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ANALYSIS OF RHEOGRAMS OF THE BLOOD OF PATIENTS WITH MYOCARDIAL ISCHEMIA AND TYPE-2 DIABETES MELLITUS WITH THE USE OF A NEW MODEL IN THE PROCESS OF PHARMACEUTICAL THERAPY

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Curves of the blood flow in patents with myocardial ischemia (MI), patients with MI and type-2 diabetes mellitus (MI + DM2), and donors have been analyzed using a rheological model proposed by the authors. The influence of the standard antianginal and antiaggregative therapy on the parameters of this model has been investigated. It has been established that the four parameters of the model are reliably changed for both groups of patients as compared to those for the healthy donors, and that, for the donors, there exists a temperature-dependent correlation between the other two parameters of the model that is absent for the patients. A criterion is proposed for estimating a normal blood-flow curve at 25°C. It is shown that the antianginal and antiaggregative therapies do not influence the parameters of the model for the patients studied.

Introduction. In patients with cardiologic pathologies [1, 2] and type-2 diabetes mellitus (DM2) [3], the viscosity of the blood and plasma is increased. In the case of DM2, the deformation ability of the erythrocytes is adversely affected [4] and their aggregation is activated, which should increase the viscosity of the blood at high [5] and low [6] rates of shear. The extracorporeal precipitation of the fibrinogen, low-density lipoproteins, total cholesterin, triglycerides, and α-lipoproteins normalizes the rheology of the blood [7]. A negative correlation between the blood viscosity and the cholesterin of the high-density lipoproteins and a positive correlation between the blood viscosity and the fibrinogen were detected. The blood viscosity correlates positively with the concentration of total protein, triglycerides, and low-density cholesterin [8]. The ratio between the low-density and high-density lipoproteins in the plasma is an important parameter determining cardiovascular risk [9].

However, the corresponding literature data are very contradictory. For example, it is reported in [10] that an increase in the concentration of triglycerides in the plasma enhances the erythrocyte aggregation but does not influence the viscosity of the blood, but the authors of [11] note that this increase leads to an increase in the viscosity of the blood and the plasma.

Since the available data on the rheology of the blood and plasma of patients with the above-indicated diseases are fairly discrepant, the aim of the present work was to investigate the curves of the blood flow in patients with MI, patents with MI + DM2, but donors with the use of a new rheological model proposed by the authors in [12, 13].

Materials and Methods. We investigated the blood of a group of donors (20 persons), a group of patients with MI (33 persons), and a group of patients with MI + DM2 (42 persons). The blood was taken by the standard method from the vein into the anticoagulant ethylenediamine tetraacetate. Cytometric indices (packed cell volume, erythrocyte concentration) were measured using a Hemacomb-10 automated hemoanalyzer. Each patient was subjected to rheological and biochemical measurements (total protein, total cholesterin, triglycerides, β-lipoproteins, α-lipoproteins) before treatment and within two weeks after it. The treatment included the taking of nitrates, inhibitors of the angiotensin-transforming enzyme, β-adrenoblockers, calcium antagonists, antiaggregation agents, anticoagulants, diuretics, and sugar-decreasing preparations (glibenclamide) in combination with a hypolipodemic diet. Large blood and plasma flows with rates of shear ranging from 1.7 to 88 sec^{-1} were measured on a VIR-78 coaxial-cylindrical vis-

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TABLE 1. Statistical Analysis of Parameters of Model (1)

Parameters of model (1)	Before treatment	After treatment	P, paired Student test (comparison before and after treatment)	P, unpaired Student test (comparison with the group of donors before* and after** treatment)
			Donors (20 persons)	
a_1	0.28 ± 0.01	—	—	—
a_2	0.25 ± 0.01	—	—	—
γ_1	3.38 ± 0.23	—	—	—
γ_2	52 ± 10	—	—	—
			MI (33 persons)	
a_1	0.23 ± 0.01	0.23 ± 0.01	0.9474	0.001^*, 0.003^{**}
a_2	0.35 ± 0.01	0.35 ± 0.01	0.7229	$1.15\cdot10^{-8*}$, $1.16\cdot10^{-7**}$
γ_1	3.68 ± 0.35	3.66 ± 0.26	0.5816	0.54^*, 0.47^{**}
γ_2	41 ± 3	43 ± 3	0.4636	0.22^*, 0.33^{**}
			MI + DM2 (42 persons)	
a_1	0.22 ± 0.01	0.24 ± 0.01	0.9355	$1.56\cdot10^{-4*}$, $5.18\cdot10^{-4**}$
a_2	0.37 ± 0.01	0.37 ± 0.01	0.6227	$2.0\cdot10^{-10*}$, 0^{**}
γ_1	3.12 ± 0.30	3.02 ± 0.30	0.7252	0.48^*, 0.60^{**}
γ_2	36 ± 3	37 ± 4	0.7131	0.35^*, 0.36^{**}

cosimeter at a temperature of 25°C. All model calculations and the statistical processing of data were carried out using the software of the graphic SigmaPlot Windows program.

Results and Their Discussion. The curves of large blood flows of patients with MI, patients with MI +DM2, and donors were estimated using an adopted variant of the model proposed by the authors in [12, 13]:

$$\ln(\eta/\eta_{pl}) = A\cdot \mathrm{Hct}^B\,,\quad A = 2.5\exp\left(a_1\exp\left(-\gamma/\gamma_1\right) + a_2\exp\left(-\gamma/\gamma_2\right)\right),\quad B = 1 + \ln(2.5/A)\,. \tag{1}$$

The parameters γ_1 and γ_2 in (1) are independent of the packed cell volume and the rate of shear and can be used for estimating the aggregation forces and the elasticity of the erythrocyte membrane at low and high rates of shear respectively. The parameter γ_1 increases with increase in the aggregation forces, and the parameter γ_2 increases when the membrane elasticity increases [13].

The parameter a_2 is also independent of the hematocrit and the rate of shear, and the parameter a_1 is a sigma function of the hematocrit with a half-inflection point in the region of Hct $\cong$ 0.3. At Hct > 0.35, the parameter a_1 of both the patients and donors is practically independent of the hematocrit. The parameters a_1 and a_2 can serve as estimates of the effective radius of the suspension-particle hydrodynamic resistance at low and high rates of shear. In this case, the parameter a_1 increases with increase in the aggregate sizes transverse to the direction of the flow, and the parameter a_2 increases with decrease in the surface/volume ratio of individual erythrocytes [14]. Our investigations have shown that the average values of the parameters a_1 and a_2 for the erythrocytes of the patients with MI and patients with MI + DM2 statistically reliably differ from those for the donors ($P < 0.001$). The average values of the parameters γ_1 and γ_2 for the erythrocytes of the patients with MI and MI + DM2 are statistically reliably close to those of the donors ($P > 0.05$, see Table 1).

A linear regression was detected for the group of donors (r = 0.96, $P < 0.01$)

$$\gamma_2 = k_1 + k_2\gamma_1\,. \tag{2}$$

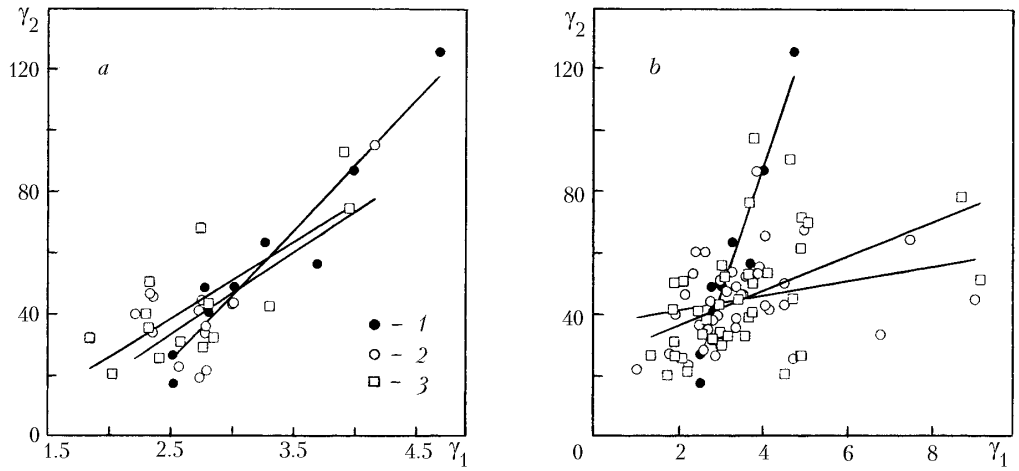

Fig. 1. Correlation dependences of the parameters γ_1 and γ_2 (1) for the group of donors (curve 1, $P < 0.01$) and absence of correlation for patients before (curve 2, $P > 0.05$) and after (curve 3, $P < 0.01$) treatment: a) MI; 2) MI + DM2.

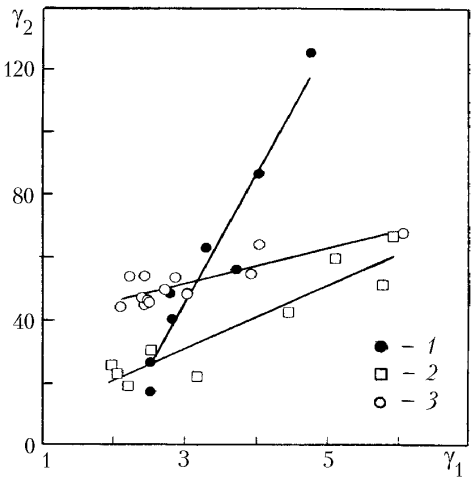

Fig. 2. Correlation dependences of the parameters γ_1 and γ_2 (1) for the group of donors at different temperatures: 1) 25; 2) 30; 3) 35°C.

Such a regression was absent in both groups of patients (Fig. 1). The coefficients k_1 and k_2 in this regression depend on the temperature: $k_1 = -82 \pm 16$ and $k_2 = 43 \pm 5$ at a temperature of 25°C. Thus, the curve of a normal blood flow at 25°C can be estimated:

$$\left|100(\gamma_2 + 82 — 43\gamma_1)/(— 82 + 43\gamma_1)\right| < 20 . \quad (3)$$

We propose to use formula (3) as a criterion for estimating the normal rheological state of the blood.

Our investigations have shown that there are no statistically reliable differences between the average values of the plasma viscosity (at $\gamma = 88$ sec^{-1}) in the patients of both groups and in the donors and of the plasma viscosity in the patients before and after treatment. We also did not detect a statistically reliable correlation between the plasma viscosity and some biochemical parameters (total protein, total cholesterin, triglycerides, α-lipoproteins), which is in contradiction with the majority of literature data, according to which these quantities are related to each other, and is consistent with the data of only a few works, e.g., [10].

The reliable decrease in the parameter a_1 in the patients, as compared to that of the donors, can be due to a decrease in the hydrodynamic resistance of the erythrocytes of the patients at low rates of shear. According to the lit-

erature data [6], the aggregation ability of erythrocytes in the case of the diseases considered is increased, which allows us to suggest that the number and length of the monetary columns is increased as compared to those of the formless erythrocyte aggregates. The reliable increase in the parameter a_2 can be due to an increase in the hydrodynamic resistance of individual erythrocytes at high rates of shear that is equivalent to the decrease in the deformability of the erythrocytes in the case of the indicated diseases, which correlates well with the literature data [4, 5].

Conclusions. The rheological model (formulas (1)) proposed by us in [12, 13] allows one to adequately diagnose the rheological disturbances of the blood and interpret the possible physical reasons for these disturbances at the cell level. It is shown that a characteristic of normal blood is a distinct correlation dependence (2) for the parameters γ_1 and γ_2, which is absent in patients with MI and MI + DM2. It is proposed to estimate the normal relation between the parameters γ_1 and γ_2 at 25°C by formula (3). It is shown that the model parameters a_1 and a_2 are reliably different for both groups of patients and the group of donors, which is due to an increase in the number and size of the monetary columns in the aggregated blood and a deterioration of the deformability (surface/volume ratio) of the erythrocytes in the patients. It should be noted that the rheological model (1) allows one to separate the plasma and erythrocyte components of the blood viscosity. Even though the model parameters of the erythrocyte component were reliably different for the patients and donors, the values of the plasma viscosity were practically the same for all three groups. The standard therapy changed neither plasma viscosity nor the rheological-model parameters.

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NOTATION

Hct, packed cell volume; P, significance level; r, correlation coefficient; $\dot{\gamma}$, rate of shear, $\sec^{-1}$; η, viscosity of a suspension, Pa·sec; η_{pl}, plasma viscosity, Pa·sec; a_1, a_2, γ_1, γ_2, parameters of (1); k_1, k_2, parameters of (2). Subscripts: pl, plasma.

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