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THE STATE OF THE BLOOD COAGULATION AND ANTI-COAGULATION SYSTEM OF PATIENTS WITH GANGRENE OF THE LOWER EXTREMITIES, CAUSED BY DIABETES MELLITUS COMPLICATED BY SEPSIS

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Abstract: Objective: to study the coagulation and anticoagulation system of blood in diabetes mellitus. Materials and methods: In 109 patients with diabetes mellitus aged 17-78 years (mostly over 35 years old) with varying degrees of severity and duration of the disease, we studied the state of blood coagulation and fibrinolysis activity, the aggregation function of platelets, erythrocytes. The results shown in the table indicate that there is a significant presence of hyperfibrinogenemia in diabetes mellitus, as pointed out by other researchers Conclusions. significant trend towards a decrease in the severity of chronic intravascular microcoagulation in patients with diabetes mellitus against the background of the use of antithrombotic therapy, the absence of side effects with the skillful use of drugs with antiplatelet and anticoagulant effects, allow us to recommend them to be included in the complex treatment of patients with diabetes mellitus.

Keywords: coagulation and anticoagulation system, diabetes, hypercoagulable state, sepsis.

Introducrion. In modern medicine, one of the most difficult and urgent is the problem of diabetes mellitus, due to its significant spread, as well as increased mortality from this disease.

Currently, the issues of the diabetes clinic have been developed in detail, a new classification has been created and metabolic processes have been well studied, much attention has been paid to the treatment of patients, many antidiabetic oral medications, various types of insulin have been created, and unsuccessful attempts at surgical treatment are being made.

Thanks to modern rational therapy of patients with diabetes mellitus, there has been a tendency to decrease the frequency of diabetic coma, but the frequency and mortality from cardiovascular (diabetic micro - and macroangiopathy) and other complications of diabetes mellitus have begun to increase.(5) There is often a combination of diabetes mellitus with ischemic heart disease, which often proceeds atypically and is not diagnosed in a timely manner, at the same time aggravating its course and leading to death. If by now the relationship between atherosclerosis and specific diabetic vascular lesions has been studied in detail, then little has been studied about the condition of the remaining internal organs (lungs, liver, stomach, kidneys, intestines), which, against the background of deep and complex metabolic disorders in diabetes mellitus, are involved in the general pathological process. (8)

In the body, the activator and inhibitory functions of the fibrinolytic system are in dynamic equilibrium. In the constant interaction of the components providing the active phase of fibrinolysis with inhibitors of this process plays an important role. This is one of the principles of the organization of the system - the principle of self-regulation (1).

Under pathological conditions, the interaction between factors leading to blood clotting and fibrinolysis is disrupted. In this case, there may be a threat of thrombosis, thromboembolic complications. In diabetes mellitus, thrombotic and thromboembolic complications are often noted.

A multi-faceted examination of patients with diabetes mellitus made it possible to approach the solution of questions about the peculiarities of violations of the functional state of internal organs and to offer pathogenetically directed therapy.

The purpose of this study: to study the coagulation and anticoagulation system of blood in diabetes mellitus.

Based on the study of the hemostasis system in diabetic patients, most researchers came to the conclusion that they have a hypercoagulable state of blood (7). The study of the coagulation system and fibrinolysis in diabetes mellitus should be given due attention not only from the point of view of timely diagnosis and prevention of their disorders, but also from the standpoint of the possible involvement of hemorheological disorders in the formation and progression of diabetic angiopathy.

Meanwhile, the results of studies of the state of hemostasis in diabetes mellitus are contradictory. The activity of fibrinolysis in this disease has not been studied enough. The practical importance and expediency in diabetes mellitus is acquired by the complexity of studying blood coagulation and fibrinolysis, which will make it possible to determine the ways of rational antithrombotic therapy in diabetic patients, aimed at preventing and treating intravascular thrombosis.

In diabetes mellitus, there is always a state of hypercoagulability in the blood, a significant tendency to hyperaggregation activity of formed elements (platelets, erythrocytes) in the bloodstream (2).

It should be emphasized that classical coagulology failed to give the clinic reliable criteria for thrombogenic danger, especially in the early preclinical stages of its occurrence. This is due to fuzziness, inconstancy, as well as insufficient reliability of changes in general coagulation parameters (Eremin G.F. et al., 1988). According to Z.S. Barkagana et al (1981), the diagnosis of thrombosis, the choice of adequate antithrombotic therapy should be based not on studies of routine coagulology, but on an assessment of the state of critical factors of thrombogenicity: soluble complexes of fibrin monomers (RCMF), antithrombin - III (AT - III), antiplasmin, products fibrin/fibrinogen degradation.

Materials and methods.

In 109 patients with diabetes mellitus aged 17-78 years (mostly over 35 years old) with varying degrees of severity and duration of the disease, we studied the state of blood coagulation and fibrinolysis activity, the aggregation function of platelets, erythrocytes. The results shown in the table indicate that there is a significant presence of hyperfibrinogenemia in diabetes mellitus, as pointed out by other researchers (6). Based on the determination of the level of SCFM in plasma, the intensity of thrombin formation in the blood, which determines fibrin formation and can influence platelet aggregation, was judged. Patients with diabetes mellitus had a significant increase in the concentration of SCFM, especially pronounced in decompensation of metabolic processes, in the presence of clinical signs of diabetic angiopathy, as well as in patients older than 40 years. The latter circumstance, in our opinion, is associated with the presence in this group of patients of clinical signs of atherosclerosis, which, as is known, proceeds with increased activity of blood coagulation. An increase in the amount of SCFM in the blood makes it possible, already at subclinical stages, to judge the activity of thrombin in the bloodstream and latent intravascular thrombus formation. These complexes, which accelerate the conversion of fibrinogen into fibrin, aggravate the state of hypercoagulability and contribute to the spread of thrombotic deposits in the bloodstream (Kovalenko A.N., 1983).

The activity of procoagulant components of hemostasis in patients with diabetes mellitus is evidenced by an increase in the content of plasma coagulation factors V and X, which was also identified by L. I. Knyazeva (1983). It is known that factor V

(proaccelerin), used for the formation of thromboplastin, is involved in the chain of reactions that promote the formation of thrombin. Its level in patients with diabetes mellitus turned out to be significantly increased compared to that in healthy individuals and patients with diabetes mellitus was significantly increased compared to that in healthy individuals and patients with atherosclerosis without signs of diabetes mellitus. Its content correlated with the severity of the disease, the state of compensation of metabolic processes, the presence of vascular changes. The content of factor X (thrombotropin) in the blood serum, a key blood coagulation factor that increases with the severity of diabetes and its decompensation, was also significantly increased. No statistically significant changes in factor II were found (Table 1). Its level did not depend on the clinical manifestations of the disease. It should be assumed that this may be due to the fact that in human blood the physiological concentration of prothrombin (factor II) is almost three times higher than the level of prothrombin required for normal blood clotting (Kudryashev B.A.).

Of practical importance is the study of AT - III in patients with diabetes mellitus, the activity of which is about 80% of the total anticoagulant activity of plasma (Barkagan ZS et al., 1982). It is a physiological inhibitor of hemocoagulation with a universal spectrum of action. A decrease in its activity of less than 85% leads to the appearance of a hypercoagulable state, and less than 40-60% to intravascular thrombosis (Mitreev Yu.G., Spesivtseva V.G., Knyazeva L.I. 1983) in patients with diabetes mellitus found a significant a decrease in its level, which directly correlated with the clinical manifestations of the disease. A particularly low concentration of AT-III (63.2%, see table) was noted in diabetic microangiopathy, which indicates a pronounced activity of the blood coagulation system with a tendency to intravascular thrombosis.

Thus, the data obtained indicate that in diabetes mellitus, pathological intravascular microcoagulation takes place, proceeding with the activation of procoagulant, platelet and erythrocyte hemostasis.

L.I. Knyazeva (1982) conducted a study of the bioelectrical properties of erythrocytes in diabetic patients - their electrokinetic potential and electrophoretic mobility in the bloodstream, which determines their physiological stability in the bloodstream. She found a significant decrease in the zeta potential and electrophoretic mobility of erythrocytes, which clearly correlated with an increase in the severity of the disease, compensation of metabolic processes and the severity of vascular changes. These changes indicated the suspension stability of the blood, the tendency of erythrocytes to aggregate in the bloodstream, which was an expression of the thrombogenic potential of the blood in these patients. Moreover, even the compensation of carbohydrate metabolism in diabetes mellitus with the help of antidiabetic hypoglycemic drugs did not ensure the normal functioning of the hemostasis system in the procoagulant, and especially in the platelet and erythrocyte parts of hemostasis.

Hemocoagulative hemostasis is a relative dynamic balance between procoagulants, plasma fibrinolytic agents, blood cells and the vascular wall. Therefore, to complete the characterization of changes in hemostasis in patients with diabetes mellitus Knyazeva L.I. (1983) determined the activity of fibrinolysis according to its objective criteria for laboratory research - the products of fibrin dehydration and fast-acting plasmin (FDP and FAP).The dataobtained indicate the stability of the content of antiplasmin in the plasma of patients with diabetes mellitus, which did not depend on the severity of the course of the disease, the degree of compensation of metabolic processes, the presence of vascular changes.

The results of the study allow us to conclude that patients with diabetes mellitus have pathologically enhanced chronic intravascular microcoagulation. In diabetes mellitus, it

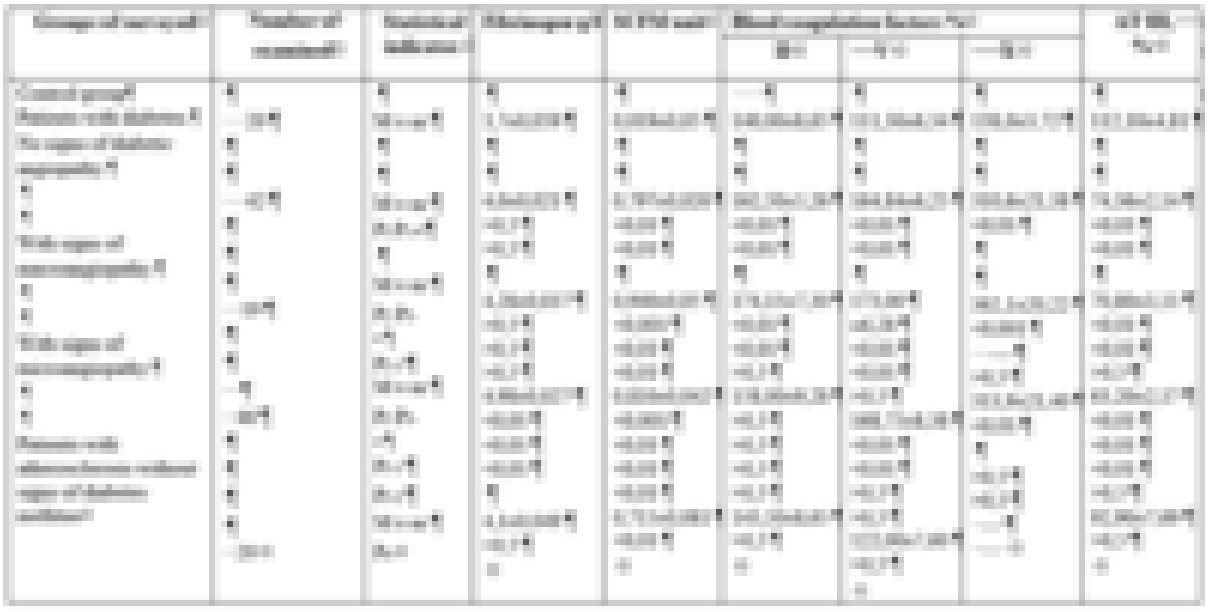
proceeds with the activation of procoagulant (a significant increase in SCFM in the blood plasma, significant consumption of AT-III, hyperfibrinogenemia), platelet and erythrocyte hemostasis (high hyperaggregation activity of platelets, erythrocytes), with a syndrome of high blood viscosity, secondary activation of fibrinolysis (according to fibrinolytic activity of the blood and the level of FDP, FAP).

It should be noted that traditional antidiabetic therapy (insulin, oral antidiabetic agents), as shown by our studies and the work of other authors (3), does not eliminate the threat of thrombosis in diabetes mellitus. Compensation of the disease only slightly reduces the intensity of chronic intravascular microcoagulation of blood, and we are talking mainly about the procoagulant, and not the cellular link of hemostasis (3, 4). This indicates the need to include antithrombotic agents in the complex therapy of patients with diabetes mellitus.

Results and discussion. In the complex therapy of patients with diabetes mellitus, we included the following drugs: diamicron (gliclazide having a hypoglycemic and rheological action), mikristin, acetylsalicylic acid, heparin or fraxiparin.Diamicron was prescribed at a dose determined by the level of blood sugar and urine (average - 40 - 240 mg); mikristin - at the rate of 20 - 30 mg per 1 kg of body weight (an average of 0.5 - 2 tablets), acetylsalicylic acid - 0.25 - 0.75 g, depending on the severity of hemorheological disorders.

Table 1

Indicators of the blood coagulation system in patients with diabetes mellitus depending on the presence of diabetic angiopathy



The course of treatment is up to 15 days. It can be repeated taking into account the state of hemostasis and fibrinolysis. Heparin was prescribed subcutaneously (around the navel) at 5 thousand units (small doses) 4 times a day (after 6 hours) for 10-12 days with gradual withdrawal of the drug, the dose was reduced by 2.5 thousand units in 2-3 day. The repetition of the course was decided individually. Heparin in small doses is well tolerated by patients, we did not observe any complications. The results of treatment with antithrombotic drugs are given in table. 2.

Table 2.

The influence of various types of therapy on the parameters of the blood coagulation system and fibrinolysis in patients with diabetes mellitus.

Indicators	Before treatment	Traditional DM therapy	Heparinotherapy		
			M ± m	P_1	P_2
Number of patients	45	25	20		
SCFM, number	55 0,0997 ± 0,047	40 0,743 ± 0,041	15 0,640 ± 0,016	>0,05	>0,05
Blood coagulation factors, % II	0,879 ± 0,014 165,26 ± 6,28	0,710 ± 0,046 159,86 ± 5,98	0,580 ± 0,014 84,71 ± 5,65	>0,05 <0,01	>0,05 <0,01
V	160,86 ± 5,35 185,65 ± 5,87	148,0 ± 6,28 167,66 ± 7,18	81,33 ± 4,34 102,0 ± 5,65	<0,01 <0,01	<0,01 <0,01
X	169,66 ± 6,25 313,9 ± 20,22	149,44 ± 6,40 307,3 ± 20,71	86,33 ± 4,56 148,5 ± 9,73	<0,01 <0,01	<0,01 <0,01
AT-III, %	362,1 ± 21,40 72,77 ± 3,15	346,36± 22,04 80,67 ± 3,89	168,4 ± 12,3 110,5 ± 3,40	<0,01 <0,01	<0,01 <0,01
	68,18 ± 3,08 183 ± 4,52	78,74 ± 2,90 198 ± 3,97	101,0 ± 7,63 210 ± 4,25	<0,01 >0,5	<0,01 <0,01
General fibrinolytic blood test.	172 ± 4,52 110,16 ± 4,79	184 ± 3,82 102,30 ± 3,29	198 ± 3,74 98,29 ± 3,51	>0,5 >0,5	<0,01 >0,5
FAP, %	105,23 ± 4,15 9,86 ± 0,96	105,59 ± 4,77 7,50 ± 1,04	99,50 ± 3,19 5,30 ± 0,70	>0,5 <0,01	>0,5 >0,5
FDP, mcg/ml	16,66 ± 1,56	11,11 ± 1,56	5,83 ± 0,98	<0,01	<0,01

Note. The numerator shows the data of patients with moderate form of diabetes, the denominator - with severe. P1 - reliability relative to the indicators before treatment, P2 - relative to the indicators of traditional antidiabetic therapy.

The results of antithrombotic therapy (antiplatelet agents, heparin, or their combination) indicate the normalizing effect of these drugs on blood coagulation, fibrinolysis, hemorheological characteristics. When included in the complex therapy for diabetes mellitus, antiplatelet agents showed apositive rheological effect in all patients. Significantly improved indicators of blood and plasma viscosity, aggregation of erythrocytes and platelets. The effect of acetylsalicylic acid, mikristin, diamicron on hemorheology was unidirectional in terms of the final effect. When using each of these drugs, increased blood viscosity in patients with diabetes mellitus decreased by more than 2 times at low shear stresses and by more than 1.5 times at high ones. We did not find significant

differences in the effect of micristin and acetylsalicylic acid on hemorheological parameters, we did not observe any complications.

When treating with small doses of heparin, its normalizing effect on the parameters of the predominantly plasma-coagulation link of hemostasis was noted. Normalization of the level of AT - III was found, that is, the anticoagulant potential of the blood was restored, the content of SCFM in the blood plasma was significantly reduced, the indicators of factors V and X, which have significant thrombogenicity, normalized. There was also a decrease in the concentration of FDP to normal values. All this testifies to the stabilization of blood coagulation and fibrinolysis in diabetic patients. Under the action of heparin, the aggregation function of platelets and erythrocytes improved, and the electrokinetic potential of the blood increased.

Conclusion. Thus, a significant trend towards a decrease in the severity of chronic intravascular microcoagulation in patients with diabetes mellitus against the background of the use of antithrombotic therapy, the absence of side effects with the skillful use of drugs with antiplatelet and anticoagulant effects, allow us to recommend them to be included in the complex treatment of patients with diabetes mellitus.

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