HEMODYNAMICS OF THE TRANSPLANTED RAT HEART

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UDC 616.12-089.843-092.9-089.168-07: 616.1-008.1

KEY WORDS: hemodynamics, transplantation of the heart.

Surgical aspects of heterotopic transplantation of the heart in rats have been sufficiently well analyzed and discussed [1]. However, no studies of the hemodynamics of the transplanted heart could be found in the accessible literature. The aim of this investigation was to study hemodynamic parameters of models of intraperitoneal transplantation of the heart and heart-lung preparation of rats.

EXPERIMENTAL METHOD

Male Wistar rats were used. The heart was transplanted into the peritoneal cavity in two versions. In version I an end-to-side anastomosis was formed between the aorta and pulmonary artery of the graft and the abdominal aorta and caudal vena cava of the recipient, respectively. In version II the heart was transplanted together with the lungs or lobes of the lung in a heart-lung preparation, by anastomosis of its aorta end-to-side with the recipient's abdominal aorta. Full details of the surgical technique of intraperitoneal transplantation of the heart were given by the writers previously [2]. On the day of investigation, under pentobarbital anesthesia (40 mg/kg, intraperitoneally) the recipient's left ventricle was catheterized through the right carotid artery (under control of the pressure curve) and the abdominal aorta was catheterized through the left femoral artery. Laparotomy was performed. The transplanted heart was removed and its left ventricle catheterized. The aortic and intraventricular catheters were connected to CP-01 electromanometers (CTC, USA). The pressure in the recipient's aorta, the blood pressure in the left ventricle of the graft and of the recipient, and the maximal rate of rise of pressure in the left ventricle dp/dt_{max}, and the heart rate were recorded on an automatic writer ("Graphtec," Japan). The cardiac output, coronary blood flow, and coronary resistance were determined by the use of labeled microspheres [6], in the modification in [3]. Plastic microspheres 15 μm in diameter, labeled with Sc-46 (NEN, USA) were used. About 100,000 microspheres were injected into the recipient's left ventricle. To determine cardiac output, simultaneously with injection of microspheres, blood was collected from the femoral artery by means of an automatic infuser. All measurements of the number of microspheres were made on a "Compugamma 1282" gamma-counter ("KLB-Wallac, Finland). Cardiac output, coronary blood flow, and coronary resistance were calculated by the following equations:

$$CO/Cr = Mi/Ms,$$

whence

$$CO = Cr \times Mi/Ms,$$

where CO denotes the cardiac output, Cr the rate of collection of the control blood sample, Mi the number of microspheres injected, and Ms the number of microspheres in the control blood sample.

$$BF/Cr = Mt/Ms,$$

Department of Cardiovascular Surgery and Laboratory of Experimental Pharmacology, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR I. A. Ashmarin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 110, No. 12, pp. 586-588, December, 1990. Original article submitted April 23, 1990.

0007-4888/90/0012-1625$12.50

TABLE 1. Hemodynamic Parameters of Recipient's (R) and Transplanted (T) Heart in the Late Stages

Rat No.	Time after transplantation, days	P_{lv}, mm Hg, T	a	dp/dt_{max}, mm Hg		Cf, ml/min/g		Coronary resistance, mm Hg/ml/min/g		Recipient's cardiac output, ml/min	HR, min^{-1}	
				T	R	T	R	T	R		T	R
1	40	140/15	155/0	5000	7500	1,66	3,71	80,27	35,83	110,98	300	400
2	45	150/5	150/0	5000	7500	3,99	14,51	23,46	6,45	144,20	280	360
3	30	55/10	90/8	1200	3000	2,23	7,13	29,12	9,12	105,90	240	280
4	165	90/5	135/0	2500	3500	0,85	3,94	99,89	21,55	125,90	290	400
5	260	80/25	100/25	2500	2500	1,62	10,95	63,10	9,36	164,00	270	390
6	20	80/25	130/4	1250	5000	1,03	5,77	84,98	15,17	71,14	250	380
7	18	100/7	110/2	3000	8500	4,43	7,83	24,81	14,04	108,48	300	380
8	25	135/5	135/0	7000	10 000	3,11	6,33	34,52	16,98	143,74	220	360
9	14	75/0	80/0	2500	3100	2,34	7,83	32,11	9,58	58,18	300	340
10	17	120/0	135/0	6000	5000	5,45	5,83	19,71	18,43	150,10	300	420
11	7	160/25	105/0	5000	6750	1,27	2,49	75,00	38,09	91,32	300	430
12	25	115/20	120/0	2700	7500	1,38	3,00	74,00	34,17	93,36	280	390
13	8	130/25	115/0	5700	5750						290	400
14	11	105/7	70/0	2500	4500						250	380
$M \pm m$	49±20 / 11±3	112±9 / 2,8±1,9	116±7 ±509	3704 ±637	5721 −0,45	2,45 ±1,38	6,61	53,41 ±8,68	19,06 ±3,36	105±10	276 ±7	379 ±10
p			<0,05			<0,05		<0,01			<0,001	

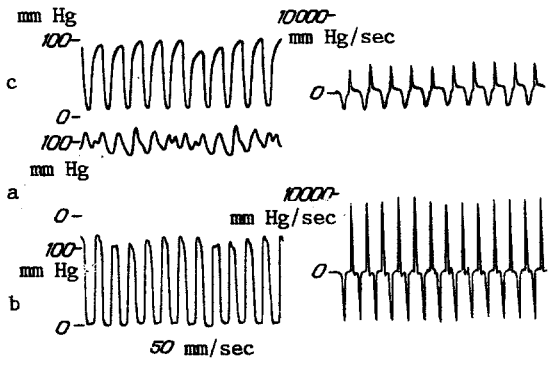

Fig. 1

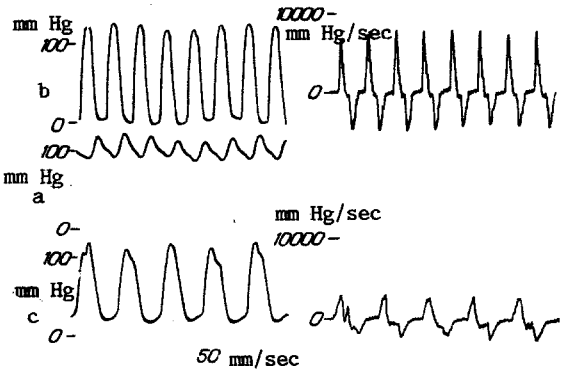

Fig. 2

Fig. 1. Pressure in recipient's aorta (a), pressure in left ventricle, and dp/dt_{max} of recipient (b) and graft (c) after transplantation of heart with lobes of the lung. 18th Day after operation.

Fig. 2. Recipient's intra-aortic pressure (a), pressure in left ventricle, and dp/dt_{max} of recipient (b) and graft (c) after transplantation of heart on two anastomoses. 25th Day after operation.

whence

$$BF = Cr \times Mt/Ms,$$

where BF denotes the blood flow in the transplant (coronary blood flow), Mt the number of microspheres in the transplant, Cr the rate of collection of the control blood sample, and Ms the number of microspheres in the control blood sample.

$$R = Pa/Cf,$$

where R denotes the resistance of the coronary bed, Pa the pressure in the recipient's aorta, and Cf the coronary blood flow.

The data were processed on a "Labtam 3015" computer (Australia). Student's t test for paired samples was used.

EXPERIMENTAL RESULTS

Altogether 14 animals were investigated. The results and times of determination of the hemodynamic parameters are given in Table 1. Transplantation of the heart on two anastomoses was performed on the animals whose serial numbers were 1, 2, 12, and 13; the heart was transplanted in conjunction with the lungs or lobes of the lung on one anastomosis in the remaining animals. A low systolic pressure in the left ventricle of the transplanted heart, together with high diastolic pressure was evidence of failure of the heart and weakening of the contractile function of the myocardium. This was the picture observed in three rats (Nos. 3, 5, and 6; in one of them, moreover, considerable ECG changes also were observed. The average values of systolic pressure in the left ventricle (PLV) of the graft and recipient were about equal, namely 112 ± 9 and 116 ± 7 mm Hg, respectively.

If cardiac function after transplantation together with the lungs or lobes of the lung was satisfactory, the systolic pressure developed by the left ventricle was high, and ejection waves of the graft were recorded on the curve of intra-aortic pressure of the recipient (Fig. 1). This ejection consisted mainly of coronary venous blood which, in this version of transplantation, returned along the vessels of the transplanted lung into the left ventricle of the graft, and was expelled by the ventricle into the recipient's aorta. A different picture was observed when the heart was transplanted into the peritoneal cavity on two anastomoses, when the coronary venous blood was expelled in the recipient's caudal vena cava. Even if the contractile function of the transplanted heart was undisturbed and there were no signs of heart failure, virtually no ejection waves of the graft were present on the intra-aortic pressure curve of the recipient (Fig. 2). The reason is that the volume of blood in the left ventricle of the graft was so small that it could not be reflected in the recipient's intra-aortic pressure. This is actually blood flowing into the left ventricle along the vessels of Thebesius, the volume of which amounts to 10-15% of the coronary blood flow [8]. The maximal rate of rise of the pressure in the left ventricle of the transplanted heart was slower than that of the recipient in nearly all cases. Only in one case, in a rat studied on the 17th day after transplantation of the heart together with lobes of the lung did it exceed this parameter of the recipient.

Significant differences also were found in the resistance of the coronary bed and the coronary blood flow. The coronary resistance of the graft was about 3 times greater than that of the recipient. The coronary blood flow in the graft was reduced by more than half compared with the recipient's heart. Regression analysis showed that the coronary blood flow and coronary resistance of the graft are independent of the times of transplantation. The coefficient of correlation in the case of the coronary blood flow was —0.326, whereas for the coronary resistance it was 0.355.

Reduction of the coronary blood flow in the transplanted heart is in agreement with data in [4], when the kinetics of radioactive thallium-201 was studied in the myocardium of the rat heart transplanted into the neck. These workers showed that primary accumulation of the isotope in the myocardium of the graft, giving an indirect idea of the coronary blood flow, was 60% of that in the recipient's myocardium.

These changes in the coronary blood flow and coronary resistance may be the result of a combination of factors: absence of pumping function of the graft, its total denervation, the nonphysiological circulation due to complex interaction between phases of cardiac activity of recipient and graft. Gregg and co-workers [5], for instance, showed on a model of surgical denervation of the heart that the denervated heart functions at a lower metabolic level than the heart with a normal innervation. Under these circumstances the coronary blood flow in the experimental dogs, both at rest and during physical work, was less by half than in control dogs.

Arteriosclerosis of the coronary, developing after allografting of the heart, does not occur after isografting. The role of this factor in the increase in coronary resistance and decrease in the coronary blood flow after transplantation of the heart into the peritoneal cavity in inbred rats can therefore be regarded as minimal.

Thus after intraperitoneal transplantation of the heart in rats, irrespective of the time after transplantation the hemodynamics of the graft undergoes significant changes in the form of weakening of myocardial contractility and reduction of the coronary blood flow and an increase in coronary resistance.

LITERATURE CITED

1. R. S. Akchurin and V. Yu. Khalatov, Khirurgiya, No. 6, 140 (1989).
2. R. S. Akchurin, V. Yu. Khalatov, and A. A. Shiryaev, Byull. Vses. Kardiol. Nauch. Tsent., No. 1, 88 (1989).
3. O. S. Medvedev, A. N. Murashev, F. E. Meertsuk, and S. F. Dugin, Fiziol. Zh. SSSR, **7**, No. 2, 253 (1986).
4. J. H. Barak, P. J. La Raica, C. A. Boucher, et al., Transplantation, **45**, No. 4, 687 (1988).

5. D. E. Gregg, E. M. Khoure, D. E. Donald, et al., Circulat. Res., **31**, No. 2, 129 (1972).
6. M. A. Heymann, B. D. Payne, J. I. E. Hoffman, and A. M. Rudolf, Cardiovasc. Dis., **20**, No. 1, 55 (1977).
7. K. G. Lurie, M. E. Billingham, S. W. Jamieson, et al., Transplantation, **31**, No. 1, 41 (1981).
8. H. E. Morgan, J. R. Neely, and Y. Kira, Basic Res. Cardiol., **79**, No. 3, 292 (1984).

ACTIVITY OF SOME ENZYMES OF CARBOHYDRATE METABOLISM IN THE LYMPH DURING A FEBRILE REACTION

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UDC 616.4-008.831:577.152.412]-02:612.57

KEY WORDS: febrile reaction, lymph, lactate dehydrogenase, alcolase.

Much research has been devoted to the study of changes in enzyme activity in the tissues and peripheral blood during the febrile reaction (FR). However, the character and direction of changes in individual enzymes in the lymph have not yet been reflected in the literature. It can be tentatively suggested that disturbances of enzyme activity of individual organs and tissues in pathological processes will be exhibited in the outflowing lymph earlier than in the blood, for enzymes, being high-molecular-weight compounds, can pass from intercellular connective-tissue spaces at their site of release into the general circulation only after they have undergone resorption from lymphatic capillaries.

For this reason we undertook a comparative study of activity of aldolase and lactate dehydrogenase (LDH) and its isozymes in the lymph and blood during the course of FR of varied duration.

EXPERIMENTAL METHOD

Experiments were carried out on 63 chinchilla rabbits weighing from 2.5 to 4.2 kg. FR was produced by intravenous injection of pyrogenal by the method described previously [7]. Animals receiving injections of pyrogen-free physiological saline, made up in bidistilled water, were used as the control. Lymph was obtained from the thoracic lymph duct (TLD) at the point where it empties into the venous angle, and blood for investigation was taken from the femoral vein. Activity of aldolase [2, 11] and LDH [9, 13] and its isozymes [8] was determined in the lymph and blood at intervals during FR of varied duration. The experimental results were subjected to statistical analysis. After the experiment the animals were killed by injection of a lethal dose of general anesthetic.

EXPERIMENTAL RESULTS

It will be clear from Tables 1 and 2 that total LDH activity in lymph from TLD was 1.6 times higher, and aldolase activity 1.5 times lower than in the blood serum.

Irrespective of the duration of FR, it was accompanied by marked activation of the enzymes tested in the body fluids. For instance, in the stage of elevation of the body temperature (2.5-3 h after the beginning of pyrogenal injection) an increase was observed in LDH activity in both lymph and blood. Activity of all the isozymes also increased, although this was more marked relatively in the case of LDH_4 and LDH_5 (by 3-4 times). In the stage of falling temperature, LDH activity in the biological fluids continued to remain high.

Department of Pathology with Pharmacotherapy Course, S. V. Kurashov Kazan' Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. D. Ado.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 110, No. 12, pp. 589-590, December, 1990. Original article submitted June 6, 1990.

 0007-4888/90/0012-1628$12.50