Prevention of Ischemic Disturbances of Contractile Function of Isolated Heart by Short-Term Total Ischemia Episodes

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Short-term total ischemia episodes restrict the drop in the force and rate of contractions of isolated rat heart during long-term reperfusion period after long-term ischemia.

Key Words: *ischemia; reperfusion; contractile function of the heart*

Effective restoration of contractile function of the heart subjected to long-term ischemia and hypothermia is a principal problem of cardiosurgery, in particular, of heart transplantation [1].

It was reported that preliminary short-term ischemia can restrict [3,5,8,9] or aggravate [4] ischemia-induced damage to the heart. Mechanisms of these effects remain unclear. The aim of the present study was to elucidate the effect of preliminary short-term episodes of total ischemia on the contractility of isolated heart subjected to long-term ischemia-reperfusion.

MATERIALS AND METHODS

Experiments were carried out on 20 male Wistar rats weighing 250-300 g. The thorax was opened under Thiopental narcosis (50 mg/kg), and the heart was removed. After a short-term arrest in a cooled solution, the heart was perfused by Langendorff [6] with Krebs—Henseleit solution saturated with O_2 (95%) and CO_2 (5%). Perfusion pressure was 60 mm Hg, and temperature of the perfusate was 37°C. Electrogram and force of heart contractions were recorded using a photoelectric isometric transducer connected to the heart apex through a rigid thread. After a 15-min perfusion, a 0-2-g load was applied and maintained to the end of the experiment.

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In the control series, the hearts were perfused for 50 min, and then the supplying tube was clamped for 30 min for modeling total normothermal ischemia. In the experimental series, rat hearts after a 15-min perfusion were subjected three times to short-term total ischemia and reperfusion and then to 30-min total ischemia, which was started on minute 50 of the experiment. The duration of short-term ischemia was determined in each individual experiment as the interval from the beginning of ischemia to the end of the rapid decrease in the contraction strength (2-3 min). The period of restoration of perfusion pressure between the successive episodes of short-term ischemia was twice as long as the preceding short-term ischemia period.

The tension, contraction strength, and velocity parameters were calculated.

RESULTS

In the control series, long-term (50 min) perfusion led to a 30% decrease in the force of contractions of isolated hearts ($p<0.01$), while after three brief periods of ischemia and reperfusion the force of contraction remained unchanged. Other parameters of cardiac contractile function changed analogously (Table 1).

Such a dynamics of the key parameters of cardiac contractility in the control series apparently resulted from inadequate perfusion conditions. In this

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TABLE 1. Effect of Ischemia Preconditioning on Parameters of Contractile Strength Curve under Conditions of Postischemic Reperfusion (n=10)

Parameter	Control			Preconditioning		
	initial	before ischemia	after reperfusion	initial	before ischemia	after reperfusion
Maximum force of contraction, g	6.9±0.4	4.9±0.2	1.6±0.3	6.0±0.5	6.6±0.4*	3.5±0.7*
%		70±7	23±5		110±4**	58±3*
Mean force of contraction, g	3.4±0.3	1.5±0.3	0.7±0.1	2.3±0.4	2.8±0.4*	1.4±0.2*
Value of the first derivative of contraction curve, $\times 10^2$ g/sec:						
maximum	45.4±4.2	23.7±5.6	8.2±1.3	34.6±5.4	40.6±5.3*	19.4±3.6**
%		47±.7	20±5		108±14*	50±8*
minimal	49.4±2.3	21.4±2.7	8.4±1.7	31.7±5.1	42.7±5.9*	20.6±4.0**
%		50±6	19±5		104±11**	65±21*
Second derivative, $\times 10^4$ g/sec^2:						
first maximum	24.1±2.5	11.9±2.1	5.2±1.2	20.4±2.8	22.3±1.2**	11.5±2.2**
minimum	19.9±1.2	9.3±1.7	3.9±0.9	13.2±1.6	20.8±4.2	8.1±1.5**
second maximum	17.7±1.0	8.7±1.0	4.1±1.3	13.4±1.2	22.1±6.4	6.7±1.4
Index of contraction[1]	655±26	546±61	468±89	649±51	729±52*	731±43*
Index of relaxation[2]	721±21	664±72	469±89	597±60	735±66	777±254
Time interval[3], $\times 10^{-3}$	12.7±0.7	14.0±0.8	34.0±12.7	13.7±0.7	12.3±0.8	14.6±1.0
%		107±21	271±93		89±6*	114±11**

Note. *p<0.05, **p<0.01 in comparison with the control. Percentage was calculated with respect to the initial values. [1]Ratio of maximum value of the first derivative to maximal force of contraction. [2]Ratio of minimal value of the first derivative to maximum force of contraction. [3]Between the first ECG R wave and the first maximum of the second derivative within one cycle of contraction and relaxation.

case, three short-term ischemia periods had a protective effect due to activation of well-known endogenous protective mechanisms [2].

This protective effect was also observed after long-term total ischemia: in experimental group the decrease in contraction force and velocity parameters was much less pronounced: by 36-44% *vs.* 77-83% in the control group.

These findings are consistent with the data obtained by others under similar experimental conditions. The absence of protective effect of brief ischemia periods reported by some researchers can be attributed to substantial differences in experimental conditions. For instance, the duration of short-term episodes of total ischemia in different studies varied from 2 to 5 min, their number varied from 3 to 6, and the duration of reperfusion 2- to 5-fold exceeded the duration of ischemic exposure [3,5,8,9].

The restriction of ischemic damage to the myocardium in experimental series may be due to higher stability of cardiomyocyte membranes, ionic transport systems, and contractile function. This assumption is confirmed by the observation that preconditioning of the heart by repeated short-term ischemia elevates the content of unsaturated fatty acids in the plasma membrane phospholipids [3] and prevents a decrease in creatine phosphate and adenine nucleotides during long-term ischemia [9].

Thus, short-term ischemia-reperfusion periods reproduced according to the above-described schedule considerably restrict the disturbances of contraction and relaxation of perfused myocardium both subjected and not subjected to subsequent sustained ischemia.

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