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Changes in the hemostasis system developing during pregnancy

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Abstract

The aim of the study was investigation of the hemostasis system in practically healthy pregnant women in the third trimester by using low-frequency vibration piezoelectric hemoviscosymetry (LVPH), comparison of the received indices with the ones of nonpregnant women. The authors have characterized in detail the main indices of hemoviscosymetry associating them with phases of hemocoagulation.

Key words: pregnancy, hemostasis.

The urgency of the problem is conditioned by significant changes in the hemostasis system during pregnancy; they are registered from the 2nd month, progress during prolongation of gestation and are directed at increasing the potential of blood coagulation and are of adaptation character in the physiological course of pregnancy. The interest to hemocoagulation in pregnancy is conditioned by high rate of thromboembolic and hemorrhagic complications in this cohort of women as well as involvement of the blood coagulation system in any critical state arising in obstetric and nonobstetric practice in pregnant women. At present the clinicians have got a lot of methods for investigating the state of the aggregate

blood condition system, however, overwhelming majority of these methods are uninformative and, moreover, giving no notion of the process dynamics. There was developed an apparatus-program complex for investigation of the blood rheological properties ARP-01M “Mednord” in Tomsk (Russia). The table 1 presents a correlation of LVPN indices with the indices of generally accepted laboratory- clinical methods of diagnosis presented by the authors of the method.

Table 1.

Correlation of LVPN indices with the indices of aggregatogram (A), coagulogram (B) and thromboelastogram (C)

A		
ICC	Spontaneous aggregation	0.76
T ₁	Spontaneous aggregation	0.59
ICC	Адp.2.5 mcg/ml	0.66
B		
CTA	TB	0.78
T3	CT	0.86
ICD	APTT	0.56
MA	F	0.67
IRCL	FA	0.83
C		
CTA	K	0.93
BCT	R	0.76
ICD	R	0.64
MA	AM	0.86
IRCL	FA	0.74

The investigation is made at the bedside of the patient. Blood taking is made by the needle of the large diameter (not less than 1 mm) without applying a tourniquet or with a short-term application of the tourniquet. The data obtained by this method cover all phases of the blood coagulation process: from the vasculothrombocytic to fibrinolysis [3, 4, 9].

Materials and methods. There were examined 50 practically healthy pregnant women with 26-30 weeks of gestation on the basis of the women's consultation center N14 of Odessa. The hemostasis system of all women was examined by the LVPN method at the same time of the day using the needle of the large diameter with a short-term application of the tourniquet.

Results and discussion. The data obtained were processed by the standard software package "MedStart" and Microsoft Excel.

M.N.Shpisman, I.I. Tyutrin and coauthors (2012) [] published referent values of the hemostasis indices in nonpregnant women – volunteers obtained by the LVPN method (Tabl.2).

Table 2.

Referent values of the hemostasis indices in nonpregnant women and in physiological pregnancy

Indices	Nonpregnant women	Pregnant women with a physiological course of gestation, M ± m
A0 (rel.u.)	191.00 [147.00; 236.00]	166.242 ± 16.166
A1 (rel.u)	154.50 [107.00; 186.00]	170.545 ± 13.033
T1 (min)	1.30 [0.80; 1.8]	1.381 ± 0.175
ICC (rel. u.)	-18.71 [-33.30; -10.67]	- 18.754 ± 0.94
CTA (rel.u)	30.3 [20.00; 34.48]	82.032 ± 2.4
T3 (min)	7.35 [6.00;14.80]	6.861 ± 0.717
ICD (rel.u)	30.30 [21.42; 36.56]	60.552 ± 4.081
A4 (rel.u)	607.00 [488.00; 689.00]	723.848 ± 26.077
T4 (min)	17.35 [16.00; 24.80]	16.845 ± 0.706
CIP (rel.u)	17.90 [14.70; 23.40]	19.242 ± 1.145
T5 (min)	30.50 [24.40; 38.10]	32.946 ± 1.654
MA (rel.u)	506.50 [422.00; 614.00]	669.091 ± 24.103
ITC (отн.ед.)	16.25 [14.49; 19.92]	26.685 ± 1.157
IRCL (%)	0.76 [-0.74; 3.16]	1.885 ± 0.4

The mean values obtained correlate with the data of changes taking place in the hemostasis system in the normal course of pregnancy [5, 6, 7, 8].

The first phase of thrombogenesis (vascular - thrombocytic) is characterized by indices of hemoviscosimogram A0, A1, T1, ICC. The index A0, which directly depends on the hematocrit value, concentration of the protein fractions and processes of the enzyme cascade of coagulation beginning immediately after blood taking is reduced by 4% in pregnant women with a physiological course of gestation in comparison with healthy nonpregnant women. It is explained by presence of oligocytemic hypervolemia as well as reduced amount of general protein due to hemodilution in the normal course of pregnancy. The indices T1 and ICC reflect the rate and intensity of the contact phase of coagulation and depend on the same characteristics of blood as A0 as well as quantitative and qualitative properties of thrombocytes. As regulation of the adhesive-aggregate function of thrombocytes takes place with the help of thromboxangenerating system of thrombocytes and prostacyclingenerating system of the placenta, the data indices are not practically changed.

The second phase of coagulation is characterized by a number of indices of hemoviscosimogram: CTA, T3, ICD, A4, T4, CIP, MA, T5. While analyzing the indices obtained by the LVPN method, the activation of II phase of hemocoagulation is clearly seen. There is elevation of the CTA index characterizing the rate of rise of thrombin formation and intensity of the proteolytic stage of the clot formation by 64%. It is confirmed by considerable activity increase of most factors of blood coagulation (XII, VIII, IX, X, V, II, XI) and factor activation occurs as a result of proteolysis of one or two specific protein bonds of the molecule with formation of the active center. This index is closely correlates with thrombin time (TT), which tends to decrease during pregnancy due to increased amount of fibrinogen. During physiological pregnancy the activity of VIII, X and XII factors significantly increases but the level of XI factor slightly decreases, which is evidence of activation of the inner way of coagulation. APTT corresponds to the index of hemoviscosimogram of ICD, which significantly

increases during the physiological course of pregnancy. On one hand, accelerated proteolysis and polymerization of the clot results from shortening of T3 and T4 intervals, on the other hand, prolongation of the T5 interval results in slowing down the clot stabilization that in total supports the process of clot formation in the organism of the pregnant woman at the safe level. The state of the fibrinolytic system characterizes the index of intensity of retraction and clot lysis (IRCL), which depends on activity of plasminogen and its activators (tissue, urokinase, kallikrein, XIIa factor). During pregnancy inhibitors of plasminogen activators are produced in the area of the placenta bed: PAI-1 in the endothelium of the vessels, PAI-2 in the placenta thromboplasts causing suppression of fibrinolysis in the physiological course of gestation. Thus, significant decrease of IRCL index is determined in women with the physiological course of pregnancy.

Conclusions.

1. During pregnancy the hemostasis system undergoes significant changes resulting in elevation of the coagulation potential.
2. The application of the new instrumental method of LVPH allows to estimate the whole kinetics of the clot formation, which extremely important for correct and effective diagnosis and treatment. The data obtained are closely correlated with the results of clinical and laboratory methods of investigation.
3. The diagnosis of the smallest changes in the hemostasis system is possible by using this method.
4. The mentioned method widens the diagnostic opportunities in obstetrics, gynecology, anesthesiology and intensive care.

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