MATHEMATICAL MODEL OF TRANSCAPILLARY ALBUMIN EXCHANGE IN PATIENTS WITH MITRAL INCOMPETENCE

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In the modern view transcapillary exchange is an active physiological process maintaining optimal constancy of composition and properties of the internal medium of cells, tissues, and organs [2]. The principal factors determining transcapillary exchange are the capillary hemodynamics, the state of the capillary connective-tissue structures (i.e., permeability in the narrow meaning of the term), and the character of the substance passing from the blood into the tissue and vice versa. It is a very difficult task to take all these factors into account during the analysis of clinical and experimental data.

A combined study of transcapillary exchange processes by the use of mathematical methods and models would seem to be promising. The object of the present investigation was to study changes in hemodynamic characteristics when transcapillary exchange is disturbed in patients with mitral incompetence using a mathematical model of the microhemocirculation developed previously [1].

EXPERIMENTAL METHOD

The method of studying vascular permeability is based on determination of the rate of transport of ^{131}I-labeled albumin in the direction from blood to tissue under clinical conditions. The background radioactivity of the patient's plasma was first determined, and 1 ml of ^{131}I-labeled albumin was then injected intravenously. The decrease in radioactivity was measured after 60, 120, and 180 min in 5-ml samples of blood plasma. A graph of albumin excretion was plotted from the results. The decrement of the fall in concentration was found by Kety's formula:

$$K_{res} = 2.3 \cdot \frac{\log C_1 - \log C_2}{t_2 - t_1},$$

where K_{res} is the resorption constant, proportional to the rate of transport of albumin from the blood into the tissues and C_1 and C_2 denote radioactivity at times t_1 and t_2 respectively.

Observations were made on 27 patients undergoing operations in the Clinic for Cardiac Surgery for mitral incompetence. The patients were divided into two groups: 1) without complications (20 cases) and 2) with postoperative complications (hepatorenal failure, lung pathology, i.e., a foremost place in pathogenesis was occupied by disturbances of the rheologic properties of the blood). The patients' condition was analyzed before and on the first and third days after operation. Parameters of the systemic hemodynamics also were determined: cardiac output (by the dye dilution method), blood viscosity (by means of coaxial cylindrical viscosimeter of Zakharchenko type), and arterial blood pressure.

EXPERIMENTAL RESULTS

The results of investigation of the patients are given in Table 1. To study the characteristics of transcapillary exchange a mathematical model of the capillary blood flow, consisting of equations of the hemodynamics and discontinuity, was used:

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TABLE 1. Results of Clinical Investigation of Patients

Parameter	Period of investigation						Normal (healthy blood donors)
	before operation		after operation				
			first day		third day		
	group 1	group 2	group 1	group 2	group 1	group 2	
Resorption capacity (K_{res})	0,060	0,060	0,086	0,100	0,069	0,050	0,080
Cardiac output (Q_V), liters/min	4,4	4,4	5,4	5,4	5,3	5,3	5,3
Blood viscosity (η_K), cP	5,9	9,2	4,0	5,9	—	—	4,2
Arterial blood pressure (P_A), mm Hg	112/74	100/64	112/67	95/65	—	—	120/75

TABLE 2. Results of Mathematical Modelling of Microcirculation in Patients with Mitral Insufficiency

Parameter	Period of investigation						Normal (healthy blood donors)
	before operation		after operation				
			first day		third day		
	group 1	group 2	group 1	group 2	group 1	group 2	
Effective permeability ($I \times 10^5$), $cm^5 \cdot sec^{-1} \cdot dynes^{-1}$	1,67	1,67	2,39	2,78	1,92	1,39	2,22
Cap. permeability ($H \times 10^{-2}$), $cm^5 \cdot sec^{-1} \cdot dynes^{-1}$	1,27	0,82	1,88	1,27	1,88	1,27	1,79
Blood press. at venous end of network (P_V), mm Hg	20,4	18,8	21,4	20,7	21,4	20,7	21,3
Vel. of blood flow at arterial end of network (Q_A), ml/sec	77,2	67,2	89,0	72,5	88,9	72,1	89,0
Filtration flow (F), ml/sec	0,505	0,488	0,739	0,846	0,594	0,424	0,684
Hydraulic resistance of capillaries (R), dynes·sec·cm^{-5}	78,7	123,0	53,2	78,6	53,2	78,6	56,0

$$\frac{dP_V}{dt} = \frac{E\delta}{\pi n r^3 l}(Q_A - Q_V) - \frac{gE\delta}{r^2}(P_A + P_V) - \frac{dP_A}{dt}, \quad (1)$$

$$\frac{dQ}{dt} = \frac{2\pi n r^2}{\rho l}(P_A - P_V) - \frac{8\eta_k}{\rho r^2}(Q_A + Q_V) - \frac{dQ_V}{dt}, \quad (2)$$

where P_A and P_V are values of the blood pressure at the arterial and venous ends of the capillary network respectively, E the modulus of elasticity, δ the thickness of the wall, r the internal radius, l the length of the capillary, Q_A and Q_B the volume velocity of the blood flow at the arterial and venous ends of the network respectively, g the coefficient of permeability of the wall, ρ the density of the blood, and η_k the viscosity of the blood. Values of Q_V and η_k were determined from the clinical data. It was considered during construction of the model that the network consists of n capillaries with constant geometry, connected together in parallel; the coefficient of permeability is constant.

The steady-state values of parameters of transcapillary exchange were determined by equations obtained from equations (1) and (2):

$$P_V = \frac{P_A(4H - I) - 4Q_V}{4H + I}, \quad (3)$$

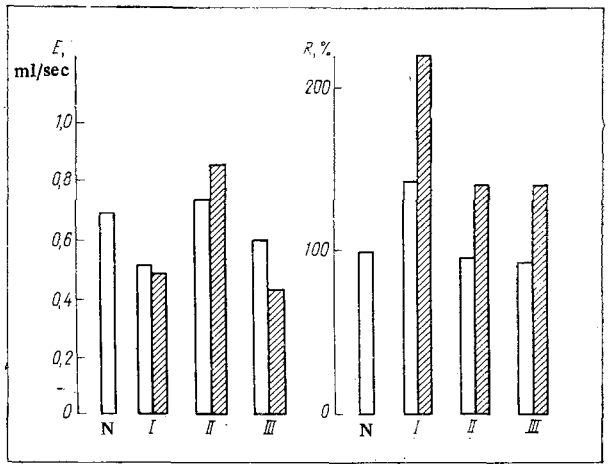

Fig. 1. Time course of changes in filtration flow of albumin and equivalent capillary bed resistance in patients with mitral incompetence. I) Before operation, II) first day after operation, III) third day after operation, N) normal. Unshaded columns — patients of group 1 and healthy subjects; shaded columns — patients of group 2.

$$F = \frac{1}{2} I (P_A + P_V), \tag{4}$$

where $F = Q_A - Q_V$ is the filtration flow, $I = 2\pi ngr\ell$ characterizes the permeability of the walls, and $H = \pi nr^4/(8\eta_k \ell)$ the conductance of the capillaries. The hydraulic resistance of the network is given by: $R = 1/H$.

As a result of the calculations values of the pressure were determined in the venous part of the capillary network, the transcapillary flow of the test substance, the blood flow at the arterial end, and the hydraulic resistance of the network were determined. The resorption constant $I = A \cdot K_{res}$, where A is a constant, was taken as the characteristic of permeability. The calculations were done for capillaries with r = 2.6 μ, t = 750 μ [3, 5], and P_A = 25 mm Hg [4]. The results of the calculations are given in Table 2.

The filtration flow of albumin, calculated by the equations of the model, was lower in patients with mitral incompetence before the operation than in healthy subjects, and the decrease was greater in patients of group 2. This effect was exhibited in conjunction with increased viscosity of the blood.

After operative correction of the vascular defect an increase was observed in the filtration flow of albumin; the flow was significantly higher, moreover, in the patients of group 2. In this case the viscosity of the blood also remained higher. On the third day after the operation a significant decrease in vascular permeability was again recorded in the patients with complications associated with changes in the rheologic properties of the blood.

The peripheral vascular resistance at all periods of observation was higher in the patients of group 2 than in healthy subjects. In the patients of group 1, however, the value of R was 6% below normal on the first and third days after the operation (Fig. 1).

It can thus be concluded that the particular features of the clinical picture of the disease correlate clearly with the parameters of rheology and of the microcirculation. The increase in aggregation of the erythrocytes and in the blood viscosity with the chronic (rheumatic) disease, accompanied by an increase in the peripheral resistance in the pulmonary circulation, may give rise to considerable abnormalities in the postoperative period, with the onset of complications affecting the lungs, liver, and kidneys, and

impairment of the results of surgical treatment. The increase in the transcapillary flow of albumin in the early postoperative period, as it must also be pointed out, is evidently connected with hemodilution during the period of artificial circulation.

LITERATURE CITED

1. O. V. Alekseev, B. I. Balanter, and I. M. Mikhailova, in: Current Problems in General Pathology [in Russian], No. 2, Moscow (1978), pp. 53-56.
2. V. P. Kaznacheeva and A. A. Dzizinskii, The Capillary-Trophic Insufficiency Syndrome [in Russian], Novosibirsk (1975).
3. K. A. Shoshenko, Blood Capillaries [in Russian], Novosibirsk (1975).
4. I. Lundvall, Acta Physiol. Scand., 86, Suppl. No. 379 (1972).
5. E. P. Salathe and K.-N. An, Microvasc., Res., 11, 1 (1976).

ROLE OF LIPID PEROXIDATION IN REGULATION OF LIVER MICROSOMAL MONO-OXYGENASE ACTIVITY OF HOMOIOTHERMIC ANIMALS EXPOSED TO COLD

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The study of the specific manifestations of long-term cold stress has shown that the pattern of function of the microsomal mono-oxygenase system, responsible not only for metabolic transformation of xenobiotics (drugs, toxins), but also for synthesis and oxidation of certain important endogenous biologically active compounds (steroid hormones, catecholamines, protaglandins), is the least studied component in the formation of the general adaptation syndrome. In investigations devoted to this problem no attempt has been made to analyze the mechanisms of regulation of the liver mono-oxygenase activity in the adapted organism [8]. Yet we know that an inseparable component against whose background adaptive reactions take place is activation of lipid peroxidation (LPO) in different organs and tissues [1, 3, 5].

The object of this investigation was to study the character of the mutual influence of two processes coupled in the system of microsomal oxidation, namely LPO and biotransformation of xenobiotics, during prolonged exposure to severe cold.

EXPERIMENTAL METHOD

Experiments were carried out on 40 male Wistar rats weighing 150-200 g. The animals were exposed to continuous cooling (excluding during meals) in a thermal chamber at −7°C for eight days. Liver microsomes were isolated by differential centrifugation. Aniline, 3,4-benzypyrene, and aminopyrine were used as substrates for microsomal mono-oxygenases. The rate of p-hydroxylation of aniline and of N-demethylation of aminopyrine [6] and the maximal velocity of the 3,4-benzypyrene-hydroxylase reaction [13] in a modification of the

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