HEMORHEOLOGICAL FAILURE IN THE PATHOLOGY OF CARDIO-VASCULAR COMPLICATIONS IN PATIENTS WITH DIABETIC FOOT SYNDROME

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Abstract
The literature that includes the study of cardiovascular complications in patients with diabetic foot syndrome was analyzed. The topicality of this problem is caused by the steady growth of diabetes mellitus morbidity among people. For today there are more than 170 mln people throughout the world with diabetes mellitus, among them 65–80 % have cardiovascular complications (myocardium infarction, acute disorder of brain blood circulation and so on).

It is established for today, that pathogenesis of diabetic foot syndrome is multi-factor one and the development of purulent-necrotic stages of DFS is connected with the combination of different factors, especially microcirculation disorder. In this article we’ll consider the mechanisms of diabetic angiopathy development, the state of platelet-vascular hemostasis link in this category of patients.

Keywords: diabetes mellitus, diabetic foot syndrome, microcirculation disorders, angiopathy, hemostasis disorders, fibrinolytic system.

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1. Introduction
Diabetes mellitus (further DM) is a clinical syndrome of chronic hyperglycemia and glycosuria, caused by insulin deficit that results in metabolism disorder in organs and tissues [1–3].

The diabetes is considered as the real vascular disease because of the frequent clinical manifestations of arterial, cardiac, brain or peripheral complications that appear at the background of glycemic control worsening.

In France the number of patients with DM is near 2,7 mln people, among them 90 % – patients with DM type 2. Near 300 000–500 000 people (10–15 %) with diabetes even do not suspect the presence of this disease. Moreover, the abdominal obesity is occurred in near 10 mln people that is a precondition of DM type 2 development. Cardio-vascular complications are revealed 2,4 times more often in patients with DM. They determine the prognosis of diabetes and favor the decrease of life-span of patients by 8 years for persons in age 55–64 years and by 4 years – for older age groups. In Ukraine the DM prevalence in recent 10 years increased in 1,5 times. In the structure of morbidity DM type 2 dominates and is 80–90 % of the whole population of patients. The most frequent and serious complication of diabetes mellitus is diabetic foot syndrome (DFS) that is revealed in 60–80 % of patients and often results in their invalidism and death [4, 5].

Nearly in 65–80 % of cases the cause of diabetics’ lethality is cardio-vascular complications, especially myocardium infarction (MI), TEPA, acute disorder of brain blood circulation, acute kidney failure. After myocardium revascularization the cardiac events more often take place in patients with DM. The possibility of 9-years survivability after coronary intervention on vessels is 68 % for diabetics and 83,5 % – for ordinary people; as the result of secondary stenosis and aggressive atheromatosis the patients with DM suffer from the repeated MI. The share of patients with diabetes in cardiologic department permanently grows and is more than 33 % of all patients. That is why diabetes is recognized as the important separate risk factor of cardio-vascular diseases formation [6–8].

For today there are more than 170 mln patients with this disease. According to the experts, the number of patients will grow till 2017 to 249 mln and till 2025 – to 300 mln people [9].

The world health organization determined the DM morbidity as global non-infectious epidemic [10].
2. Aim of research

The analysis of accessible information sources about the features of hemostasis system in formation of pathology of cardio-vascular complications in patients with diabetic foot syndrome.

3. Materials of research and their discussion

The development of DFS complication is based first of all on the disorders of hemostasis system, because they precede the other disorders, typical for diabetes mellitus [11].

In the study of development of angiopathy of the lower extremities at DM the more and more importance is given to the changes in blood coagulation system, so the changes in both platelet-vascular hemostasis link and in plasma one are typical for patients with DM that, in its turn, leads to microcirculation disorder [12–14].

Metabolic disorders, growing at DM favor the cellular hypoxia that is a universal activating and injuring factor [15]. That is why the study of vascular-platelet hemostasis state becomes especially topical.

Among the causes of diabetic anginopathies development the leading role is given to the raise of platelets functional activity, which molecular mechanism is explained by accumulation of oxygen free radicals that leads to intensification of peroxide oxidation of the lipids of plasma and cellular membranes [16, 17]. The reflection of this process is the raise of malonic dialdehyde concentration, where it is a final product of reioxide oxidation of lipids at cyclooxygenase cascade of arachidonic acid in platelet membrane of patients with carbohydrate metabolism concentration [3, 18, 19]. The increase of glycogen quantity in cellular cytoplasm, the raise of cytoplasmatic Са+ that induces biosynthesis of thromboxane of blood platelets and raises the aggregation activity of platelets take place in platelets membrane of patients with DM as the result of metabolic disorders [20].

The change of platelet function in patients with DM leads to the decrease of membranes permeability, metabolic processes disorder that alongside with endothelium ability to synthesize anti-aggregation agents raises the risk of vascular complications [21].

According to the modern notions, pathogenesis of DM chronic complications is considered from the position of glucose toxicity theory, according to that, the chronically increased glucose level in blood is a main factor that induces the different biochemical and structural changes in cells and tissues [22].

Taking the view of this theory, the one of main pathogenetic mechanism of diabetic anginopathy at DM type 2 is the changes in the system of hemostasis microcirculation link [23, 24].

The raise of activity of the processes of non-enzymatic glycosilation of proteins and lipoproteins leads to the disorder of the functions of cellular and also basal membranes of vessels. The change of functional activity of the components of vascular wall disturbs the normal interaction between endothelium cells and blood cells that favors the development of hypercoagulatory syndrome, changes the parameters of vascular tonus regulation and as the result leads to the vascular pathology development [23, 24].

The most role in hemocoagulatory processes development in patients with DFS is played by activation of plasma factors, conditioned by the active “fibrinolization” – the process of inflammation and change of hemostasis plasma link at the expanse of expressed hyperfibrinogenemia (fibrinogen concentration raises in 1,5–2 times comparing with organism norm before fibrinolysis system exhaustion) [12, 25, 26]. The combination of these changes with significant activation of XIII factor testifies to the tendency to the most heavy hypercoagulatory changes in patients and is characterized with the high probability of intravascular thrombosis on the background of endothelium injury.

The other leading factor in the development of hemostasis disorders is the change of balance between coagulating and anti-coagulating blood systems that is proved by the essential decrease of antithrombin III activity and acts at microcirculation level [11, 25, 16].

The development of critical ischemia of the lower extremities is mainly connected with vascular factor and thrombophilia, also conditioned by the organism fibrinolization, fibrinolysis inhibition and deficit of activity of the natural anti-coagulation agents that is explained in first turn by heavy metabolic disorders and intoxication [25].

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Despite the proved inclination to the thrombus-creation at DM type I and II, the regularities of changes of hemostasis system indices in the age aspects were not fully studied that complicates the diagnostics of vascular complications. The feature of blood coagulation system in healthy people older than 40 years is inclination to hypercoagulation. The inclination to hypercoagulation that is increased in young age, after 26 years is typical for patients with DM type II [27–31].

N. A. Nitstsa in the work, devoted to the analysis of platelet hemostasis in children with insulin dependent DM, made a conclusion that in children with insulin dependent DM of the different severity and duration of disease, on the background of its compensation or subcompensation, the serious disorders of platelet hemostasis were revealed. These changes take place already at the moment of setting diagnosis and grow at the increase of disease duration that indicates the raise of thrombogenic potential and injury of vascular wall, starting from the disease debut and further increase of vascular changes [30].

The studies, carried out by G. G. Petrik and S. V. Butaev, prove that the gender differences are characterized with more cholesterol concentration in combination with more expressed aggregation activity of platelets at DM type I, with increased fibrinogen concentration at DM type II in women. The essential age differences in metabolism and hemostasis parameters at DM type I and II were not revealed [31].

The described changes in hemostasis system occupy the one of leading places at the development of purulent-necrotic complications of diabetic foot [32].

For today it is established, that DFS pathogenesis is multi-factor one and at the development of DSF purulent-necrotic stage many factors are combined, especially the microcirculation disorders at the foot level [33, 34]. The series of factors take part in the formation of this link of DFS pathogenesis: atherosclerotic injury of great vessels, decrease of collateral blood circulation and reduction of vascular reserve, immune mechanisms, metabolic disorders of basal membrane of capillaries, intensification of adhesive and aggregation properties of platelets and leukocytes, changes of erythrocytes structure and disturbance of hemocoagulatory blood properties [35].

It was proved, that fibrin and fibrinogen concentration in blood plasma and also aggregation properties of platelets are increased in 78 % of patients with DFS [36]. Certainly, it creates conditions for microthromboses in microcirculation channel: the structure of vascular wall is changed, blood flow is slowed, rheological properties of blood are worsened. Normalization of at least one of these factors can rather effectively reduce manifestations of purulent-necrotic process in foot.

Taking into account the fact, that fibrinolytic system of organism is directed on the natural lysis of fibrin, created in the process of thrombus formation, the elaboration of methods of fibrinolytic system correction is topical [37].

The inalienable components of fibrinolytic system that at the normal state provide the permanence of hemostasis and prevent the excessive thrombolysis are inhibitors of enzymes of fibrinolytic system. They include α2-macroglobulin and α1-antitrypsin. The complexes, created by these substances and plasmin, do not cause fibrinogen and fibrin breakdown but are caught by phagocytes of reticuloendothelial system. Just the presence of these compounds in the blood plasma prevents the development of the uniform elements stasis and pathological microthrombosing with the signs of intravascular blood coagulation syndrome. At the same time fibrinolysis inhibitors not only provide elimination of excessive plasmin from the bloodstream but also participate in reparation of tissues in macrophagic reactions [38].

It was revealed that patients with purulent-necrotic forms of DFS on the background of severe intoxication are characterized with significant inhibition of platelets functions. It is manifested from the one side by the decrease of aggregation activity of platelets, from the other one – by the decrease of aggregation speed [25].

Thus, for optimization of the complex treatment of patients with purulent-inflammatory complication of diabetic foot it is expedient to take into account the values of biochemical and immunological blood parameters, to assess the inflammation process activity, the presence of endogenous intoxication, the disorders of platelet-vascular hemostasis system [39–41].
4. Conclusions

On the base of analysis of accessible scientific sources we made a conclusion that the data of hemocoagulation and microcirculation in patients with purulent-necrotic forms of diabetic foot are contradictory and the platelet-vascular hemostasis remains insufficiently studied. Like before the assessment of platelet-vascular hemostasis is carried out using the old, low-informative methods that do not give on-line information about the state of adhesion and aggregation of platelets, the problem about interconnection between platelet-vascular hemostasis with plasma one is not solved that essentially complicates the integral understanding of hemocoagulation in patients with purulent-necrotic complications of diabetic foot and the influence of its disorders on the course of this disease.

It indicates the necessity of complex study of coagulation in perioperative period and differential correction of disorders that is a topical problem of anesthesiology and intensive care.

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