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LEFT VENTRICULAR PUMPING FUNCTION AND CONTRACTILITY CHANGES AFTER MYOCARDIAL ISCHEMIA EVOKED BY CORONARY ARTERIAL EMBOLIZATION BY MICROSPHERES IN ANESTHETIZED RATS

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KEY WORDS: coronary vessels; embolization; myocardial ischemia; microspheres; contractility; pumping function of the heart

Microspheres inserted through a catheter into one coronary artery without thoracotomy are being used on an ever increasing scale in recent years to create a model of myocardial ischemia [4-7]. However, research of this kind has been undertaken only on large animals, such as dogs or pigs, mainly because of the difficulty of catheterizing single coronary arteries in small animals. This paper describes a relatively simple method of inducing a measured degree of embolization of the coronary vessels by means of microspheres in anesthetized rats and gives the results of the study of the effect of measured myocardial ischemia on the pumping function of the heart.

EXPERIMENTAL METHOD

Under pentobarbital anesthesia (40 mg/kg) catheters were inserted into the abdominal aorta of Wistar rats through the femoral artery and into the left ventricle through the right carotid artery. Measured embolization of the coronary vessels was produced with the aid of

TABLE 1. Basic Parameters of BP and of Left Ventricular Function in Control Rats (n = 6) and in Rats with Embolization of the Coronary Vessels (n = 16)

Parameter	Control group	Experimental group
Average BP, mm Hg	117±9	108±4
P_s of LV, mm Hg	135±7	134±4
EDP of LV, mm Hg	3,8±0,9	5,0±0,5
dP/dt_{max}, mm Hg/sec	7625±1284	6974±282
$dP/dt_{max}/P$ (1/sec)	55,5±7,9	51,6±1,5

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TABLE 2. Maximal Pressure in Left Ventricle (P_{max}) and First Derivative of Intraventricular Pressure (dP/dt_{max}) during Occlusion of Ascending Aorta in Control Rats (n = 6) and Rats with Embolization of the Coronary Vessels (n = 16)

Parameter	Control group		Experimental group	
	1st occlusion	6th occlusion	1st occlusion	6th occlusion
P_{max}, mm Hg	255±16	255±11	263±5	174±8*, **
dP/dt_{max} mm Hg/sec	10 583±1 261	10 208±1 058	11 086±322	5 624±408*, **

Legend. *p < 0.05) Relative to 1st occlusion (experimental group); **p < 0.05) compaared with control group.

microspheres 15 μ in diameter, which were injected into the left ventricle in a dose of 100,000-200,000 during compression of the ascending aorta for 10 sec. In the experiments of series I the microspheres were injected 4 times at intervals of 10 min (2nd, 3rd, 4th, and 5th occlusions). The 1st and 6th occlusions were controls. The left ventricular pressure was recorded by means of a CP-01 electromanometer (Century Technology Co., USA). The ascending aorta was occluded as follows. The arch of the aorta was compressed against the spine by means of a special L-shaped probe, inserted into the thorax by puncture in the 3rd right intercostal space, without opening the chest [2]. The contractile function of the left ventricle was assessed by measuring the maximal systolic pressure (P_{max}) developed by the left ventricle and the maximal rate of rise of the intraventricular pressure (dP/dt_{max}) during occlusion of the ascending aorta [3]. Rats of the control group underwent six occlusions of the aorta without injection of microspheres.

Curves of arterial and left-ventricular pressure were analyzed by "Labtam 3015" computer, by means of a program which enabled the numerical values of the average arterial pressure (BP), systolic pressure (P_s), and end-diastolic pressure (EDP) in the left ventricle (LV), the maximal rate of rise of the pressure in LV (dP/dt_{max}), and the contractility index ($dP/dt_{max}/P$) to be determined for each cardiac cycle. The results were subjected to statistical analysis by Student's paired and unpaired t test.

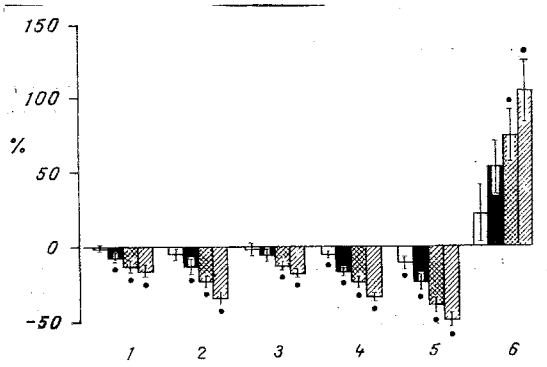

Fig. 1. Changes in basic and maximal contractility of left ventricle (during compression of aorta) after measured coronary embolization. Abscissa: 1) P_s (basic), 2) dP/dt (basic), 3) dP/dt/P (basic), 4) P_{max} (occlusion), 5) dP/dt_{max} (occlusion), 6) EDP (basic); ordinate, changes relative to initial level (%). Unshaded columns — changes after 1st embolization (in left ventricle there are 52,000 microspheres/g); columns shaded black — after 2nd embolization (105,000 microspheres/g in left ventricle); cross-hatched columns — after 3rd embolization (145,000 microspheres/g in left ventricle); obliquely shaded columns — after 4th embolization (178,000 microspheres/g in left ventricle). *p < 0.05 compared with initial values.

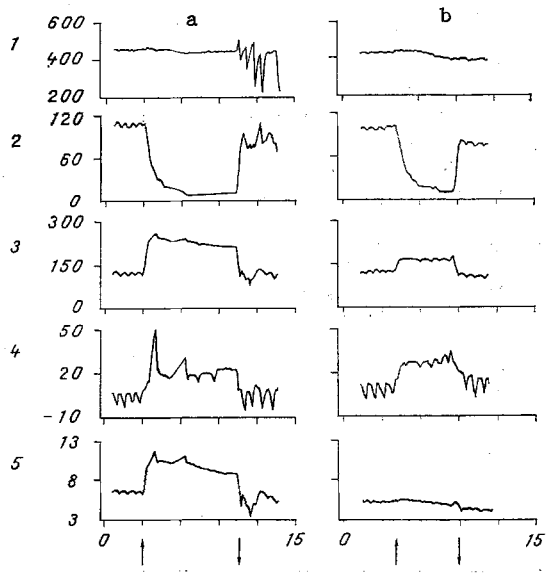

Fig. 2. Changes in left ventricular function BP, and heart rate (HR) in response to occlusion of ascending aorta before (a) and after (b) embolization of coronary vessels by microspheres. Arrows indicate period of occlusion of ascending aorta. Abscissa, time, sec; ordinate: 1) HR (beats/min), 2) HP (in mm Hg), 3) P_S (in mm Hg), 4) EDP (in mm Hg), 5) dP/dt_{max} (× 1000/sec).

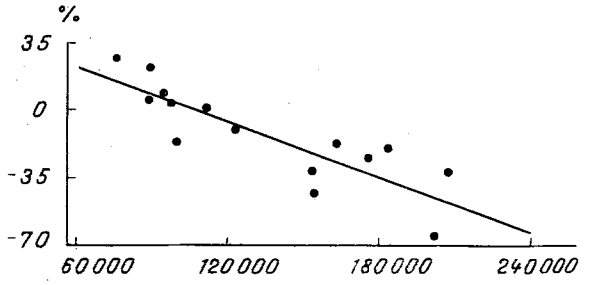

Fig. 3. Dependence of changes in cardiac output (in % of initial value) on number of microspheres entering left ventricle during embolization. Abscissa, number of microspheres, in thousands; ordinate, %.

EXPERIMENTAL RESULTS

Basic parameters of left ventricular function in the control and experimental animals with embolization of the coronary vessels are shown in Tables 1 and 2. Six occlusions of the ascending aorta, each for 10 sec, were not accompanied by any changes in the basic parameters of left ventricular contractility or changes in the response to compression of the aorta, in the control animals. During measured embolization of the coronary vessels a progressive, dose-dependent fall of systolic pressure in the left ventricle and in the contractility index was found (Fig. 1), together with a rise of the EDP in LV. A significant fall of the basic values of the parameters of LV function was discovered after the 2nd or 3rd embolization. Typical changes in the response of LV to short-term occlusion of the aorta before and after fourfold embolization of the coronary vessels are illustrated in Fig. 2. A small but significant fall of P_{max} during occlusion of the aorta was found even after the first embolization. In the experiments of series II the effect of coronary embolization

on the pumping function of the heart was studied. Dependence of changes in the cardiac index on the number of microspheres immobilized in the left ventricular myocardium is shown in Fig. 3. A significant decrease of the cardiac index was observed only after about 150,000 microspheres/g had entered LV. In this series of investigations strong correlation was not found between the decrease in basic contractility of LV and the number of microspheres deposited in LV ($r = 0.31$), which can be explained by the action of regulatory mechanisms, on account of which this parameter can remain unchanged even in the presence of relatively large lesions of LV. It was shown, for instance, that the basic hemodynamic parameters are reduced in rats with chronic myocardial infarction if weight of the infarcted zone of the myocardium exceeds 46% of the weight of the left ventricle [8]. Meanwhile relatively strong correlation was found between changes in the contractility index and changes in the cardiac index.

The results show that the model described above can be used to induce measured ischemization of the myocardium in small animals, so that it can be used to study the pathophysiology of acute myocardial ischemia and, for example, to study the relationship between changes in myocardial contractility and the pumping function of the heart, and also for the screening of new therapeutic substances for the treatment of this pathology.

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PHARMACOLOGICAL AND HYPOTHERMIC SUPPORT FOR EXPERIMENTAL DRY HEART OPERATIONS

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The method of no-perfusion hypothermic protection of the patient against hypoxia during operations on the dry heart has already proved its worth in clinical practice. A combination of pharmacological and hypothermic support enables the circulation to be arrested for 30 min or longer, thus providing conditions for the correction of complex heart defects [2]. However, improvement of the method cannot be achieved without an experimental model enabling the various aspects of hypothermia to be studied.

Most experimental investigations of the heart during hypothermia have been carried out on the isolated organ, a heart-lung preparation [3, 4, 8, 12], or an animals cooled with the aid of an artificial circulation apparatus [10, 11]. There have been only a few investigations

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