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STATE OF MICROCIRCULATION IN PATIENTS WITH GENITAL CONDYLOMAS OF THE ANOGENITAL AREA AND CHARACTERISTICS OF EFFICIENCY OF TREATMENT AT THE PERIOD OF PREOPERATION

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Abstract

Introduction. Determination of the state of microcirculation in patients with genital warts (GW) of the anogenital area and the effectiveness of correction at the stage of preoperative treatment.

The aim of the study. Determination of the state of microcirculation in patients with genital warts (GW) of the anogenital area and the effectiveness of correction at the stage of preoperative treatment.

Materials and methods. 105 patients (63 – 60 % women; 42 – 40 % men) with genital warts with anogenital lesions were examined and treated: single acute warts – 36 (34,29 %); multiple acute warts – 66 (62,86 %); giant Bushke-Levenstein warts – 3 (2,86 %.). Control group consisted of 20 healthy people (women 10 – 50 %; men 10 – 50 %). Assessment of local circulatory status was determined by laser Doppler flowmetry with a wavelength of 0,63 μm (in the red range). The indicator of microcirculation (IM) – amplitude of oscillations of blood circulation in real time and its average value (M) were determined; standard deviation (SD) of the amplitude of blood flow fluctuations from the mean value of M; C_v – coefficient of variation - reflects the relationship between perfusion and its variability: $C_v = \sigma / M \times 100$ %

The examination was performed in two clinical groups during the initial examination, after 2 weeks of preoperative preparation and in the dynamics of observation in the postoperative period. All patients received immunomodulatory, antiviral and topical therapy for two weeks, which included antiseptic and hyaluronic acid. The first group included 70 patients who were prescribed Tivortin Aspartate (L-arginine Aspartate) 2 weeks before surgical treatment. The second group consisted of 35 patients and was comparative in monitoring the effectiveness of treatment.

Results and Discussion. The state of microcirculation among healthy subjects was characterized by variability in the amplitude of oscillations with preserved active and passive regulatory mechanisms.

In patients with single acute warts, blood circulation corresponded to the spastic form of disorders, which was characterized by: low amplitude of oscillations M – (4,60 ± 0,06) pf.un. ($p < 0,05$), decrease in SD – (0,56 ± 0,03) pf.un. ($p < 0,05$) and C_v – (12,23 ± 0,58) % ($p > 0,05$). Patients with multiple GW were characterized by a hyperemic type of microcirculation, which accompanies the inflammatory process and, but occurs due to decreased venous circulation: M – n (12,29 ± 0,32) pf.un. ($p < 0,05$), SD – (0,66 ± 0,03) pf.un. ($p < 0,05$), C_v – (5,52 ± 0,22) % ($p < 0,05$). In patients with giant Bushke-Levenstein warts, changes in blood flow varied from hyperemic type with values of M – (18,92 ± 0,55) perfusion units ($p < 0,05$), SD – (0,55 ± 0,21) pf.un. ($p < 0,05$), C_v – (2,95 ± 1,17) % ($p < 0,05$); to stagnant in the combination of Bushke-Levenstein warts with necrosis and phlegmon of the perineum: M – (19,81 ± 0,13) pf.un. ($p < 0,05$), SD – 0,40 pf.un., C_v – 2,0 %.

Positive changes in microcirculation at the end of preoperative preparation were more pronounced in the first group, where L-arginine aspartate was used, which was manifested in a significant increase in C_v, SD and variability of M.

Conclusions. Changes in microcirculation in patients with acute genital warts of the anogenital area are realized in 3 variants: spastic – in patients with single GW, hyperemic - in patients with multiple GW, stagnant, which acquired maximum disorders in patients with giant Bushke-Levenstein warts.

L-arginine has a positive effect on microcirculation in the focus, and regardless of the initial type (hyperemic or spastic, stagnant), contributes to its changes towards normalization. This efficiency can be explained from the standpoint of the direct effect of L-arginine as a nitrogen donor on the active mechanisms of regulation of microcirculation.

Significant changes in microcirculation towards normalization with less pronounced positive dynamics in patients of the second clinical group, due to the indirect effect on the

state of microcirculation due to the influence of systemic antiviral treatment, local therapy on the pathological process.

Key words: genital warts of the aogenital area; the giant Bushke-Levenstein condyloma; laser Doppler flowmetry; microcirculation; L-arginine.

Annotation. At present, much attention is paid to the study of the state of microcirculation in various pathological processes. A number of surveys of domestic and foreign scientists have appeared, which testify to the influence of microcirculatory disorders on the course of diseases [3]. In turn, there are inverse data on the impact of surgery on the state of microcirculation in the postoperative period and methods of prevention of complications. Factors influencing the state of microcirculation include the presence of intoxication, hypothermia, metabolic disorders, coagulation. Among iatrogenic factors the choice of surgical access, method and scope of surgical intervention are highlighted, the impact of drugs, the body's response to surgical trauma, which is equated to the systemic inflammatory response syndrome involving the sympathetic autonomic system, endocrine and immune status [3].

No less important are the methods of correction of microcirculation disorders because the effect of drugs on pre- and postcapillary sphincters can predict the level of effectiveness of therapy [4].

Among the variety of methods for determining the state of microcirculation is the method of laser Doppler flowmetry (LDF), which allows you to monitor the perfusion of peripheral tissues in the current time in the dynamics of the disease and its control during treatment under the influence of drugs [1, 2, 4]. The method is based on the determination of tissue perfusion by blood by measuring the Doppler frequency shift that occurs when probing the tissue with laser radiation, followed by registration of radiation reflected from moving and stationary components of the tissue. The received signal reflects the features of blood flow in microvessels in the amount of up to 1,5 mm3 of the examined tissue [1, 6].

In a section of regulation of blood flow there are 2 types of mechanisms: active and passive. Passive mechanisms include a group of external factors that are formed outside the microcirculatory tract: cardiac rhythm at the "entrance" to the microcirculatory channel and venular rhythm at the "exit" from it. To the active - factors that directly affect the vessels of the microcirculatory tract due to changes in vascular resistance to blood flow due to changes in tone and complex system of sympathetic and endothelial regulation [1, 6].

The aim of the study. Determination of the state of microcirculation in patients with genital warts (GW) of the anogenital area and the effectiveness of correction at the stage of preoperative treatment.

Materials and methods. 105 patients with acute wart (GW) with anogenital lesions were examined and treated, among which single acute wart (GW) – 36 (34,29 %); multiple GC – 66 (62,86 %); giant Bushke-Levenstein warts – 3 (2,86 %.). The control group consisted of 20 healthy individuals. 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 criteria for exclusion from the main group were the presence of diabetes, pregnancy, HIV, syphilis, oncological pathology of the skin of the anogenital link, rectum, genitals. All patients were not vaccinated.

Assessment of local blood circulation was determined by laser Doppler flowmetry (LDF), which was performed during the initial examination, after 2 weeks of preoperative preparation and in the dynamics of observation in the postoperative period.

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 superficial blood circulation, which was fixed on the skin of the perineum for 3 minutes.

Microcirculation index (MI), which is the magnitude of the amplitude of blood circulation fluctuations in real time, was determined. We studied the parameters M, SD and Cv [1, 2, 4], which allow a general assessment of the state of microcirculation, where:

M (perfusion units – pf.un.) is the average value of the amplitude of oscillations, depending on the concentration of erythrocytes. A change in M in the direction of increase or decrease indicates an increase or decrease in perfusion. This figure depends on the state of arteriolar vascular tone and / or decreased blood flow in the venules. Increase in M occurs in cases of decreased vascular tone or blood stasis in the venules, which leads to an increase in the concentration of erythrocytes in the volume of tissue examined.

σ («flax», SD) (perfusion units – pf.un.) is the standard deviation of the amplitude of blood flow oscillations from the mean M, which characterizes the temporal variability of perfusion, which is provided by neurogenic and miogenic tone, and reflects the average modulation of blood flow in the frequency range. The greater the value of σ is, the greater the depth of blood flow modulation. A decrease in σ indicates the suppression of active vasomotor mechanisms of blood flow modulation or the prevalence in the system of regulation of tonic sympathetic influences.

Cv – coefficient of variation – reflects the relationship between perfusion and its variability: Cv = σ / M×100 %. Increase Cv reflects the improvement of the microcirculation, which is associated with an increase in SD due to activation of endothelial secretion, neurogenic and myogenic control mechanisms with virtually unchanged value of M.

Our proposed treatment design included antiviral / immunomodulatory therapy, topical (antimicrobial and anti-inflammatory therapy), and surgical treatment. Systemic antibiotic therapy was prescribed according to the indications. Condyloma excision was performed by electrocoagulation using the device BOWA (Germany) with mandatory histological verification of removed tissues

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 area were 47 (67,14 %), single AW – 21 (30,0 %), Bushke-Levenstein warts – 2 (2,86 %).

The second clinical group included 35 patients, including patients with multiple lesions of the perianal area – 19 (54,29 %), single – 15 (42,86 %), Bushke-Levenstein warts – 1 (2,86 %).

In order to affect the microcirculation of all patients of the first group, 2 weeks before surgery and 10 days in the postoperative period was prescribed "Tivortin aspartate" (L-arginine aspartate). The drug was administered in a single dose of 5,0 ml, corresponding to 1,0 g of L-arginine, orally, 4 times daily with meals. Arginine is a nitrogen donor for the enzyme NO synthase, which is required for the synthesis of nitric oxide by endotheliocytes, thereby having the effect of pronounced vasodilation by inhibiting the synthesis of endothelin-1, the latter is a powerful vasoconstrictor. Arginine reduces oxidative stress level by inhibiting the synthesis of asymmetric dimethylarginine. Stimulates the activity of the thymus gland; affecting the synthesis of T lymphocytes. Arginine has antioxidant, immunomodulatory, membrane stabilizing, cytoprotective and detoxifying effects. The drug can affect the synthesis of a number of hormones and biologically active substances [5].

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 indicators of the variance series and according to the Student's criterion. The reliability interval was obtained with a probability of 95 % ($p < 0,05$).

The obtained results and their discussion. Surveys showed that in patients with perianal GW the state of microcirculation was significantly different from that in the control group.

The state of microcirculation in the control group was characterized by variability in the amplitude of oscillations. The average microcirculation (M) indicator was equal to (6,57 ± 0,10) pf.un. with high values of SD – (1,95 ± 0,06) pf.un. and the coefficient of variation (C_v) – (29,13 ± 0,93) %, indicating the variability of blood circulation with preserved active and passive mechanisms of regulation.

Data on the state of blood circulation in the main group differed reliably from the control group and depended on the nature of the spread of GW and the presence of secondary inflammation.

Blood circulation in single GW in comparison with the control group was characterized by a decrease in all three indicators: M – (4,60 ± 0,06) pf.un. ($p < 0,05$), SD – (0,56 ± 0,03) pf.un. ($p < 0,05$) and Cv – (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 GW.

At the same time in the group of patients with multiple GW there was a significant increase in IM with average values of M – (12,29 ± 0,32) pf.un. ($p < 0,05$), which was characterized by monotony, SD – (0,66 ± 0,03) pf.un. ($p < 0,05$) with low Cv – (5,52 ± 0,22) % ($p <0,05$). This type of microcirculation in patients with multiple GW corresponds to the hyperemic type of microcirculation, which occurs due to increased blood flow with slow outflow due to reduced venous circulation.

The most pronounced changes in IM were observed in patients with giant Bushke-Levenstein warts, in which in different areas there were changes in blood flow from increased hyperemic with values of M – (18,92 ± 0,55) pf.un. ($p < 0,05$), SD – (0,55 ± 0,21) pf.un. ($p < 0,05$), Cv – (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) pf.un. ($p < 0,05$), SD – 0,40 pf.un, Cv – 2,0 %, which was observed in one patient.

When determining the state of microcirculation at the end of preoperative preparation, we observed positive changes in both groups.

In the first group, regardless of the variant of initial blood circulation, we observed significant positive changes in microcirculation compared to the initial 68 (97,14 %) patients. Exceptions were 2 (2,86 %) cases in patients with Bushke-Levenstein warts, where there was a weak positive trend, but without significant differences.

In patients of the first group with multiple GW and hyperemic variant of microcirculation after two weeks of preoperative preparation M – (9,60 ± 0,20) pf.un. ($p < 0,05$), i.e., decreased by 21,9 %. SD increased by 59,1 % with values (1,05 ± 0,03) pf.un. ($p <$

0,05), which indicates the elimination of the venous component in the form of delayed blood flow, which is inherent in the inflammatory type of microcirculation. There was also a significant increase in C_v by 100 % - (11,05 ± 0,36) % ($p < 0,05$).

In patients of the first group with single GW, with a spastic variant of microcirculation in contrast, we observed an increase in M by 20,4 % - (5,54 ± 0,06) pf.un. ($p < 0,05$), which indicates the elimination of vasoconstriction due to the influence of arginine on the active parts of the mechanism of regulation of microcirculation. The level of SD increased more than 1,5 times and was equal to (1,49 ± 0,03) pf.un. ($p < 0,05$). C_v – (26,95 ± 0,52) % ($p < 0,05$).

In two patients with giant Bushke-Levenstein warts there was a statistically insignificant tendency to normalize microcirculation: M – (18,45 ± 0,98) ($p > 0,05$); SD – (0,90 ± 0,01) ($p > 0,05$); C_v – (4,88 ± 0,33) % ($p > 0,05$). In our opinion, this is due to the peculiarities of the pathogenesis of this form of GW, expressed by tissue infiltration; the presence of secondary bacterial contamination and phlegmon of the perineal tissues, which was observed in one patient.

In patients of the second group with multiple GW and hyperemic type of microcirculation at the end of preoperative preparation also showed a decrease in M by 15,1 % – (10,44 ± 0,56) pf.un.in comparison with initial values (p 0,05). SD had a significant increase (0,92 ± 0,04) ($p < 0,05$) pf.un. relative to the initial values, but significantly different from the indicator in the first group ($p < 0,05$). C_v increased due to a decrease in M and was equal to (18,33 ± 0,66) % ($p > 0,05$) and differed significantly from the initial values and values in the first group ($p < 0,05$).

In patients of the second group with single GW and the inherent spastic variant of microcirculation, there was an increase in M relative to baseline values by 9,1 % – (5,02 ± 0,04) perfusion units ($p > 0,05$) but was not reaching the values in the first group ($p < 0,05$). The average SD indicator had a significant positive dynamic and was equal to (0,92 ± 0,04) perfusion units ($p < 0,05$), significantly different from the first group ($p < 0,05$). Cv was equal to (18,33 ± 0,66) % ($p < 0,05$).

In 1 (2,86 %) patient of the second group with giant Bushke-Levenstein warts after postoperative preparation, we did not observe credible changes in microcirculation relative to the initial data.

Conclusions.

Changes in microcirculation in patients with acute genital warts of the anogenital area are realized in 3 variants: spastic – in patients with single GW, hyperemic – in patients with

multiple GW, stagnant, which acquired maximum disorders in patients with giant Bushke-Levenstein warts.

L-arginine has a positive effect on microcirculation in the focus, and regardless of the initial type (hyperemic or spastic, stagnant), contributes to its changes towards normalization. This efficiency can be explained from the standpoint of the direct effect of L-arginine as a nitrogen donor on the active mechanisms of regulation of microcirculation.

Credible changes in microcirculation towards normalization with less pronounced positive dynamics in patients of the second clinical group, due to the indirect effect on the state of microcirculation due to the influence of systemic antiviral treatment, local therapy on the pathological process.

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