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Research Article

Endothelial Dysfunction in the Pathogenesis of Chronic Inflammatory Processes of the Internal Genital Organs in Women

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Abstract

The objective of the work: to study the changes of the functional activity of the endothelium and the plasma-coagulation link of hemostasis in women with chronic inflammatory processes of the internal genital organs (CIPIGO) with and without varicose veins of the small pelvis (VVSP).

Materials and methods: 68 women with chronic inflammatory processes of the internal genital organs against the background of varicose veins of the small pelvis (group 1); 52 women with chronic inflammatory processes of the pelvic organs without varicose veins of the small pelvis (group 2); 30 practically healthy women (control group) were examined before and after the treatment. The age of women was between 18 and 45 years old. All the patients of the study groups received the treatment offered by us, which included a diosmine-containing phlebotropic preparation normoven, 500 mg twice a day in continuous mode and a donor of nitric oxide tivortin aspartatum, 5 ml 3 times per os for 14 days each month during six months.

Determination of concentration of endothelin-1, prostacyclin was performed by immunoassay using a set of reagents from the firm “Biomedica” (Austria); the determination of D-dimers in blood plasma was performed by latex-test of the firm “Organon-Tekhnika”.

Results of work. In women with CIPIGO with and without VVSP, the increased production of endothelin-1, which has a pro-aggregate and pro-inflammatory effect, was determined. At the same time, the decrease of the synthesis of prostacyclin, which has anti-aggregant properties, was noted. In evaluating the indicators of coagulograms in patients of the studied groups, the propensity for hypercoagulation was revealed, as evidenced by an increase in the level of fibrinogen and a rise of index of the phospholipid-dependent coagulation tests. The decrease of the percentage of fibrinolytic blood activity and the increase in plasma concentration of the molecular marker of thrombophilia D-dimer can be considered as activation of intravascular coagulopathy and the presence of endothelial dysfunction.

Conclusions: 1. Our studies found endothelial dysfunction and violations of the plasma-coagulation linkage of hemostasis in both studied groups. 2. After the performed treatment, the improvement of the functional activity of the endothelium and normalization of the main parameters of the plasma-coagulation linkage of hemostasis were observed.

Keywords

chronic inflammatory processes of internal genital organs; varicose veins of the small pelvis; endothelium

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Problem statement and analysis of the recent research

Inflammatory processes of female genital organs remain one of the most serious problems in modern gynecology [6, 7].

Considering the problem of CIPIGO against the background of VVSP and studying the pathogenetic mechanisms of the development of these diseases, it would be advisable to determine the state of vascular endothelium, as the origin of its dysfunction is in the basis of the development of the most common vascular diseases, the characteristic sign of which is the violation of microcirculation, changes of the processes of angiogenesis and the formation of vasoactive substances [1-5, 8-10].

Endothelium – is not only a semi-permeable membrane, which provides the nonwettability of the vessel, but it is also an active endocrine organ, scattered in all tissues [1, 2, 5]. One of the main functions of the endothelium is the balanced extraction of regulatory substances that determine the integral function of the circulatory system [2, 5].

Objective of the work is to study the changes of the functional activity of the endothelium and the plasma-coagulation link of hemostasis in women with chronic inflammatory processes of the internal genital organs (CIPIGO) with and without varicose veins of the small pelvis (VVSP).

1. Materials and methods

68 women with chronic inflammatory processes of internal genital organs against the background of varicose veins of the small pelvis (group 1); 52 women with chronic inflammatory processes of the pelvic organs without varicose veins of the small pelvis (group 2); 30 – practically healthy women (control group) were examined before and after the treatment. The age of women was between 18 and 45 years old. All patients of the research groups received the treatment offered by us, which included a diosmine-containing phlebotropic medicine (normoven) of 500 mg twice daily in continuous mode and a donor of nitric oxide (tivortin aspartatum) of 5 ml 3 times a day per os for 14 days of each month during the six months.

Determination of concentration of endothelin-1, prostacyclin was performed by immunoassay using a set of reagents from the firm "Biomedica" (Austria); the determination of D-dimers in blood plasma was carried out by latex-test of the firm "Organon-Tekhnika".

2. Results of the research and their discussion

In women with CIPIGO with and without VVSP, the increased production of endothelin-1, which has the pro-aggregant and pro-inflammatory effect, was determined. At the same time, the decrease of the synthesis of prostacyclin, which has anti-aggregant properties, was noted. Prostacycline – vasoactive endothelial factor, one of the final products of metabolism of arachidonic acid, is formed in endothelial cells of media and adventitia of vessels [2].

In women of the control group, the concentration of endothelin 1 was 2.81±0.04 pg/ml, and prostacyclin – 235.31±1.56 pg/ml.

The content of endothelin-1 in blood serum of women of the first and second groups was significantly higher and was 4.21±0.07 pg/ml and 3.57±0.02 pg/ml, respectively.

The parameters of the level of prostacyclin in the group 1 were – 184.51±1.15 pg/ml, in the group 2 – 221.40±2.13 pg/ml (Table 1).

Taking into account the fact that such vasoactive substances as endothelin-1 and prostacyclin directly influence on the rheological properties of blood, namely regulating thrombosis, all the women of the research groups were performed the study of coagulogram parameters.

There is a statistically significant increase of the following indices: time of venous blood clotting was – 9.50±0.05 min in the first group and 9.10±0.02 min in the second group, and in the control group this index was 8.30±0.02 min; activated partial thromboplastin time (APTT) – was 38.41±0.02 sec in women with CIPIGO on the background of VVSP; 38.11±0.02 sec – in women with CIPIGO without varicose veins of the small pelvis, whereas in the control group it was 36.21±0.01 sec; activated time of recalcification (ART) – was 71.60±0.06 sec and 69.2±0.04 sec in the patients of the first and second groups respectively, against 60.00±0.04 sec in the control group.

The indicator of the prothrombin index was higher in women of the group 1 – 98.41±0.05% and 97.12±0.03% respectively in the second group, compared with the control group – 91.50±0.02%. There was a statistically significant increase in the concentration of fibrinogen both in the first (3.80±0.02 g/l) and in the second group (3.40±0.02 g/l), relative to the control group (2.8±0.04 g/l). A decrease of the protein C level was observed compared with healthy women, in the first group the rate was 145.60±2.4%, in the second group – it was 136.50±2.4%.

In women of the studied groups, a decrease of the percentage of fibrinolytic blood activity was observed. Thus, in the first group this index was 13.80±0.02%, in the second group it was 13.10±0.01%, compared with 15.2±0.03% in the control group women.

It was also considered appropriate for us to estimate the concentration of a specific marker of functional activity of the endothelium – the D-dimer in a blood plasma. The statistically significant increase of the indicators was observed in both research groups: 0.76±0.08 μg/ml in the first group and 0.71±0.02 μg/ml in the second group; while in women of the control group – 0.38±0.02 μg/ml.

Thus, in evaluating of the indicators of the coagulogram in patients of the studied groups, the tendency to hypercoagulation was revealed, as evidenced by an increase of the level of fibrinogen and an increase of the index of phospholipid-dependent coagulation tests. Reduction of the percentage of fibrinolytic blood activity and increase of the concentration of the D-dimer thrombophilic molecular marker in the blood plasma can be considered as activation of intravascular coagulation and the presence of endothelial dysfunction.

Analyzing hemostatic data in the dynamics after the treatment, there was a statistically significant improvement of the blood rheological properties. The decrease of the blood coagulation time was established – 8.4±0.03 min in the first group and 8.2±0.02 sec in the second group. ART after the treatment was in the first group 63.2±0.03 sec, in the second group – it was 61.3±0.02 sec, APTT –36.8±0.02 s and 36.1±0.02 sec respectively. The prothrombin index after the treatment was 93.3±0.02% in the first group and 91.6±0.03% in the second group. Statistically, the fibrinogen concentration index, namely, 2.9±0.01 g/l in women with CIPIGO on the background of VVSP and 2.8±0.03 g/l in women with isolated CIPIGO, was statistically lower. Protein C was 120.4±2.1% and 119.5±2.2%, respectively.

The percentage of fibrinolytic blood activity was significantly higher after the cancellation of the proposed treatment and was 15.9±0.02% in the first group and 15.41±0.04% in the second group. The D-dimmer index was statistically significantly lower and was 0.39±0.02 μg/ml and 0.38±0.02 μg/ml, respectively. Changes of endothelin-1 and prostacyclin after the treatment are shown in the table.

From the performed studies it can be concluded that the ability of endothelial cells to maintain the balance of constric-

Table 1. Indicators of functional activity of the blood serum endothelium in women of the studied groups

Indicators, pg/ml		Groups of women		
		CIPIGO with VVSP n= 68	CIPIGO without VVSP n=52	Control group (n=30)
Endothelin-1	before treatment	4.21±0.07 p<0.001	3.57±0.02 p<0.001	2.81±0.04
	after treatment	2.91±0.02 p<0.05	2.84±0.03 p<0.01	
Prostacyclin	before treatment	184.51±1.15 p<0.001	221.40±2.13 p<0.001	235.31±1.56
	after treatment	227.20±2.01 p<0.01	230.3±1.15 p<0.05	

Note. p – is the reliability of the difference between the norm and the pathology.

tors and dilators in conditions of constant changes in blood flow and blood flow properties is not infinite, and therefore endothelium dysfunction occurs. In this context, obviously, the venous hypertension, blood stasis and ischemia of the vascular wall, which receives nutrients directly from the venous blood, are predominant. Violation of regional blood flow is accompanied by a decrease of oxygen tension in venous blood and endothelial hypoxia. All these processes lead to a violation of the protective properties of the vascular wall, its anticoagulant and anti-inflammatory activity, the regulation of the tone of the vascular wall and the adhesion of the leukocytes.

3. Conclusions

1. Our studies found endothelial dysfunction and violations of the plasma-coagulation linkage of hemostasis in both studied groups.
2. After the performed treatment, the improvement of the functional activity of the endothelium and normalization of the main parameters of the plasma-coagulation linkage of hemostasis were observed.

4. Prospects for further research

To perform an analysis between changes in the indexes of endothelial functional activity and plasma-coagulation link of hemostasis with changes in the hemomicrocirculatory bed of the adventitia of varicose veins of the small pelvis and hemomicrocirculatory bed of the bulbar conjunctiva.

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