

proteolytic activity of blood in case of high level of comorbidity is probably very complex, universal and non-specific, especially in case of the cardiovascular system diseases prevalence. However, it is important that they are integral components of high cardiovascular risk in these patients. In a complex regimen of their treatment in the context of CVR prevention they should be kept in mind as the metabolic basis of a number of disorders and the means of metabolic and rheological correction should be used.

Conclusions

1. The comorbidity occurs in patients with osteoarthritis with age, increase in disease severity and duration mainly due to the cardiovascular system disorders, metabolic syndrome, digestive system diseases and increased levels of cardiovascular and gastrointestinal risks.

2. Age-increasing levels of comorbidity in patients with osteoarthritis are accompanied by significant progressive decrease in fibrinolytic properties of blood, increased levels of fibrinogen and increased blood proteolytic activity.

3. Disorders of proteolysis and fibrinolysis in the blood of this group of patients are one of the pathophysiological components of high cardiovascular risk and vascular-metabolic disorders in different tissues and organs. They should be taken into account in the implementation of preventive measures and as an addition to the used rheological means of metabolic action.

Prospects for further research

Different medication with vascular-metabolic-rheological properties is advisable to be tested to determine criteria and duration of its use in the treatment of patients with OA and high comorbidity.

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Peculiarities of Hemostasis System in Pregnant Women with Fetal Loss Syndrome on the Background of Thrombophilia

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Abstract. The results of studying the status of hemostasis system in pregnant women with fetal loss syndrome and thrombophilia are demonstrated.

The objective of the research was to study the peculiarities of hemostasis system in pregnant women with fetal loss syndrome on the background of thrombophilia.

Materials and methods. There were examined 60 pregnant women with fetal loss syndrome and thrombophilia and 30 healthy pregnant women without aggravated anamnesis. All women underwent examination using clinical and laboratory methods.

Results and discussion. The disorders of the vascular-platelet and coagulation elements of hemostatic process being characterized by hypercoagulation, reduction in natural anticoagulants, intensification of thrombosis processes were determined.

Conclusions. In pregnant women with fetal loss syndrome on the background of thrombophilia disorders of the vascular-thrombocytic and coagulation elements of hemostatic process were observed.

Keywords: pregnancy; hemostasis system; fetal loss syndrome; thrombophilia.

Problem statement and analysis of the recent research

The relevant problem of modern obstetrics is the management of pregnancy in women with fetal loss syndrome. To prevent miscarriage or premature delivery, special importance is given to prenatal observation, timely diagnostics and correction of detected disorders.

According to literature data, 40% of perinatal losses are

associated with the presence of thrombophilia [1, 2]. Pregnancy is a condition that can be called a certain “examination” for the presence of hereditary (genetic) or acquired thrombophilia as it is accompanied by physiological hypercoagulation thereby contributing to the realization of latent thrombophilia not only in the form of thromboses and thromboembolia, but also obstetric complications [3].

The probability of fetal loss or the development of placental insufficiency in women with thrombophilia is very high. This obstetric pathology may be caused by antiphospholipid syndrome, hyperhomocysteinemia, hereditary disorders of hemostasis. The coexistence of these pathological conditions significantly increases the risk of pregnancy complications [4].

The status of hemostasis system determines the course and consequences of pregnancy for both mother and fetus. Lately, peculiar attention has been given to the study of hemostasis system indices as an important component in the development of obstetric complications. Due to the imbalance of procoagulant and anticoagulant mechanisms, thrombophilia may lead not only to the development of thrombosis during pregnancy and postnatal period, but also to different placental vascular complications that may cause disorders of implantation and fetus development [5]. Therefore, the study of hemostasis parameters in pregnant women with thrombophilia is an urgent scientific problem.

The objective of the research was to study the peculiarities of hemostasis system in pregnant women with fetal loss syndrome on the background of thrombophilia.

Materials and methods

There were examined 90 pregnant women who were divided into three groups: Group I consisted of 30 pregnant women with fetal loss syndrome and inborn thrombophilia; Group II consisted of 30 pregnant women with fetal loss syndrome and acquired thrombophilia; Group III (the control group) included 30 healthy pregnant women without aggravated anamnesis.

The diagnosis of fetal loss syndrome was made based on the presence of history of three and more spontaneous miscarriages occurring up to 8 weeks of gestation, and/or at least one pregnancy loss during the period of more than 8 weeks, including stillbirth (babies born dead after 22 weeks of gestation or weighting more than 500 grams) and neonatal death (death of a newborn born after 22 weeks of gestation or weighting more than 500 grams within 7 days after birth). Anatomical, genetic, infectious and hormonal reasons of fetal loss were excluded.

The study of hemostasis system consisted of studying the procoagulant component, namely the activated recalcification time (ART), the partial thromboplastin time (PTT), fibrinogen levels, the prothrombin index (PTI) according to Quick, as well as the thrombocytic component, namely the number of thrombocytes in peripheral blood, and the anticoagulant component, namely, the activity of antithrombin III (AT III). The determination of blood thrombophilic status was based on the detection of thrombophilia marker - D-dimer. The increase in the concentration of D-dimer by more than 1.0 µg/ml indicated the presence of thrombophilia.

The diagnosis of antiphospholipid syndrome (APS) was made in case of increased levels of antiphospholipid antibodies (APA) or lupus anticoagulant and fetal loss syndrome. Laboratory diagnostics of APS was confirmed by APA indices during blood testing.

The results of the research were statistically processed using the Student’s t-test.

Results and discussion

The average age of women of Group I was 31.8±6.0 years; the average age of women of II was 29.6±4.0 years; the average age of women of Group III was 27.4±4.8 years.

The indices of hemostasis system are presented in Table 1. In pregnant women of

all groups, there was observed an increase in the overall coagulation potential since the first trimester as evidenced by the increase in the concentration of the main clot-forming substrate – fibrinogen. Moreover, during the first trimester, this index in pregnant women with thrombophilia (Group I – 4.1±0.4 g/l, Group II – 3.9±0.3 g/l) was significantly higher as compared to the indices of the control group (3.2±0.2 g/l; p<0.05).

During the third trimester and before delivery, there was observed an increase in fibrinogen levels by 1.5 times (Group I – 6.2±0.6 g/l, Group II – 5.8±0.4 g/l) as compared to the results of healthy women (3.8±0.2 g/l; p<0.05).

The level of fibrinogen is one of the most important parameters characterizing the status of hemostasis system. The concentration of fibrinogen in the blood plasma changes dramatically in different pathological conditions. Fibrinogen is involved in the final stage of blood sedimentation. The change in its content in the plasma indicates a disorder of the hemostatic process, especially in case of disseminated intravascular coagulation. The degree of hyperfibrinogenemia indicates the severity of the pathological process. Therefore, the data on the content of this protein in the blood plasma have a prognostic value [1].

There was noted an insignificant increase in the PTI in healthy pregnant women during the third trimester of pregnancy (100.6±3.1%) as compared to the indices of the first and second trimesters (96.1±4.7% and 99.8±2.5%, respectively) which points to the activation of extrinsic coagulation pathway during delivery [7]. The significant increase in the PTI was observed in patients with thrombophilia at all the stages of examination (during the first trimester, the index in Group I was 98.4±2.6%, in Group II, it was 99.5±3.2%; during the second trimester, the index in Group I was 101.7±3.5%, in Group II, it was 102.3±2.3%; during the third trimester, the index in Group I was 105.9±2.6%, in Group II, it was 106.8±2.2%; p<0.05). Changes in the PTI indicated the increased activity of extrinsic coagulation pathway factors.

In healthy pregnant women, the obtained indicators were within the reference range, however, there was a tendency towards their reduction (during the first trimester, the ART was 69.1±1.4 seconds, the APTT was 37.2±1.5 seconds; during the second trimester, the ART was 65.6±1.5 seconds, the APTT was 36.6±1.9 seconds; during the third trimester, the ART was 60.1±1.7 seconds, the APTT was 34.3±1.4 seconds). In pregnant women of both Group I and Group II, there was observed a significant reduction in the aforementioned parameters (p<0.05) indicating the hypercoagulation shift being interpreted as a risk factor for thrombosis. The reduction in the ART index indicated the activation of plasma and thrombocytic factors of blood

Table 1. Indices of hemostasis system during the 1st, 2nd and 3rd trimesters

Index	Group of women n			I			II			III		
	30			30			30			30		
	Trimester			Trimester			Trimester			Trimester		
	1	2	3	1	2	3	1	2	3	1	2	3
PTI, %	98.4±2.6	101.7±3.5	105.9±2.6	99.5±3.2	102.3±2.3	106.8±2.2	96.1±4.7	99.7±2.5	100.6±3.1			
Fibrinogen, g/l	4.1±0.4*	5.1±0.5*	6.2±0.6*	3.9±0.3*	4.7±0.3*	5.8±0.4*	3.2±0.2	3.6±0.3	3.8±0.2			
ART, seconds	63.3±2.1*	62.5±1.8*	51.7±0.8*	62.5±2.1*	60.5±1.7	51.69±1.3*	69.1±1.4	65.6±1.5	60.1±1.7			
APTT, seconds	33.6±1.7*	32.9±1.6*	31.4±1.1*	35.1±1.3*	33.2±2.1*	30.7±1.8*	37.2±1.5	36.6±1.9	34.3±1.4			
Thrombocytes (PLT) x10 ⁹ /l	220.3±10.9	218.1±7.6	209.6±8.3*	230.0±10.5	226.5±11.7	210.1±9.7*	232.1±8.3	238.6±5.7	243.7±9.6			
D-dimer (µg/ml)	1.2±0.1*	1.6±0.3*	2.1±0.4*	1.5±0.3*	1.8±0.2*	2.2±0.1*	0.5±0.4	0.8±0.5	1.1±0.1			
AT III (%)	86.5±4.8*	84.6±3.5*	82.4±4.7*	87.8±3.2*	82.5±5.7*	81.5±7.7*	110.3±7.8	108.6±9.8	105.3±4.8			

Note: * - statistically significant difference as compared to the control group (p<0.05)

coagulation as well.

The indices of platelet count ($\times 10^9/l$) in women of all groups during pregnancy were within normal range. However, it should be noted that before delivery there was a tendency towards their reduction in Group I (209.6 ± 8.3) and II (210.1 ± 9.7) while in Group III (243.7 ± 9.6) there was a tendency towards their increase.

The activation of hemostasis system that leads to the development of thrombosis is accompanied by the appearance of the specific markers in the blood flow which reflect the degree of increase in hemostatic blood potential. In particular, the level of D-dimer indicates the intensity of the processes of thrombogenesis and fibrinolysis. Since the early pregnancy term, the index of D-dimer increases gradually and the highest indices are observed in women with complicated course of pregnancy: preeclampsia, diabetes mellitus, renal diseases etc. [6].

The average concentration of D-dimer in healthy pregnant women was $0.5 \pm 0.4 \mu\text{g/ml}$ during the first trimester; during the second trimester, it was $0.8 \pm 0.5 \mu\text{g/ml}$; during the third trimester, it was $1.1 \pm 0.1 \mu\text{g/ml}$. Pregnancy dynamics showed a significant increase in the level of D-dimer in groups of women with thrombophilia as compared to the indices of healthy pregnant women: during the first trimester, the index of Group I was $1.2 \pm 0.1 \mu\text{g/ml}$, in Group II, it was $1.5 \pm 0.3 \mu\text{g/ml}$; during the second trimester, the index of Group I was $1.6 \pm 0.3 \mu\text{g/ml}$, in Group II, it was $1.8 \pm 0.2 \mu\text{g/ml}$; during the third trimester, the index of Group I was $2.1 \pm 0.4 \mu\text{g/ml}$, in Group II, it was $2.2 \pm 0.1 \mu\text{g/ml}$, ($p < 0.05$).

In both Group I and Group II, changes in the anticoagulant system were observed as well. Since the first trimester, there was observed the reduction in AT III activity in patients with thrombophilia (Group I – $86.5 \pm 4.8\%$, Group II – $87.8 \pm 3.2\%$) as compared to the control group ($110.3 \pm 7.8\%$, $p < 0.05$). According to literature data, the reduction in the level of AT III, in case of systemic inflammation in particular, is associated with increased consumption of anticoagulation factors under conditions of coagulation cascade activation, its destruction under the influence of elastase (the product of activated neutrophils), as well as disturbance of its synthesis [7]. During the second trimester, the activity of AT III was $84.6 \pm 3.5\%$ in Group I and $82.5 \pm 5.7\%$ in Group II, $108.6 \pm 9.8\%$ in the control group, ($p < 0.05$). During the third trimester, the index of AT III activity was $82.4 \pm 4.7\%$ in Group I and $81.5 \pm 7.7\%$ in Group II, $105.3 \pm 4.8\%$ in the control group ($p < 0.05$).

Conclusions

Thus, in pregnant women with fetal loss syndrome on the background of thrombophilia, the disorders of the vascular-platelet and coagulation elements of hemostatic process being characterized by hypercoagulation, reduction in natural anticoagulants (increased levels of fibrinogen, the PTI, decrease in the ART, the APTT, platelet count, AT III activity), intensification of thrombosis processes (increased level of D-dimer) were observed.

Prospects for further research

This study gives the possibility to implement the algorithm for examination of women with a history of fetal loss syndrome and co-existent thrombophilia thereby preventing thrombophilic complications during pregnancy.

Practical recommendations

Based on the results of the research, we propose to include dynamic examination of hemostasis system into the algorithm for management of women with fetal loss syndrome on the background of thrombophilia since the early terms of pregnancy to evaluate thrombophilia activity as well as to predict pregnancy consequences, to prescribe and evaluate the effectiveness of pathogenetic therapy.

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Особливості системи гемостазу у вагітних із синдромом втрати плода на фоні тромбofilії

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Резюме. Вступ. У роботі проведено визначення стану системи гемостазу у вагітних із синдромом втрати плода на фоні тромбofilії.

Метою дослідження є вивчення особливостей системи гемостазу у вагітних із синдромом втрати плода на фоні тромбofilії.

Матеріали і методи дослідження. Обстежено 60 вагітних із синдромом втрати плода на фоні тромбofilії та 30 здорових вагітних без втрат плода в анамнезі. Усіх вагітних обстежували загальноклінічними та лабораторними методами.

Результати дослідження та їх обговорення. Встановлено порушення у судинно-тромбоцитарній та коагуляційній ланках гемостазу, які характеризуються гіперкоагуляцією, зниженням резерву природних антикоагулянтів, інтенсифікацією процесів тромбоутворення.

Висновки. У вагітних із синдромом втрати плода на фоні тромбofilії спостерігаються порушення у судинно-тромбоцитарній та коагуляційній ланках гемостазу.

Ключові слова: вагітність, система гемостазу, синдром втрати плода, тромбofilія.

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Особенности системы гемостаза у беременных с синдромом потери плода на фоне тромбофилии

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Резюме. Вступ. В работе проведено определение состояния системы гемостаза у беременных с синдромом потери плода на фоне тромбофилии.

Целью исследования является изучение особенностей системы гемостаза у беременных с синдромом потери плода на фоне тромбофилии.

Материалы и методы исследования. Обследовано 60 беременных с синдромом потери плода на фоне тромбофилии и 30 здоровых беременных без потерь плода в анамнезе. Всех беременных обследовали общеклиническими и лабораторными методами.

Результаты исследования и их обсуждения. Установлены нарушения в сосудисто-тромбоцитарном и коагуляционном звене гемостаза, которые характеризуются гиперкоагуляцией, снижением резерва естественных антикоагулянтов, интенсификацией процессов тромбообразования.

Выводы. У беременных с синдромом потери плода на фоне тромбофилии наблюдаются нарушения в сосудисто-тромбоцитарном и коагуляционном звене гемостаза.

Ключевые слова: беременность, система гемостаза, синдром потери плода, тромбофилия.

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