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The state of hemostasis in pregnant women with hydramnion

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Abstract

Purpose. To determine the state of various stages of hemostasis in pregnant women with hydramnion as a risk factor for premature detachment of the placenta.

Results. There was investigated the state of hemostasis in pregnant women with hydramnion by low piezoelectric thromboelastography (LPTEG) and standard coagulogram. According to the LPTEG results this group of women was found to have increased plasma coagulation potential manifested in elevated constant thrombin activity (TAC) by 76.8%, the intensity of coagulation drive (ICD) by 74.9%, maximum clot density (MA) by 16.8%, shortening of coagulation time (T3) by 7.8% and inhibition of fibrinolysis manifested by decrease in retraction intensity and clot lysis (RICL) by 67.7% ($p<0.05$).

Conclusions. The state of hemostasis in pregnant women with hydramnion is characterized by increased plasma coagulation and inhibition of fibrinolysis potential that are factors of preparing the woman's body for the upcoming birth to control and minimize blood loss.

Keywords: pregnancy, hydramnion, hemostasis, thromboelastography.

During pregnancy a woman's body undergoes a number of adaptative - adjusting processes, involving many organs and systems. These physiological changes are aimed at ensuring adequate course of the gestational period, fetal growth and development, and preparing the body for childbirth and lactation [1, 4].

The system of hemostatis during pregnancy also undergoes significant changes, which are the body's adaptive response of women to the process of fetal development and a possible blood loss during childbirth. During pregnancy the state of the so-called "physiological hypercoagulation" characterized by a "mild" thrombosis to reduce blood loss during childbirth is formed in women [3].

Laboratory findings of pregnant and non-pregnant women are substantially different, so it is important to determine their significance for the correct interpretation of the results [2].

The Purpose of this study was to determine the state of various stages of hemostasis in pregnant women with hydramnion as a risk factor for premature detachment of the placenta.

Materials and methods. There was studied a group of women in the gestation period of 28-40 weeks with hydramnion as a risk factor for premature placental detachment (study group, n = 40), which was compared with a group of non-pregnant women (n = 36) without concomitant severe chronic diseases. The system of hemostasis was studied by the method of low-frequency piezoelectric thromboelastography (LPTEG) and standard clot tests - coagulograms [2, 5].

Results and discussion. The LPTEG method gave the results, which can characterize the state of the vascular - platelet, coagulation and fibrinolytic links of hemostasis. The LPTEG indices obtained in the study of hemostasis of non-pregnant women and women of the main group are shown in the table 1.

Table 1

Value of thromboelastography indices in the study group and non-pregnant women.

Indices	Non-pregnant women (n = 36), M±m	Study group (n = 40), M ± m
A0, rel.units, initial index of blood aggregation state	211.43±12.71	186.91 ± 15.43
A1, rel.units, amplitude of the contact phase	182.95±13.76	150.27 ±14.97

of coagulation		
T1, min., time of the contact phase of coagulation	1.58±0.11	1.51 ± 0.09
ICC, rel.units, intensity of the contact phase of coagulation	12.29±1.17	14.82 ± 1.52
TAC, rel.units, thrombin activity constant	27.64±4.83	48.86 ±4.56*
T3,min., time of coagulation	7.39±0.21	6.81 ± 0.1*
ICD, rel.units, intensity of coagulation drive	29.83±8.06	52.17 ± 2.15*
A4, rel.units	615.39±47.43	724.63± 38.19
T4,min., time of clot polymerization	17.41±1.38	16.54 ± 2.34
ICP, rel.units, intensity of clot polymerization	17.09±2.21	19.72 ± 3.93
T5,min., time of clot formation	32.40±2.09	36.50 ± 1.53
MA, rel.unit, maximal s clot density	563.26± 29.87	657.98 ± 22.91*
ITC, rel.units, intensity of total coagulation	15.48±2.96	20.84 ± 3.54
RICL, %, retraction intensity and clot lysis	0.96±0.19	0.31 ± 0.23*

Note: *- reliable difference of the mean data by Student's criteria, $p<0.05$ in comparison with non-pregnant women

When comparing the thromboelastogram indices of non-pregnant and pregnant women of the main group there were obtained data that characterize differences in separate links of hemostasis.

The vascular- platelet link of hemostasis is characterized by such factors as the time of the contact phase of coagulation T1 and intensity of the contact phase of coagulation ICC, reflecting the rate (T1) and intensity (ICC) of the contact phase of coagulation and depend on the quantitative and qualitative properties of the platelets and hematocrit value, concentrations of protein fractions and processes of enzymatic coagulation cascade that begins immediately after blood sampling. The pregnant women of the main group compared to non-pregnant women had the index T1 reduced from 1.58 ± 0.11min to 1.51 ± 0.09 min during the study, ICC increased from 12.29 ± 1.17 rel.units to 14.82 ± 1.52 rel.units, but these changes were statistically insignificant ($p>0.05$).

The plasma phase of coagulation is characterized by the following indices of thromboelastogram as constant thrombin activity (TAC), clotting time (T3), the intensity of

coagulation drive (ICD), amplitude of clot polymerization (A4), time of clot polymerization (T4), intensity of clot polymerization (ICP), maximum clot density (MA), the formation of fibrin-platelet coagulation structure (T5), the intensity of total coagulation (ITC).

When comparing indices obtained by the LPTEG method in the main group with that of non-pregnant women there was observed activation of the plasma link of hemocoagulation. This is reflected in statistically reliable ($p<0.05$) changes in such factors as the constant activity of thrombin, coagulation intensity drive, maximum clot density, blood clotting time. The index of constant thrombin activity that characterizes the rate of increasing thrombin formation and intensity of the proteolytic stage of clot formation, statistically reliably increased from 27.64 ± 4.83 rel.units in nonpregnant women to 48.86 ± 4.56 rel.units in the main group ($p<0.05$). This indicates the activation of the external way of blood coagulation. The intensity index of coagulation drive is also statistically significantly increased from 29.83 ± 8.06 rel.units to 52.17 ± 2.15 rel.units. This indicates the activation of the internal way of blood coagulation characterizing integrative pro- and anticoagulant effect on the process (rate) of the blood clot formation. There are also statistically reliable ($p<0.05$) changes in the chronometric index T3 that characterizes the clotting time. It is shortened from 7.39 ± 0.21 min to 6.81 ± 0.1 min, indicating the coagulation acceleration during polymerization of fibrin. The maximum density of the clot MA is statistically reliably ($p<0.05$) increased from 563.26 ± 29.87 rel.units to 657.98 ± 22.91 rel.units, indicating hardening of the blood clot.

There are also changes in the fibrinolytic link of hemostasis of pregnant women, manifested by the index of intensity of retraction and clot lysis, which depends on the activity of plasminogen and its activators (tissue, urokinase, kallikrein, XIIa factor). There is RICL decrease from $0.96 \pm 0.19\%$ in non-pregnant women to $0.31 \pm 0.23\%$ in pregnant women in the control group, and these changes are statistically reliable ($p<0.05$). Reduction of the RICL index shows the inhibition of fibrinolysis in pregnant women, which reduces the rate of the blood clot lysis and is one of the factors in the preparation of the body of a pregnant woman for a possible blood loss during childbirth. These changes in the fibrinolytic activity are related to the functioning of the placenta, which is the source of inhibitors of the tissue plasminogen activator that inhibit fibrinolysis and activity level, which are particularly increased in the third trimester of pregnancy.

Thus, according to the LPTEG results the hemostasis system in pregnant women with hydramnion is characterized by the physiological hypercoagulation state most pronounced in the plasma link of hemostasis and reduction of the fibrinolytic activity. These changes are factors of the hemostasis system preparation for childbirth to reduce blood loss.

The pregnant women of the main group were also examined using standard coagulograms, the results of which are shown in the Table. 2.

Table 2

Coagulogram indices in nonpregnant and women of the main group.

Index	Non-pregnant women, M±м	The main group, M±м
Thrombocytes, g/l	293±27.82	221±26.51
Thrombocyte aggregation with ADP,%	59.23±5.81	60.1±5.36
Time of blood coagulation (Lee-White) (min)	7.08±0.2	6.61±0.12*
Prothrombin index (PI),%	89.24±4.17	105.6±7.02*
International normalized ratio (INR)	1.1±0.06	0.9±0.08*
Activated partial thromboplastin time (APTT), sec	38.74±3.02	29.41±2.82*
Thrombin time (TT), sec	15.31±1.89	15.08±2.71
Fibrinogen, g/l	2.98±0.71	4.82±0.53*
Euglobulin lysis, min	196.59±17.65	261.62±23.24*
Hagemann-dependent fibrinolysis, min	8.76±0.93	11.72±1.08*
Dimers of fibrin (D-dimers), ng/ml	86.52±20.64	487.6±63.18*

*- statistically significant differences between nonpregnant women and women of the main group.

As a result of comparison of coagulograms of non-pregnant women and women of the main group the following data were obtained. The vascular- platelet hemostatic link does not undergo significant changes: platelet count decreases from 293 ± 27.82 g/l in nonpregnant women to 221 ± 26.51 g/l in pregnant women due to oligocythemic hypervolemia; platelet aggregation activity of ADP increases slightly from 59.23 ± 5.81% to 60.1 ± 5.36%, but these changes are statistically insignificant ($p>0.05$).

The plasmic link of hemostasis experiences more pronounced changes, which are as follows. Time of blood coagulation after Lee-White in pregnant women is shortened from 7.08 ± 0.2 min to 6.61 ± 0.12 min, changes are statistically reliable ($p<0.05$). This test is more characteristic of the first phase of coagulation hemostasis - formation of prothrombin. It also determines shortening of the activated partial thromboplastin time from 38.74 ± 3.02 s to 29.41 ± 2.82 s, indicating the increase of internal pro-coagulating factors of hemostasis link and characterizes the activity of factors I, V, VIII, IX, X, XI, XII. These changes are statistically reliable ($p<0.05$). The increased prothrombin index from 89.24 ± 4.17% to 105.6 ± 7.02 % is also statistically reliable ($p<0.05$) indicating increased activity of coagulation factors that are responsible for external way of blood clotting, characterizes the first and second phases of plasma hemostasis and shows the activity of the prothrombin complex (factors II, V, VII, X). The international normalized ratio also characterizes the phase of thrombin formation of plasma hemostasis but it changes slightly - moderately shortened from 1.1 ± 0.06 to 0.9 ± 0.08 ($p<0.05$) in pregnant women with hydramnion.

Thrombin time, indicating the state of the final stage of clotting cascade - conversion of fibrinogen into fibrin under the influence of thrombin in pregnant women in the control group is slightly shortened from 15.31 ± 1.89s to 15.08 ± 2.71 s, and these changes are statistically unreliable ($p>0.05$). The fibrinogen level in the control group is statistically reliably increased from 2.98 ± 0.71 g/l to 4.82 ± 0.53 g/l ($p<0.05$).

The fibrinolytic link of hemostasis also undergoes significant changes. The time of euglobulin lysis is extended from 196.59 ± 17.65 min in nonpregnant women to 261.62 ± 23.24 min in women of the main group ($p<0.05$). The time of Hagemann - dependent fibrinolysis (XIIa dependent lysis) is also extended from 8.76 ± 0.93 min to 11.72 ± 1.08 min, the changes are statistically reliable ($p<0.05$). Inhibition of fibrinolysis is associated with a significant increase in the concentration of inhibitors: inhibitor of plasminogen activator of type 1 (PAI-1) that is released from the endothelial cells, and especially the inhibitor of plasminogen activator of type 2 (PAI-2), which is produced by the placenta. Inhibition of fibrinolysis is the main cause of hemostatic balance displacement toward the hypercoagulation state. The concentration of D - dimer during pregnancy is also increased from 86.52 ± 20.64 ng/ mL to 487.6 ± 63.18 ng/ ml and statistically reliable ($p<0.05$), mainly due to the acceleration of fibrinogen exchange but not to increased fibrinolysis.

Thus, while summarizing the results of the hemostasis study in non-pregnant women compared to pregnant women with hydramnion we can assert unidirectional changes in the hemostatic system during the study by thromboelastography and coagulograms. The

vascular-platelet hemostasis link does not undergo statistically significant changes in the indices in the study by both methods. There is a potential increase in plasma coagulation, resulting, according to the LPTEG in statistically reliable ($p<0.05$) increase in such indices as constants of thrombin activity, intensity of coagulation drive, maximum density of the clot, and shortening of blood coagulation time. Coagulometric studies correlate with LPTEG changes and consist in statistically reliable increase in such indices as activated partial thromboplastin time, prothrombin index, reduction of the international normalized ratio, increased fibrinogen level, shortening of blood coagulation time after Lee-White. There is also suppressed fibrinolysis activity that indicates statistically reliable ($p<0.05$) decrease in intensity of retraction and clot lysis, according to the LPTEG data and is confirmed by extension of time of euglobulin and Hagemann-dependent lysis.

Thus, changes in the hemostatic system of pregnant women with hydramnion are balanced at a new level, due to functioning of the feto-placental complex. Increased plasma coagulation potential and inhibition of fibrinolysis are factors preparing the woman's body for the upcoming birth to control and minimize blood loss.

Conclusions:

1. Increased plasma coagulation potential was established in pregnant women with hydramnion, which was manifested by constant increase in thrombin activity TAC by 76.8%, the intensity of coagulation drive ICD by 74.9%, maximum density of the clot MA by 16.8%, shortening of blood coagulation time T3 by 7.8% and inhibition of fibrinolysis, as evidenced by decrease in intensity of retraction and clot lysis RICL by 67.7% ($p<0.05$). Thus, increased plasma coagulation potential and inhibition of fibrinolysis are factors preparing the woman's body for the upcoming birth to control and minimize blood loss.
2. The method of low-frequency piezoelectric thromboelastography along with standard coagulographic tests can fully and rapidly reproduce the hemostatic state of various hemostatic links.

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