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Research Article

Characteristics of Violations in the Aggregate State of Blood Regulation System of Women with a High Degree Anemia on the Background of Endometrium Hyperplastic Processes

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Abstract
Endometrial hyperplasia is a benign pathology of the uterine mucosa, characterized by certain histological changes, characterized as simple and complex, non-atypical and atypical forms. Hyperplastic processes of endometrium, according to various authors, in the structure of gynecological pathology make up 15 to 40%. Clinically, the endometrial hyperplasia manifest by uterine bleeding. Maternal bleeding that is not susceptible to hormonal, symptomatic, and hemostatic therapy, leads to chronic post-hemorrhagic anemia and is the indication for surgical intervention. Consequently, systemic disorders of the hemostasis parameters on the background of uterine bleeding with endometrial hyperplasia, in particular the regulation of the aggregate state of blood systems, require further research to identify new pathogenetic links and develop correction methods.
Materials and methods. State of platelet-vascular hemostasis was assessed by the percentage of platelets adhesion in the blood and by the index of spontaneous platelet aggregation. Total potential coagulation of blood, plasma fibrinolytic activity, plasminogen potential activity, antiplasmin, fibrinogen in blood plasma, the activity of antithrombin III, the concentration of soluble fibrin monomer complexes in the blood was determined by reagents made by Simko Ltd company (Ukraine). Using the ”Thromboelastohraph ACG” machine we identified parameters of thrombin clotting rate, thromboelastograph K constant, specific platelets convolution constants, α-angle and coagulation composite index.
Results. In women with anemia of III-rd degree against background of the uterine bleeding, at high activity of primary hemostasis, structural and chronometric hypocoagulation develops; it is predefined by the acute decreasing of fibrinogen in the blood. The principal reason of hypofibrinogenaemia is the excessive activating of non-fermentative fibrinolysis. In conclusion, changes in the system of regulation of the aggregate state of blood in women with severe degree of anemia are the display of subclinical inopexia that develops as a result of thrombocytes high functional activity.

Keywords
aggregate state of the blood; endometrial hyperplasia

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Problem statement and analysis of the recent research

Endometrial hyperplasia (EH) - is a benign pathology of the uterine mucosa, characterized by certain histological changes, characterized as simple and complex, non-atypical and atypical forms. Hyperplastic processes of endometrium, according to various authors, in the structure of gynecological pathology make up 15 to 40%.Most cases of endometrial hyperplasia result from high levels of estrogens, combined with insufficient levels of the progesterone-like hormones which ordinarily counteract estrogen's proliferative effects on this tissue. This may occur in a number of settings, including obesity, polycystic ovary syndrome, hyperinsulinemia etc [2, 4, 6].

Clinically, the endometrial hyperplasia is manifested by uterine bleeding [5, 7]. The degree of severity of EH determines the intensity and duration of bleeding, anatomical substrate of this are hyperplastic endometrium, hemorrhages and necrosis of cells. Maternal bleeding that is not susceptible to hormonal, symptomatic, and hemostatic therapy, leads to chronic post-hemorrhagic anemia and is the indication for surgical intervention [1, 3]. Consequently, systemic disorders of the hemostasis parameters on the background of uterine bleeding with endometrial hyperplasia, in particular the regulation of the aggregate state of blood system require further research to identify new pathogenetic links and develop correction methods.

1. Materials and methods

State of platelet-vascular hemostasis was assessed by the percentage of platelets adhesion in the blood and by the index of

spontaneous platelet aggregation. Total potential coagulation of blood, plasma fibrinolytic activity, plasminogen potential activity, antiplasmin, fibrinogen in blood plasma, the activity of antithrombin III, the concentration of soluble fibrin monomer complexes in the blood was determined by reagents made by Simko Ltd company (Ukraine). Using the ≪Tromboelastohraph ACG≫ machine we identified parameters of thrombin clotting rate, tromboelastograph K constant, specific platelets convolution constants, α-angle and coagulation composite index.

2. Results

Women with third degree of anemia combined with uterine bleeding revealed a clear chronometric hypocoagulation: plasma recalcification period was in 1.62 times higher comparing with control data; prothrombin ratio was 1.47 times higher than the control and thrombin clotting time extended relative to the reference level at 54.14% (Table 1). Inhibition of thrombogenesis intensity against internal through prothrombin complex formation was confirmed by a significant increase in activated partial thromboplastin time. The immediate cause of low fibrinogen level in blood plasma in women with anemia III level against background of uterine bleeding was the excessive blood plasma fibrinolytic system activation: total fibrinolytic activity increased by 1.80 times due to a significant increase of the non-enzymatic fibrinolysis intensity, whereas fibrin enzymatic lysis did not differ significantly from the control data.

We should draw attention on blood changes of women with a high degree fibrinolysis products of anemia: soluble fibrin monomer complexes in blood plasma increased by 3.84 times, plasma content of fibrin/fibrinogen degradation products also increased more than 3 times. Otherwise enzymatic fibrinolysis reserves remained: plasminogen potential activity corresponded to the control level and intensity of Hageman-dependent fibrinolysis exceeded the control data.

Women with III anemia degree, suffering from uterine bleeding of various origins, showed a significant thrombinogenesis speed decrease. Thromboelastohraph constant k is almost 2 times higher than the control data. The maximum amplitude of thromboelasthographic curve decreased significantly, indicating a degree of independence between depression of blood clot density and the functional state of platelets. It has been estimated that in women with a high degree of structural anemia hypocoagulation was not accompanied by platelets activity decrease but conversely specific platelet clotting constant decreased.

3. Conclusions

Therefore, changes in fibrinolytic blood potential in women with anemia III degree has a secondary character, due to activation of thrombin- and fibrin-genesis by external way mechanisms. Chronometric hypercoagulation develops as a result of blood coagulation activation by external mechanism of prothrombinase formation, accompanied by a decrease of anticoagulative capacity and a significant increase in adhesional-aggregational properties of platelets.

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Table 1. The condition of blood coagulation and anticoagulation ability of women with uterine bleeding ($x \pm S_x$)

Indicators studied	Control data (n=30)	Anemia of III-rd degree (n=30)
Recalcification period, sec	82.34±4.61	133.42±7.49 p<0.001
Prothrombin time, sec	20.09±0.67	29.55±1.42 p<0.001
Thrombin time, sec	11.04±0.75	15.71±0.95 p<0.001
Activated partial thromboplastin time, sec	33.83±0.96	46.41±3.19 p<0.001
Percentage of adhesive thrombocytes, %	35.44±2.37	71.42±5.18 p<0,001
Index of platelet aggregation spontaneous, units	4.08±0.44	10.21±0.65 p<0.001
Antithrombin III, %	96.74±3.79	62.51±3.79 p<0.001
Activity of the XIII factor, %	101.52±5.26	76.91±3.28 p<0.001
Fibrinogen concentration in blood plasma, g/l	3.91±0.31	2.01±0.26 p<0.001
Total fibrinolytic activity, E440/ml/h	4.52±0.52	8.26±0,72 p<0,001
Non-enzymatic fibrinolysis, E440/ml/h	0.61±0.07	2,92±0.25 p<0.001
Enzymatic fibrinolysis, E440/ml/h	4.01±0.47	4.94±0.57 p>0.001
Antiplasmines, %	101.70±7.44	129.67±7.98 p<0.001
Soluble fibrin monomer complexes, mkg/ml	2.08±0.19	7.99±0.76 p<0.001
Fibrin/fibrinogen degradation products, mkg/ml	1.04±0.08	4,05±0,52 p<0.001
Plasminogen potential activity, min	15.02±2.10	17.80±2.94 p>0.05
Hageman-dependent fibrinolysis, min	15.97±2.96	10.07±1.71 p<0.001

Notes:
p - the degree of probability of difference of indicators in comparison with control;
n - is the number of observations.