MYOCARDIAL INFARCATION IN RATS: RIGHT VENTRICULAR HYPERTROPHY AS A CRITERION OF POSTINFARCTION LEFT VENTRICULAR FAILURE

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KEY WORDS: myocardial infarcation; heart failure; right ventricular hypertrophy; antioxidant dibunol

The development of experimental myocardial infarction (MI) in rats is accompanied by an increase in weight of the heart, mainly on account of the right ventricle (RV), whereas the weight of the left ventricle (LV) of the heart does not change significantly [8-10]. The aim of this investigation was to study correlation between the disturbance of myocardial contractility of LV and the development of hypertrophy of RV in rats with occlusion of the coronary artery. The cardiodynamics of animals with MI was corrected by the use of dibunol (ionol), which prevents depression of contractility in experimental myocardial ischemia [5] and improves the parameters of myocardial contractility in patients with MI [2].

EXPERIMENTAL METHOD

Experiments were carried out on 112 male Wistar rats weighing 220-300 g. MI was induced by high ligation of the anterior descending branch of the left coronary artery [3]. The animals were killed on the 3rd, 7th, 15th, and 30th days after occlusion of the coronary artery, the infarct was measured [10], and RV and the free wall of LV with the ventricular septum were weighed separately. The ventricular index (VI) was determined as the ratio of the weight of RV to the weight of LV [6]. The index of right ventricular hypertrophy was an increase of VI by more than 3σ compared with intact rats [7]. In experiments on animals with MI of 30 days' duration, the contractility of LV was determined in some rats in a state of relative rest, after injection of noradrenalin hydrotartrate (1 μg/kg, intravenously) and on the creation of the maximal resistance load by compressing the aorta for 30 sec. The function tests were carried out under pentobarbital anesthesia (40 mg/kg, intraperitoneally), with an open chest and artifical ventilation. The systolic and end-diastolic pressure (SP and EDP) in LV, and its maximal rate of rise ($+dp/dt_{max}$) and fall ($-dp/dt_{max}$) were recorded.

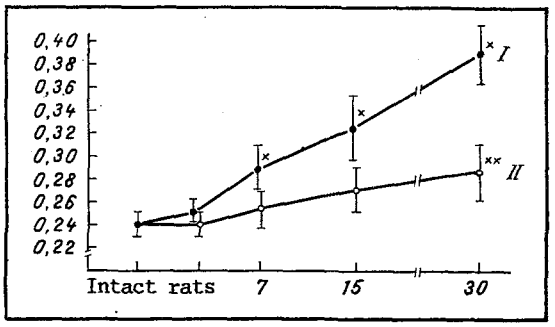

Fig. 1. Time course of VI during development of MI in rats. Abscissa, time after induction of experimental MI, days; ordinate, VI, relative units. I) Control animals with MI; II) MI + dibunol (30 mg/kg). *$p < 0.05$ compared with intact rats, **$p < 0.05$ compared with control at same time of investigation.

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TABLE 1. Contractile Function of LV of Rats on 30th Day of MI at Rest and during Maximal Loading by Compression of Aorta (M ± m)

Parameter	Series of animals	Stage of experiment		
		relative rest	maximal value during aortic compression	25 sec of aortic compression
SP, mm Hg	I	121,2±3,9	248,2±2,4	216,5±6,0
	IIA	68,8±4,0	142,7±7,7	129,2±11,2
	IIB	92,5±6,5*	195,3±9,6*	165,7±6,5*
	III	88,6±4,0*	186,6±10,1*	177,0±6,4*
EDP, mm Hg	I	7,8±0,4	—	30,0±1,9
	IIA	20,4±4,8	—	44,3±5,4
	IIB	7,6±0,4*	—	40,1±2,7
	III	7,6±0,9*	—	46,9±7,2
$+dp/dt_{max}$, mm Hg/sec	I	3548±160	8846±429	5645±404
	IIA	2124±127	4620±319	2935±328
	IIB	3036±166*	6366±655*	4236±304*
	III	3107±164*	5981±843	4596±411*
$-dp/dt_{max}$, mm Hg/sec	I	2426±80	4075±147	2845±150
	IIA	1264±103	1976±156	1591±181
	IIB	1774±129*	2730±100*	2171±145*
	III	1720±89*	2419±183	2052±125*

Legend. I) Intact animals (n = 12); IIA) control animals with hypertrophy of RV h (n = 16); IIB) control animals without hypertrophy of RV(n = 6): III) animals receiving dibunol in a dose of 30 mg/kg (n = 8); *$P_{IIB,III-IIA} < 0.05$.

There were three series of experiments: I) intact animals, II) control animals with simulation of MI, III) animals receiving daily intraperitoneal injections of dibunol in a dose of 30 mg/kg after induction of experimental MI. The results were subjection to statistical analysis by the usual methods [7].

EXPERIMENTAL RESULTS

The development of MI in rats of the control series was accompanied by a statistically significant increase in VI, which was most marked in the group of animals with MI of 30 days' duration (Fig. 1). On the 30th day of MI hypertrophy of RV was observed in 12 of the 20 rats (subgroup IIA), in which VI was 0.50 ± 0.03 (0.24 ± 0.01 in intact animals; $p < 0.001$). The remaining eight animals of this series did not develop hypertrophy of RV (subgroup IIB), as shown by the closely similar values of VI in this subgroup (0.25 ± 0.01) to those of intact rats.

The size of the infarct in rats of the control series on the 30th day varied from 7.6 to 58.6% (mean 37.6 ± 3.4%) of the size of LV. In the subgroup with hypertrophy of RV the size of the zone of myocardial necrosis (45.9 ± 2.4%) was significantly greater ($p < 0.01$) than in the animals without hypertrophy of RV (28.3 ± 4.6%); positive correlation was observed between the size of the focus of necrosis and the value of VI ($r = 0.73$, $p < 0.01$; Fig. 2).

In the control series of experiments, on the 30th day reduction of the force and velocity of contraction of the heart muscle was observed compared with intact animals both at rest and during loading tests. Depression of myocardial contractility under these circumstances was much more marked in rats with hypertrophy of RV. For instance, in rats with hypertrophy of RV in the initial state reduction of SP, $+dp/dt_{max}$, and $-dp/dt_{max}$ by 30-40% was observed and EDP was 3 times higher than in rats without hypertrophy of RV (Table 1). Evidence of marked depression of the contractile function of LV in rats with hypertrophy of RV was given by the time course of the contractility parameters during loading tests. For instance, after injection of noradrenalin into rats with hypertrophy of RV, there was a less abrupt rise of SP, $+dp/dt_{max}$, and $-dp/dt_{max}$ (by 26.6 ± 6.6, 24.4 ± 5.7, and 28.1 ± 8.5%, respectively) than in animals without hypertrophy (by 40.6 ± 5.9, 32.7 ± 7.6, and 33.7 ± 6.6% respectively). During creation of the maximal load on the heart by compression of

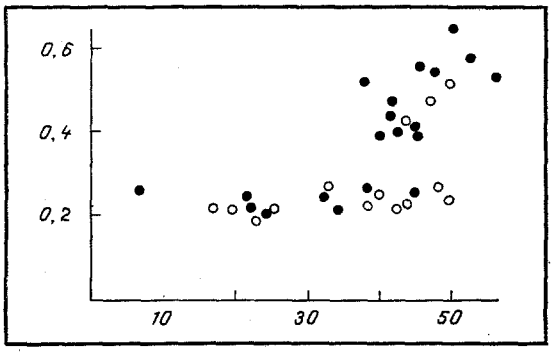

Fig. 2. Relationship between size of myocardial infarct and VI on 30th day of MI. Abscissa, size of infarct, % of size of LV; ordinate, VI, relative units. Here and in Fig. 3, filled circles indicate control animals with MI, empty circles indicate receiving dibunol in a dose of 30 mg/kg after induction of experimental MI.

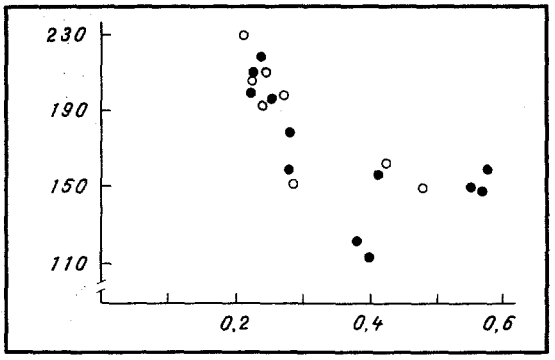

Fig. 3. Relationship between VI and maximal developed SP in LV during aortic compression in rats. Abscissa, VI, relative units; ordinate, SP, mm Hg.

than in animals without hypertrophy; negative correlation was observed in this case between the value of VI and the maximal developed SP in LV ($r = -0.67$, $p < 0.02$; Fig. 3).

On the 30th day of MI marked evidence of heart failure was obtained in the rats with hypertrophy of RV: reduction of the force and velocity of contraction of the left ventricular myocardium, an increase of EDP in LV [1, 4], reduction of the compensatory powers of the myocardium [4] and of its sensitivity to the inotropic action of catecholamines [11].

Hypertrophy of RV is thus an indicator of postinfarction left ventricular failure associated with depression of the pumping function of LV and the development of pulmonary hypertension. The absence of any marked depression of myocardial contractility in rats with MI without hypertrophy of RV confirms this conclusion. Further evidence in the same direction is given by the results of experiments with dibunol, in which, although the zone of necrosis was the same size as in the control series on the 30th day of MI (37.2 ± 2.5%), no marked reduction of contractility of LV compared with control rats with hypertrophy of RV (subgroup IIA) was observed either in the initial state or during function tests (Table 1). Under these circumstances VI on the 30th day of MI in the experiments with dibunol was lower than in the control (Fig. 1), whereas hypertrophy of RV was observed in only three of the 14 rats ($p < 0.05$ compared with the control series). It will be noted that among animals in which the focus of necrosis exceeded 37.4% in size (the threshold of development of hypertrophy of RV in the present experiments), hypertropy of RV was observed in 12 of the 14 rats of the control series and in three of the nine animals in the experiments with dibunol (Fig. 2).

Improvement of contractility of the intact myocardium, observed in the experiments with dibunol, when the focus of necrosis was the same size as in the control series, prevents the

development of postinfarction heart failure and hypertrophy of RV. Consequently, the development of right ventricular hypertrophy depends not only on the size of the infarct, but also on the functional state of the residual left ventricular myocardium.

LITERATURE CITED

1. Yu. V. Belov and B. V. Shabalkin, Kardiologiya, No. 7, 18 (1985).
2. A. P. Golikov, V. Yu. Polumiskov, A. A. Berestov, and V. A. Ryabinin, Kardiologiya, No. 1, 15 (1984).
3. A. Kh. Kogan, Modeling of Myocardial Infarction [in Russian], Moscow (1979).
4. F. Z. Meerson, Adaptation, Disadaptation, and Failure of the Heart [in Russian], Moscow (1978).
5. F. Z. Meerson, L. M. Belkina, A. A. Ugolev, et al., Kardiologiya, No. 10, 81 (1980).
6. L. M. Nepomnyashchikh, E. L. Lushnikova, and G. I. Nepomnyashchikh, Morphometry and Stereology of Hypertrophy of the Heart [in Russian], Novosibirsk (1986).
7. I. V. Polyakov and N. S. Sokolova, A Practical Aid to Medical Statistics [in Russian], Leningrad (1975).
8. W. Hort, S. de Canalis, and H. Just, Arch. Kreisl.-Forsch., 44, 288 (1964).
9. T. D. Norman and C. R. Coers, Arch. Pathol., 69, 181 (1960).
10. M. A. Pfeffer, J. M. Pfeffer, M. C. Fishbein, et al., Circulat. Res., 44, 503 (1979).
11. J. A. Thomas and B. H. Marks, Am. J. Cardiol., 41, 233 (1978).

ELECTRICAL ACTIVITY OF THE HEART DURING ANTI-ISCHEMIC PROTECTION OF THE MYOCARDIUM

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About 50 methods and modifications of cardioplegia have been suggested to protect the myocardium against ischemia during open heart operations [11], for many investigations have shown that prolonged ischemia of the heart without special protection gives rise to irreversible changes in it. The effectiveness of cardioplegia is assessed on the basis of the results of clinical, biochemical, electrophysiological, functional, and morphological investigations [1, 3, 7, 9, 10, 12-15].

The aim of this investigation was to determine to what extent the effectiveness of cardioplegia can be judged from the electrical activity (EA) of the heart, and how its parameters may be analyzed.

EXPERIMENTAL METHOD

Three series of experiments were carried out on 54 mongrel dogs. Animals weighing 4-10 kg served as heart donors, dogs weighing from 18 to 30 kg as perfusion donors. Trimeperidine (7.0 mg/kg), droperidol (0.5 mg/kg), and atropine (0.2 mg/kg) were injected intramuscularly. The operations were performed under intravenous general anesthesia (pentobarbital, 25-30 mg/kg) with artificial ventilation of the lungs.

In series I (nine experiments) a heart-lung preparation was isolated from the heart donor, the ascending aorta was cannulated, and a high-potassium (25 meq/liter) cardioplegic

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