The results also deserve attention from the general biological point of view: The first phase, in which LPO is inhibited, is the stage of mobilization of protective mechanisms and activation of antistressor systems; the second phase develops as a result of overcoming of the activity of the antistressor system due to the continued exposure to stress.

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EFFECT OF DIFFERENT REPERFUSION SCHEDULES ON RESTORATION OF MYOCARDIAL CONTRACTILITY AFTER TOTAL ISCHEMIA

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KEY WORDS: heart; ischemia; reperfusion; contractility.

Reperfusion of the ischemic myocardium often causes additional disturbances of its structure and metabolism [6, 10] accompanied by arrhythmias, the development of contracture, and incomplete recovery of its contractile function (CF) [7, 9, 11]. Excessive reoxygenation of the myocardium and accumulation of intracellular calcium [4] play an important role in the onset and development of reperfusion disturbances, and for that reason the use of antioxidants [7], of Ca^{++}-antagonists [8, 13], and of reperfusion hemodilution [12] diminishes the damaging action of reperfusion. These data suggest that delayed recovery of CF of the ischemic myocardium, determining the intensity of energy expenditure in the initial period of reperfusion, may improve the restoration of CF at the end of reperfusion. In this investigation energy expenditure in the initial period of reperfusion was reduced by the use of a reperfusion solution with modified ionic composition or the initial rate of perfusion was limited.

EXPERIMENTAL METHOD

Experiments were carried out on guinea pigs weighing 200-300 g, anesthetized with urethane (1.25-1.50 g/kg). The isolated hearts were perfused in the retrograde direction through

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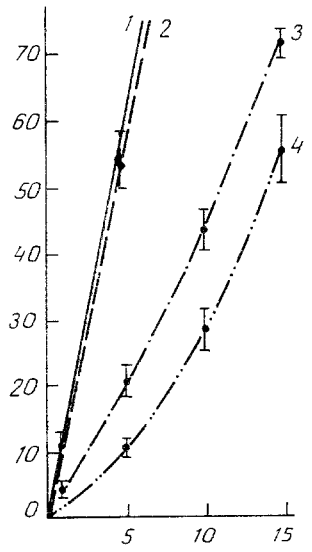

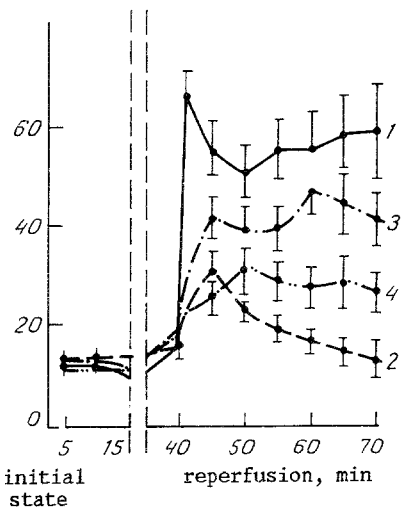

Fig. 1 Fig. 2

Fig. 1. Total perfusion volume (PV, ml/g) during control (1), two-stage (2), and gradual reperfusion at an initial rate of 4 ml/min (3) and 2 ml/min (4). Abscissa, duration of reperfusion, min; ordinate, PV, ml/g.

Fig. 2. Diastolic pressure (DP, mm Hg) with different perfusion schedules (legend as to Fig. 1). Ordinate, DP, in mm Hg.

the aorta with Krebs' solution (37°C), with constant volume velocity of 10.5 ± 0.6 ml/(min·g) by means of a pump. The initial level of perfusion pressure was 75 ± 3 mm Hg. The composition of the solution was given previously [11]. The isovolumic pressure in the left ventricle was recorded by means of a "Gould Statham P23Db" strain-gauge transducer on a "Gould Brush 2200" instrument. CF was calculated as the product of the developed pressure and the heart rate (HR).

After stabilization of CF for 20-30 min perfusion of the heart was completely stopped for 25 min, to produce normothermic ischemia, which was followed by reperfusion for 30 min. The volume velocity in the hearts with control (n = 12) and two-stage (n = 7) reperfusion was constant and did not differ from the initial level. In the last series, during the first 5 min of reperfusion a solution with the addition of 30 mM sodium glutamate was used (the NaCl concentration was reduced correspondingly), the KCl concentration was increased up to 9 mM, the $MgSO_4$ concentration was doubled, and the concentrations of $CaCl_2$ and Na_3EDTA were reduced by half. After the 5th minute and until the end of the experiment the heart was perfused with a solution with the same composition as the original solution. In experiments with gradual reperfusion two different schedules of gradual restoration of volume velocity were used. In the control series (I) of experiments (n = 10) the initial rate of perfusion (4 ml/min) was unchanged for 8 min and completely restored after 15 min of reperfusion. In series II (n = 8) the initial rate of perfusion was reduced eightfold (to 2 ml/min) compared with the initial rate, and it was increased by 2 ml/min every 4th minute of reperfusion. The total volumes of perfusion fluid corresponding to these schedules were different mainly during the first minutes of perfusion only (Fig. 1), and by the 30th minute they amounted to 212 ± 8 and 186 ± 18 ml/g with moderate and low initial rates, and in the control and during two-stage reperfusion they amounted to 330 ± 17 and 315 ± 15 ml/g respectively.

The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Initial values of HR and CF before ischemia were about equal in all series of experiments, namely 247 ± 7 min^{-1} and 23.0 ± 0.6 mm Hg/min × 10^{-3} respectively. The diastolic

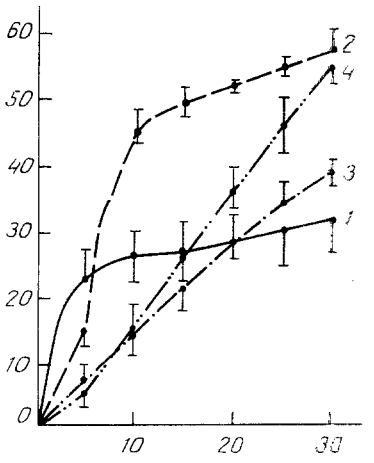

Fig. 3. Restoration of contractile function (CF, %) with different reperfusion schedules (legend as to Fig. 1). Abscissa, duration of reperfusion, min; ordinate, CF, %.

pressure (DP) after 25 min of total ischemia showed a very small, but not significant, increase — on average by 6 ± 2 mm Hg, a result characteristic of the guinea pig myocardium [3].

The reperfusion period was equal in the different series of experiments. In series I (control) with a constant rate of perfusion, rapid (toward the end of the first minute) restoration of HR to its initial level and a sharp increase in DP (Fig. 2) were observed, and during the subsequent reperfusion both parameters remained virtually unchanged. The increase in CF in the control, which was fastest initially (Fig. 3), later became much slower, and by the end of reperfusion CF amounted to 33 ± 5% of the initial value. The first period of two-stage reperfusion with the modified solution was accompanied by slow recovery of HR (to 191 ± 10 min^{-1} by the 5th minute) and of CF, and also by a very small rise of DP (Fig. 2). After replacement of the solution by the original solution, HR was restored quickly and CF increased considerably (Fig. 3). Toward the end of two-stage reperfusion DP was virtually completely restored (Fig. 2), whereas CF recovered to 59 ± 2% of its initial value (Fig. 3).

In both series with gradual reperfusion and with a reduced initial velocity, slow recovery of HR (by the end of the 20th minute) and of CF was observed, but the rise of DP was smaller (Figs. 2 and 3). During reperfusion with a low initial rate, a smaller rise of DP (Fig. 2) and better recovery of CF — to 56.2% of the initial level (Fig. 3) were observed.

The positive effect of gradual reperfusion was due not so much to a decrease in the total volume of solution passing through the heart during reperfusion but rather to limitation of the volume of perfusion in the initial period. This effect may probably be associated mainly with diminution of the damaging action of reoxygenation of the ischemic myocardium. The data obtained are in agreement with results in which reperfusion oxygenation was reduced due to hemodilution [12]. Besides excessive reoxygenation, the initial rate of elution of various ions and metabolites accumulating in the myocardium during ischemia [1, 5] is evidently important also. Most of them (K^+, H^+ ions) have a negative cardiotropic action, and breakdown products of adenine nucleotides may also be reutilized during reperfusion [2]. Rapid elution of these substances, on the one hand, impairs resynthesis of high-energy phosphates [5, 8] and, on the other hand, it promotes intensive energy expenditure and the onset of arrhythmias [1, 3]. The results of experiments in which a modified solution was used for two-stage reperfusion confirm the importance of reduction of energy expenditure in the initial period of restoration of CF. The discovery made in this series that reperfusion contracture was considerably reduced, deserved special attention, for it is particularly important in connection with the improvement of restoration of the pumping function of the heart. The results of these experiments may be useful for optimizing reperfusion of the ischemic myocardium.

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MEDIUM MOLECULAR WEIGHT BLOOD PEPTIDES AS FACTORS MODIFYING ERYTHROCYTE MEMBRANES IN BURNS

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KEY WORDS: burns; erythrocytes; medium molecular weight peptides.

General ideas formulated previously on the mechanisms of involvement of medium molecular weight peptides (MMWP) in the process of burn autointoxication postulate a direct role of erythrocytes in the distribution of biologically active MMWP in the body fluids [5]. The efficacy of detoxication by transfusion of washed erythrocytes confirmed the validity of these suggestions [4]. At the same time, it was evident that direct proof of interaction between MMWP and erythrocytes was necessary. Obtaining such proof also is important in connection with analysis of the possible mechanisms of the change in morphological and functional characteristics of erythrocytes and their membranes in burns.

EXPERIMENTAL METHOD

Electrophoretic mobility (EPM) of the erythrocytes was measured by means of a horizontal chamber of Kharamonenko's design. EPM was measured in phosphate buffer (pH 7.4) at 22-24°C [3, 6]. Meanwhile, in some experiments the effect of MMWP on acid resistance of the erythrocytes was studied [2].

The investigations were conducted on noninbred male albino rats weighing 150-200 g. In all series of experiments the initial level of EPM of the erythrocytes was measured beforehand, and was 1.30 ± 0.02 $\mu \cdot V^{-1} \cdot sec^{-1} \cdot cm$ ($n = 107$). MMWP was obtained from blood plasma of intact and burned animals by the method in [1]. The fractions were numbered in order of elution from the column. Four concentrations of MMWP were used (from blood of intact animals — normal, from blood of burned animals — burn). Concentration 1 corresponded to the concentration of MMWP in plasma, whereas concentrations 2, 3, and 4 were 2.5, 5, and 10 times higher respectively than the MMWP level in the plasma of the experimental animals. For the control, erythrocytes were incubated for 4-6 h in plasma of intact animals, in phosphate buffer with

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