus gland, affecting the synthesis of T lymphocytes. Arginine has antihypoxic, antioxidant, immunomodulatory, membrane stabilizing, cytoprotective and detoxifying effects. The drug is able to affect the synthesis of a number of hormones and biologically active substances.

According to the treatment design, patients were divided into **2 clinical groups**.

The first group included 70 patients, among whom patients with multiple lesions of the perianal region were 47 (67,14 %), single – 21 (30,0 %), Bushke-Levenstein warts – 2 (2,86 %). All patients of the first group, except for antiviral and topical therapy, were given L-arginine aspartate 2 weeks before surgery and 10 days in the postoperative period. The drug was administered in a single dose of 5,0 ml, corresponding to 1,0 g of L-arginine, orally, 4 times a day with meals.

The **second clinical** group included patients with multiple lesions of the perianal region – 19 (54,29 %), single – 15 (42,86 %), Bushke-Levenstein warts – 1 (2,86 %), who did not receive L- arginine. Otherwise, the treatment regimen did not differ.

The **obtained results and their discussion.** The analysis of the somatic status of patients with AW of the anogenital region revealed a high level of chronic diseases, which were observed in 96 (91,43 %). At the same time, 24 (22,86 %) patients presented themselves as somatically healthy, did not seek medical help, which contributed to the chronicity of the pathology. The high frequency of pathology of the digestive system, which was 81 (77,14 %), is noteworthy. On average, one patient in the main group had 2,16 cases of pathology of the digestive system and 3,41 cases of general somatic pathology. In contrast to the main group, the control level of somatic pathology was significantly lower. On average, in the control group per subject there were 0,9 cases of pathology of the digestive system and 1,2 of general somatic pathology, which is lower than in the main, respectively, 2,4 and 2,8 times ($p < 0.05$). The presence of a high level of chronic somatic and infectious pathology in patients with AW area gives reason to think about the presence of chronic immune disorders which are a risk factor for AW in infected HPV and lead to the manifestation of the pathological process.

When examining the immune status of 100 % of patients with AW anogenital area was observed significantly lower compared to the control group, the total number of lymphocytes,

equal to (1,63 ± 0,07) × 10^9 /L at (2,15 ± 0,1) × 10^9 /L ($p < 0,05$), which indicates the homogeneity of the group on this basis and can be used as a prognostic factor. The relative number of lymphocytes corresponded to the lower limit of the reference values – (28,75 ± 1,75) %, while in the control group it was 1,3 times higher and equal to (35,95 ± 1,61) % ($p < 0,05$). The presence of absolute and relative lymphopenia can be explained from the standpoint of the influence of long-term viremia on immune homeostasis.

Immunological examination in patients of the main group in comparison with the control revealed a proportional decrease in the absolute number of T-lymocytes (CD3 +) and their populations. The number of T-lymocytes (CD3 +) was 1,6 times lower and was equal to (0,70 ± 0,02) × 10^9 /L against (1,13 ± 0,07) × 10^9 /L ($p < 0,05$). The absolute level of (CD4 +) (T-helpers / inducers) compared with the control group was reduced by 1,6 times – (0,42 ± 0,01) × 10^9 /L in the control (0,66 ± 0,05) × 10^9 /L ($p < 0,05$). The level of CD8 + (T-suppressors / killers) also differed and was 1,5 times lower, respectively – (0.28 ± 0,01) × 10^9 /L at (0,43 ± 0,03) × 10^9 /L ($p <0,05$) in the control.

The relative number of T-lymphocyte populations also differed significantly. The level of CD3 + in the main group was equal to (41,64 ± 0,41) %; in the control – (49,45 ± 0,8) % ($p < 0,05$). CD4 + (25,19 ± 0,45) % and (30,15 ± 0,64) % ($p < 0,05$), respectively. According to CD8 + in the main (16,48 ± 0,36) % and in the control (19,40 ± 0,52) ($p < 0,05$). All subjects showed an imbalance in the subpopulation of T lymphocytes with a proportional decrease of 1,2 times. At the same time, the level of CD3 + was reduced relative to the reference values in 100 % of patients, which indicates statistical homogeneity of the population. According to CD4 + indicators, there were 33 (36,7 %) reductions. The level of CD8 + was reduced by 29 (32,2 %). Immunoregulatory index did not differ significantly and was equal in the main group (1,64 ± 0,06) %, in the control – (1,55 ± 0,08) % ($p > 0,05$), but in the main group of its increase relative to the reference values were observed in 18 (20,0 %), while in the control only in one case (5,0 %) due to its reduction.

At the same time, the level of B-lymphocytes (CD 22) was changed against the background of T-lymphopenia. An increase in the total number of B-lymphocytes relative to the reference values was observed in 81 (90,0 %) patients of the main group and only in 3 (15,0 %) ($p < 0,05$) in the control with values, respectively (0,52 ± 0,02) × 10^9 /L and (0,45 ± 0,03) × 10^9 /L ($p < 0,05$). The relative composition was also changed in the direction of increase: (30,41 ± 0,52) % at (20,4 ± 0,38) % in the control ($p < 0,05$), indicating the presence of chronic inflammation and / or viral inflammation with depletion of the T-link of immunity

In accordance with the increase in B-lymphocytes, we observed changes in the link of humoral immunity. The indicators of Ig A and Ig G showed a significant increase. The level of Ig A was equal to (1,84 ± 0,03) g/L in the group of patients and (1,36 ± 0,05) g /L in the control group ($p < 0,05$). Ig G, respectively (13,96 ± 0,20) g /L and (11,6 ± 0,35) g /L ($p < 0,05$). The level of Ig M in both groups probably did not differ, but in the main group tended to decrease and was equal to (1,12 ± 0,03) g /L and (1,29 ± 0,17) g /L, respectively ($p > 0,05$).

In the study of the cytokine profile in patients of the main group we found a significant increase in the level of pro-inflammatory interleukin IL-8, pro- and anti-inflammatory IL-4 and tumor necrosis factor (TNFa) The level of IL-4 was 2,4 times higher than in the control respectively (4,14 ± 0,24) pg/ml and (1,73 ± 0,13) pg/ml ($p < 0,05$). Comparison of IL-4 levels with the level of CD 22, IgG, IgA confirms its role in the stimulation of the humoral immune system, as a compensatory response to the depletion of the T-link in a chronic inflammatory process [5].

IL-8 levels were increased 1,9-fold, respectively (29,82 ± 3,15) pg/ml and (15,18 ± 1,82) pg/ml ($p < 0,05$). Increase in TNFa – 3,0 times – (7.64 ± 0.93) pg/ml against (2,55 ± 0,22) pg/ml ($p < 0,05$). The level of IL-6 in patients with AW was 2,7 times higher – (3,77 ± 0,45) pg/ml, while in the control – (1,62 ± 0,15) pg/ml ($p < 0,05$).

Analyzing the cytokine profile data, we found the dependence of IL-6, IL-4 and IL-8 levels on the prevalence of AW and the presence of concomitant perifocal inflammation. Thus, the highest values were in patients with giant Bushke-Levenstein warts, which were accompanied by necrosis, secondary inflammation, severe tissue infiltration. While in patients with single AW cytokine status did not differ significantly from the values in the control group.

Surveys showed that in patients with AW, the state of microcirculation was significantly different from that in the control group.

The state of microcirculation in the control group was variable. The average microcirculation (M) was equal to (6,57 ± 0,10) perfusion units (p.u) with a high standard deviation (σ) – (1,95 ± 0,06) p.u and a coefficient of variation (K_v) – (29,13 ± 0,93) %, which indicates high modulation of blood circulation.

Data on the state of blood circulation in the main group differed significantly from the control and depended on the nature of the spread of the pathological process. Circulation in single AW in comparison with the control group was characterized by a decrease in all three indicators: M – (4,60 ± 0,06) p.u ($p < 0,05$), σ – (0,56 ± 0,03) p.u ($p < 0,05$) and K_V – (12,23

± 0.58) % ($p > 0,05$). This variant of microcirculation is most consistent with the spastic form and, in our opinion, may be one of the factors in the implementation and spread of AW.

At the same time in the group of patients with multiple AW there was a significant increase in M with average values of M – (12,29 ± 0,32) p.u ($p < 0,05$), which was characterized by monotony, σ – (0,66 ± 0,03) p.u ($p < 0,05$) with a low K_V – (5,52 ± 0,22) % ($p < 0,05$). This type of blood flow in patients with multiple AW corresponds to the hyperemic type of microcirculation that accompanies the inflammatory process, and is characterized by increased blood flow with slowed outflow due to decreased venous circulation.

The most pronounced changes in M were observed in patients with giant Bushke-Levenstein warts, in which in different areas there were changes in blood flow from increased hyperemic with average values of M – (18,92 ± 0,55) p.u ($p < 0,05$), monotonicity σ – (0,55 ± 0,21) p.u ($p < 0,05$), K_V – (2,95 ± 1,17) % ($p < 0,05$); to a stagnant form at a combination of Bushke-Levenstein's condyloma with a necrosis and a phlegmon of area of a perineum: M – (19,81 ± 0,13) p.u ($p < 0,05$), monotonicity σ – 0,40 p.u., K_V – 2,0 %. In these patients, we observed maximal values of interleukin levels, which ranged from IL-4 to (6,74 – 8,64) pg/ml; IL-8 – (104,0 – 140,7) pg/ml; IL-6 – (12,90 – 26,91) pg/ml; TNFα – (23,57 – 27,1) pg/ml.

When comparing the course of the postoperative period, we observed a slower elimination of symptoms of post-traumatic reaction in patients of the second clinical group. The intensity of pain in the first group averaged (4,74 ± 0,24) points and ranged from weak and insignificant 1 - 4 points, which accompanied 23 (32,86 %) patients, moderate – 5 - 6 points in 28 (40,0 %) to strong – 7 - 8 points – 18 (25,71 %) and intolerable – 1 (1,43 %). In the second group, the average values of pain intensity were higher – (5,54 ± 0,29) points (p_1, $p_2 > 0,05$) due to an increase in cases of moderate and severe pain, which was determined with the following frequency: mild and minor – 6 (17,14 %), moderate – 17 (48,47 %), strong – 11 (31,43 %), intolerable – 1 (2,86 %). In both groups, excruciating pain accompanied the postoperative period in patients with giant Bushke-Levenstein warts, which required the appointment of narcotic analgesics on the first day. In the postoperative period in the first group the pain persisted for up to 4 days – (2,93 ± 0,09) days, in the second - up to 5-8 – (5,88 ± 0,17) days ($p < 0,05$).

Post-traumatic perifocal reaction was observed in both groups. But these symptoms were eliminated in the first group for 3-5 days – (3,94 ± 0,10), while in the second for 6-9

days – (7,01 ± 0,18), (p < 0, 05), which significantly increased the length of stay in the hospital.

In total, postoperative wound healing in 102 patients occurred according to the biological type of "healing under the scab". In 2 patients with giant Bushke-Levenstein warts, healing was secondary, due to the large volume of excision in both cases and the presence of phlegmon of the anogenital region in the patient of the first group. Complete epithelialization of the postoperative wound with discharge of the scab in patients of the first group occurred on average after 12 - 14 days – (12,97 ± 0,11) days in the second after - 14 - 18 – (15,62 ± 0,26) (p < 0,05).

The term of wound healing in patients with giant Bushke-Levenstein warts was continued in the first group in a patient without purulent-septic complications and suturing for 14 days, and in a patient with complicated perineal phlegmon process up to 4 months. In the second group, the process of complete epithelialization occurred after 24 days.

We monitored the dynamics of the interleukin profile on the 10th day of the postoperative period, namely in the phase of proliferation of postoperative wound healing. During treatment, we observed a decrease in cytokine levels, which was more pronounced in the first group.

The average values of TNFa levels in patients of the first group on the 10th day of the postoperative period decreased in and were equal to (1,56 ± 0,14) pg/ml (p_1 < 0,05). Clinically, this was manifested by an acute recurrence of the disease in men and women with multiple HA 12 and 14 days after surgical destruction and was accompanied by multiple formations. The level of IL-4 in the first group on the 10th day of the postoperative period was equal to (1,73 ± 0,07) pg/ml (p_1 < 0,05)

There was also a decrease in the level of IL-6 and IL-8, respectively (1,35 ± 0,22) pg/ml (p_1 <0,05) and (8,34 ± 0,54) pg/ml (p_1 <0.05).

In the second group on the 10th day of the postoperative period, the dynamics of TNFa was more appropriate – (2,17 ± 0,12) pg/ml (p_2 < 0,05) (p_1, p_2 < 0,05).

There was a positive dynamics in the level of interleukins. IL-4 with values (2,0 ± 0,08) pg/ml (p_2 < 0,05) (p_1, p_2 > 0,05); IL-6 – (1,60 ± 0,11) pg/ml (p_2 < 0,05) (p_1, p_2 > 0,05); IL-8 – (12,47 ± 0,53) pg/ml (p_2 < 0,05) (p_1, p_2 <0,05). In the second group, recurrence of the disease was observed in 3 (8.57%) after 1-3 months: in one man and woman with multiple genital warts and women with single.

On the background of therapy in patients of the first group with multiple AW (n = 47) on the 10th day of the postoperative period on the background of complex therapy with L-

arginine, we observed positive changes in the mean microcirculation, characterized by increased variability of M - flaxmotions (7,34 ± 1,02) p.u, relative to the initial values (p_1 < 0,05). At the same time, there was a significant increase in σ – (1.37 ± 0.03) p.u (p_1 < 0,05) and K_v, which was equal to (19,08 ± 0,58) %, indicating the restoration of microcipculation. At single AW at all patients of the first group (n = 21) the shift of indicators of microcirculation towards normalization was also noted: M – (6,21 ± 0,07) p.u (p_1 < 0,05); σ – (1,73 ± 0,04) p.u. (p_1 < 0,05); K_v – (27,91 ± 0,71) % (p_1 < 0,05).

In the second group in patients with multiple AW (n = 19) the average microcirculation was equal to M – (8,27 ± 0,42) p.u (p_2 < 0.05) (p_1, p_2 > 0,05); σ – (1,37 ± 0,05) p.u (p_2 < 0,05) (p_1, p_2 > 0,05); K_v – (17,82 ± 1,11) % (p_2 < 0.05) (p_1, p_2 > 0,05). In patients of the second group with single AW (n = 15) there were also significant positive changes: M – (5,60 ± 0,06) p.u (p_2 < 0,05) (p_1, p_2 < 0,05); σ - (1,19 ± 0,05) p.u (p_2 < 0.05) (p_1, p_2 < 0.05); K_v – (21,27 ± 0,85) % (p_2 < 0,05) (p_1, p_2 < 0,05).

Among patients of both groups with giant Bushke-Levenstein warts more pronounced positive dynamics occurred in the first group (one case in each), respectively, M – (10,99 ± 0,4) p.u (p_1 < 0,05) and (11,02 ± 0,27) p.u (p_2 < 0,05) (p_1, p_2 > 0,05); with a slight increase in σ and K_v, more pronounced in the first group.

Conclusions. In patients with AW, there are shifts in the links of cellular and humoral immunity, manifested by depletion of cellular immunity – general lymphopenia, T-lymphopenia with a decrease in their absolute and relative numbers in all subpopulations, increased levels of B-lymphocytes with significant and Ig A. The proportional decrease in absolute and relative indicators of the lymphocyte pool with a significant increase in the level of B-lymphocytes and immunoglobulins in patients of the main group gives reason to consider it a consequence of the impact of HPV on this link.

Significant increase in the level of cytokines IL-4, IL-6, IL-8 and TNFa in patients with AW reflects the prevalence of AW and corresponds to the nature of the perifocal inflammatory process, which should be used as a factor in predicting the postoperative period and treatment effectiveness.

Changes in microcirculation in patients with AW of the anogenital region depend on the spread of AW and concomitant factors, such as perifocal inflammation due to bacterial contamination. Changes in microcirculation are realized in 3 variants: spastic - in patients with single AW, hyperemic - in patients with multiple AW, stagnant, which acquired maximum disorders in patients with giant Bushke-Levenstein warts.

The obtained results showed a significantly higher efficiency of complex treatment of acute genital warts of the anogenital region in the group of patients receiving a nitrogen donor L - arginine. In the group of patients receiving L-arginine (n = 70), there were 2 (2,86 %) relapses. In the control (n = 35) group – 3 (8,57 %) ($p < 0,05$).

The use of nitrogen donor (L-arginine) in complex therapy allows to eliminate subjective symptoms, signs of secondary bacterial contamination in the preoperative period, postoperative pain, post-traumatic stress and to provide a significantly higher rate of epithelization, which optimizes the patient's stay. prognosis for recurrence of AW.

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