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NV Drohomyretska  
SHEI "Ivano-Frankivsk  
National Medical University,  
Ukraine

NI Henyk  
SHEI "Ivano-Frankivsk  
National Medical University,  
Ukraine

## The role of the hemomicrocirculatory system in the pathogenesis of chronic inflammatory processes of the internal genital organs in women

NV Drohomyretska and NI Henyk

### Abstract

**The objective of the research:** To study the peculiarities of violations of the hemomicrocirculatory bed of the bulbar conjunctiva in women with isolated chronic inflammatory processes of the internal genital organs and against the background of varicose veins of the small pelvis before and after the treatment.

**Material and methods:** There were examined before and after the treatment 54 women with chronic inflammatory processes of the internal genital organs against the background of varicose veins of the small pelvis (group I); 46 women – with chronic inflammatory processes of the pelvic organs without varicose veins of the small pelvis (group II); 30 – practically healthy women (control group). The age of women was between 18 and 45 years old. All patients of the study groups received the treatment offered by us, which included a diosmin-containing phlebotropic medicine of 500 mg twice a day in a continuous mode and a 5-ml nitric oxide donator for 3 times daily per so for 14 days each month during six months.

Bulbar microscopy was performed with the help of SHCHL-2B slit lamp. The results of microscopy were evaluated according to the system of V.S. Volkov *et al.* (1976). Morphometry of the micro-vessels of the conjunctiva of the eyeball was carried out using photographic negatives based on the increase of SHCHL-2B.

**Results:** It was determined that in both of the examined groups there was a violation of hemomicrocirculation, which was systemic. After the performed treatment, the positive dynamics of changes in the hemomicrocirculatory bed was noted, especially in the group of patients with chronic inflammatory processes of the pelvic organs without varicose veins of the small pelvis. In the group of patients with chronic inflammatory processes of internal genital organs, which developed against the background of varicose veins of the small pelvis, positive intravascular and extravascular changes were revealed. The shape and size of the micro-vessels changed slightly.

### Conclusions

1. Violation of hemomicrocirculation is one of the main components of the pathogenesis of chronic inflammatory processes of internal genital organs, both against the background of varicose veins of the small pelvis and without varicose veins of the small pelvis.
2. Changes in hemomicrocirculation in chronic inflammatory processes of the internal genital organs against the background of varicose veins of the small pelvis and without varicose veins of the small pelvis are systemic in nature, as evidenced by the data of bulbar microscopy of the conjunctiva.
3. After the performed treatment offered by us, the improvement of hemomicrocirculation occurs, especially in the group of patients with chronic inflammatory processes of the internal genital organs without varicose veins of the small pelvis.

**Keywords:** Chronic inflammatory processes of internal genital organs, varicose veins of the small pelvis, hemomicrocirculatory bed, bulbar conjunctiva

### Introduction

Chronic inflammatory diseases of female genital organs occupy a leading place in the structure of gynecological pathology in the reproductive age (60-65%), and is the cause of female infertility and disorders of menstrual function [6, 9]. The topicality of the preservation and restoration of reproductive health of women in recent years is being paid particular attention in connection with the increase of number of chronic inflammatory diseases of the organs of small pelvis in women with a lack of knowledge of the pathogenetic mechanisms of inflammatory reactions, which creates significant difficulties of early diagnosis, with insufficiently high effectiveness of treatment [3, 5, 6, 9]. An important link in the pathogenesis of chronic inflammatory processes of the internal genital organs (CIPIGO) is a violation of the hemostasis system, which manifests itself in the development of hypercoagulation against the background of reducing the anticoagulation potential and inhibition of fibrinolysis.

Correspondence  
NV Drohomyretska  
SHEI "Ivano-Frankivsk  
National Medical University,  
Ukraine

The system of blood supply to the pelvic organs is impaired, the elasticity of the arteries and arterioles decreases, there are the signs of hypotension and complicated blood outflow from the arterial part to the veins, blood flow is reduced. The basis of slowed blood flow and stagnant phenomena in the pelvic organs includes anatomical changes in veins, sclerotic processes in vessels of the microcirculatory bed, connective tissue enlargement, atherosclerosis and varicose venules' dilation. Violation of regional hemodynamics worsens tissue trophism, promotes the appearance of zones of anemia or venous congestion in the organs of small pelvis, the development and maintenance of inflammatory and dystrophic changes in the receptor apparatus of the uterine appendages, provoking pain syndrome [3, 9]. Microcirculatory disorders often determine the course of many pathological processes. Microcirculatory system – is a complex structure that responds to all pathological processes in the preclinical period and takes on the first blow. The study of microhemocirculation will enable to solve important for practical medicine questions of pathogenesis of many diseases, prevention and therapy of regional circulatory disorders [8].

It has been determined that the hemomicrocirculatory bed (HMCB) consists of separate units – micro-districts. Each unit represents a certain multi-component complex of micro-vessels (arterioles, precapillaries, capillaries, postcapillaries, venules), nerve conductors, cells, fibrous formations and intercellular substance. Each microdistrict is separated from neighbouring one and has isolated ways of inflow and outflow of blood and metabolic waste products. Numerous data show that all the links of a multi-component microcirculatory bed function mutually consistently as a single system [1, 2, 4, 7, 8].

At the level of HMCB the capillary exchange and functioning of internal respiration, which support tissue and hemodynamic homeostasis, are carried out. Along with this, it is believed that HMCB, in turn, is the first to respond to the various pathological factors of the external and internal environment. Such response to pathological stimuli is manifested by stereotypical reactions that can be realized in the form of spasm of arteries, arterioles and pre-capillaries, slowing of blood flow, aggregation and stasis of formed elements, paresis of arteriole walls, pre- and post-capillaries with subsequent enlargement of their lumen, plasmorrhagia, erythrocytes' diapedesis etc. Such changes in microcirculation are schematically divided into: intravascular disorders: a) aggregation of red blood cells; b) violation of homeostasis, thrombosis; c) embolism; d) changes in blood flow velocity; vascular disorders: a) degenerative changes in the vascular wall (unevenness of the caliber, convolution, saccules, microaneurysm, vascular glomeruli, elastosis, elastophyrosis); b) dynamic vasomotor changes (dilation or constriction of micro-vessels, changes in capillary perfusion, retrograde blood flow); c) changes in vascular permeability (from pathological filtration of the liquid part of the blood to the diapedesis of the formed elements through the vascular wall); d) microscopic changes in the shape and function of the vascular endothelium; extravascular violations: a) micro-hemorrhagia into the perivascular space; b) perivascular edema; c) pathology of micro-lymphocirculation; d) damage to the perivascular connective tissue; e) development of neurodystrophic tissue processes; e) deposition of hemosiderin in perivascular tissues [4, 8].

An analysis of the nature of vascular, intravascular and extravascular changes in the microcirculation system makes it

possible to conclude that with each disease in the components of microcirculation there are both pathological and adaptive changes. The division, arising in the conditions of pathology, changes in micro-vessels to the pathologic and adaptive ones has an important methodological value, as it contributes to a more in-depth analysis of the pathogenetic mechanisms that underlie a particular disease and makes it possible to clarify the preconditions that provide compensation for violations of hemomicrocirculation, as well as the reasons that lead to a “breakdown” of compensation, development of irreversible hemodynamic changes in organs and tissues [8].

One of the methods of studying microcirculation is conjunctival biomicroscopy, which makes it possible to analyze changes in the shape of micro-vessels and the nature of blood flow not only visually, but also with the help of photoregistration, which greatly increases the objectivity of information [1, 2, 4, 8].

Hemomicrocirculatory status of the conjunctiva reflects the degree of clinical manifestations in diseases of the cardiovascular system and other organs. New data confirm the view of the diagnostic and predictive value of conjunctival biomicroscopy. With its help, a few days before the clinical manifestations of medication allergy were determined. In the initial stages of diabetes mellitus, hypertension, arterial hypertension, vascular changes in the conjunctiva were more pronounced than in the vessels of the eyeground. In hypertension of young people, this method detected vascular disorders in earlier stages of the disease. The possibility of this method use for assessment the efficacy of the treatment is evidenced by the reversal development of such changes as micro-aneurysms, venous twisting, reduction of the capillary channel [8].

It should be noted that in available literature we did not meet data on the use of bulbar microscopy to study microcirculatory changes in chronic inflammatory processes of internal genital organs in women with varicose veins of the small pelvis (VVSP).

Biomicroscopy of bulbar conjunctiva gives an opportunity to evaluate the state of rheological properties of blood, to determine the visibility of blood flow in different parts of the blood vessels of the microcirculation, to detect some changes in interstitial circulation and the effectiveness of the performed therapy.

The purpose of the research is to study the peculiarities of violations of the hemomicrocirculatory bed (HMCB) of bulbar conjunctiva in women with isolated chronic inflammatory processes and against the background of varicose veins of the small pelvis (VVSP) before and after the treatment offered by us.

**Materials and methods:** there were examined (before and after the treatment) 54 women with chronic inflammatory processes of the internal genital organs against the background of varicose veins of the small pelvis (group I); 46 women – with chronic inflammatory processes of the pelvic organs without varicose veins of the small pelvis (group II); 30 – practically healthy women (control group). The age of women was between 18 and 45 years old. All patients in the study groups received the offered by us treatment, which included a diosmin-containing phlebotropic medicine of 500 mg twice a day in continuous mode and a 5-ml nitric oxide donor for 3 times daily per se during 14 days each month for six months.

Bulbar microscopy was performed with the help of SHCHL-2B slit lamp. The results of microscopy were evaluated

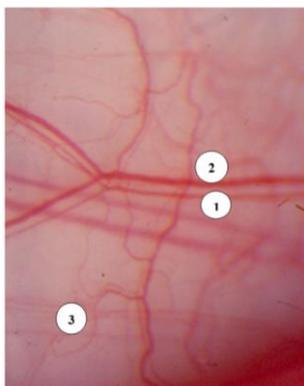
according to the system of V.S. Volkov *et al.* (1976). Morphometry of the micro-vessels of the conjunctiva of the eyeball was carried out using photographic negatives taking into account the magnification of SHCHL-2B.

### Results of the research and their discussion

For the hemomicrocirculatory bed, the conjunctiva of the eyeball (CEB) is characterized by the terminal type of branching of the micro-vessels, so the modular organization is not clearly expressed. Small arteries that penetrate the CEB and are radial with respect to the pupil branch dichotomically, giving several orders (4-5) of arterioles' different diameter. The arterioles of the first order include the vessels that give rise to the pre-capillaries, the first-order venules – the vessels that are formed as a result of the post-capillaries' fusing. Larger micro-vessels (usually of the 3<sup>rd</sup> order of branching) are not divided into subgroups, they are limited in size: for arterioles in the range of 20-40 microns, for venules – 28-65 microns. Arterioles in most cases are accompanied by one, sometimes two, venules of the same name with them in order. The pre-capillary arterioles are usually characterized by the fact that they are located at some distance from the post-capillary venules. The connection between these micro-vessels is carried out through a network of capillaries. The pre-capillary arteriole, together with capillaries and post-capillary venule, form a local subunit of HMCB, which provides the corresponding tissue micro-region. The microcirculatory unit consists of one pre-capillary arteriole, which gives rise to an average of 2-3 capillaries, which in turn have 1-2 orders of dichotomous branching. The blood that flows out of them comes mainly into 2-3 post-capillary venules. The length of the subunit of MCB is 1400-1800×600-900 microns. With age these relations change [Fig.1]

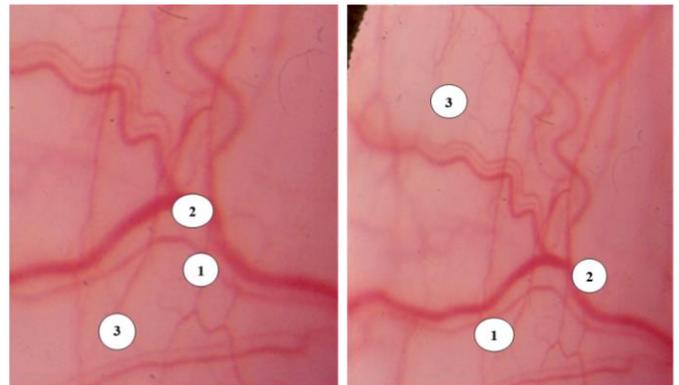
To study the peculiarities of conjunctival microcirculation, we have examined 30 practically healthy women aged 18 to 45 years. The quantitative and qualitative analysis of micro-photographs of the conjunctival vascular network was carried out.

In practically healthy women of reproductive age in biomicroscopy, the rapid, homogeneous, laminar conjunctival blood flow is determined. There are no signs of perivascular edema and intravascular aggregation of red blood cells. Arterioles ( $21.11 \pm 0.51 \mu\text{m}$ ) and venules ( $37.60 \pm 0.51 \mu\text{m}$ ) are parallel vessels with a ratio of diameters of 1:2. Capillary network ( $6.8 \pm 0.02 \mu\text{m}$ ) is formed due to the sequential branching of arterioles. The conjunctival index is  $2.20 \pm 0.20$  points



**Fig 1:** The state of conjunctival hemomicrocirculation in practically healthy women: N., 31 years old, 1-arteriole, 2-venule, 3-capillary. Mag.×40.

Patients with CIPIGO against the background of VVSP during bulbar microscopy there were marked changes in the HMCB, which are apparently related primarily to the varicose extension, and then – to the chronic inflammatory process. The unevenness of the caliber of the vessels of the conjunctiva and the sharp convolution of the venules impressed. Perivascular edema and venous enlargement were observed. The diameter of the latter ones was  $48.62 \pm 1.85 \mu\text{m}$  ( $P < 0.001$ ), the diameter of arterioles was  $24.36 \pm 0.95 \mu\text{m}$  ( $P < 0.01$ ). Capillaries with a diameter of  $9.28 \pm 1.16$  microns ( $P \leq 0.05$ ) had a net structure in small areas. Blood flow was slowed, in capillaries – intermittent one. CI was  $9.83 \pm 0.91$  points. Partial: CI 1-  $1.5 \pm 0.22$  points, CI 2-  $7.0 \pm 0.32$  points, CI 3-  $1.33 \pm 0.21$  points (Fig. 2)



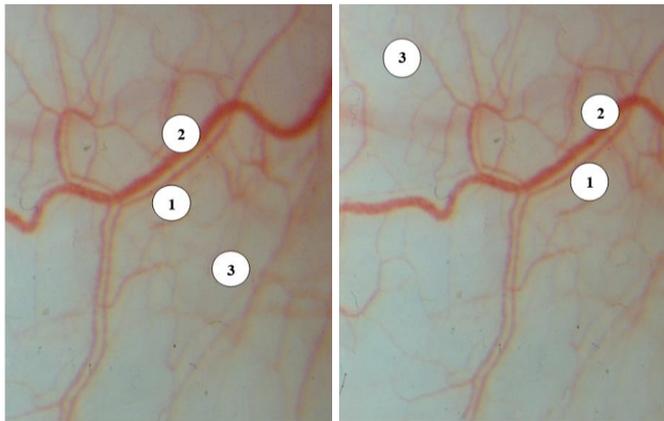
**Fig 2:** The state of conjunctival hemomicrocirculation in a patient L., 30 years old, with CIPIGO against the background of VVSP: a) before the treatment; b) after the treatment. 1-arteriole; 2-venule; 3-capillary. Mag.×40.

While performing the bulbar microscopy for women in this group 6 months after the treatment, we could see that perivascular edema was not expressed, blood flow has normalized, but the convolution and unevenness of the vessels' caliber remained. The diameter of the venule somewhat decreased –  $41.66 \pm 1.73 \mu\text{m}$  ( $P < 0.05$ ); arterioles –  $21.6 \pm 0.51$  microns, capillaries –  $6.52 \pm 1.05$ . The CI was  $8.17 \pm 0.70$  points ( $P < 0.001$ ) compared with the data before the treatment. Such a slight drop in the CI occurred, mainly due to CI 1 and CI 2.

Positive hemodynamics of the HMCB of CEB after the performed treatment shows the improvement of hemodynamics of the pelvic veins, which in turn leads to the improved tissue trophism by reducing hypoxia, and prevents the progression of dystrophic changes.

In women of the group II there were minor changes in the conjunctival blood vessels. The architectonics of the vascular pattern almost did not change. The perivascular edema was observed along the individual vessels, the venous portion of the bed was full-blooded, somewhat expanded, the venule diameter was  $39.64 \pm 0.85 \mu\text{m}$ , the blood flow slowed down. The diameter of the arterioles – was  $20.00 \pm 1.49 \mu\text{m}$ , the diameter of the capillaries –  $8.75 \pm 0.56$ . (Fig. 3) The overall CI before the treatment was  $6.80 \pm 0.98$  points. Partial CI: CI 1-  $1.40 \pm 0.40$  points, CI 2-  $4.40 \pm 0.40$  points, CI 3-  $1.20 \pm 0.20$  points. In the dynamics after the performed therapy, we noticed a significant improvement in the state of HMCB of CEB. Perivascular edema along the vessels of the conjunctiva of the eye is absent, the diameter of the venules has somewhat decreased ( $38.93 \pm 0.51 \mu\text{m}$ ;  $P < 0.001$ ). In the capillaries and venules there was a homogeneous laminar blood flow. The diameter of the arterioles was  $20.71 \pm 0.46 \mu\text{m}$ , the diameter of

the capillaries was  $7.9 \pm 0.42 \mu\text{m}$  ( $P < 0.05$ ). The general conjunctival index was  $4.80 \pm 0.37$  points, the partial: CI 1-  $0.80 \pm 0.37$  points, CI 2-  $3.67 \pm 0.40$  points, CI 3-  $0.40 \pm 0.24$  points.



**Fig 3:** State of conjunctival hemomicrocirculation in a patient L., 30 years old with CIPIGO without VVSP: a) before the treatment; b) after the treatment. 1-arteriole; 2-venule; 3-capillary. Mag.  $\times 40$ .

Thus, after the performed treatment, we have found positive changes in the HMCB of the CEB, both in the I and in the II groups.

Based on our research, we can conclude that our treatment for women in both groups affects one of the main components of the pathogenesis of development of chronic inflammation of the internal genital organs and varicose veins of the small pelvis.

### Conclusions:

1. Violation of hemomicrocirculation is one of the main components of pathogenesis of chronic inflammatory processes both against the background of VVSP and without VVSP.
2. Changes in hemomicrocirculation in chronic inflammatory processes both against the background of VVSP and without VVSP are systemic, as evidenced by the data of bulbar microscopy of the conjunctiva.
3. After the treatment offered by us, an improvement of hemomicrocirculation is observed, especially in the group of patients with CIPIGO without VVSP.

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