EFFECT OF ESSENTIALE-FORTE ON NUCLEIC ACID SYNTHESIS AND SOME HEMODYNAMIC PARAMETERS OF THE DAMAGED RABBIT MYOCARDIUM

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KEY WORDS: essentiale-forte; nucleic acid; phospholipids; infarct

Recent investigations [1, 3] have shown that myocardial infarction due to coronary occlusion is accompanied by intensification of lipid peroxidation (LPO), which in turn is accompanied by delipidization and by marked phospholipid deficiency in cell membrane structures [6, 11]. There is evidence of the important role of phospholipids as effectors for several enzymes, such as RNA-polymerase [7], DNA-polymerase [8], succinate dehydrogenase, mitochondrial ATPase, pyrophosphatase, cytochrome c-oxidase [4, 5, 9], etc. They also demonstrate the importance of these lipids in the organization of the phospholipid component of bilayer membranes and in the mechanism of restoration of function of the muscle cells of the damaged heart [2].

The aim of this investigation was to study the action of exogenous essential phospholipids on the state of nucleic acid synthesis in the myocardium and on certain hemodynamic parameters in myocardial infarction caused by coronary occlusion.

EXPERIMENTAL METHOD

Experiments were carried out on 50 Chinchilla rabbits weighing 2-2.5 kg. A model of myocardial infarction was produced by occlusion of the anterior descending branch of the left coronary artery. The animals were divided into five groups: intact; with myocardial infarction, untreated; with myocardial infarction, treated with essentiale-forte (EF) in ampuls; with myocardial infarction and treated with a combination of EF and α-tocopherol; with myocardial infarction and treated with EF in combination with α-tocopherol and sodium nucleate (1 ampul of EF contains 250 mg of essential phospholipids, 25 mg of pyridoxine chloride, 10 μg of cyanocobalamin, and 2.5 mg of nicotinamide). Administration of EF to the experimental animals from the 1st through the 15th day after creation of the myocardial infarct took the form of single daily intravenous injections in a dose of 0.25 ml/kg body

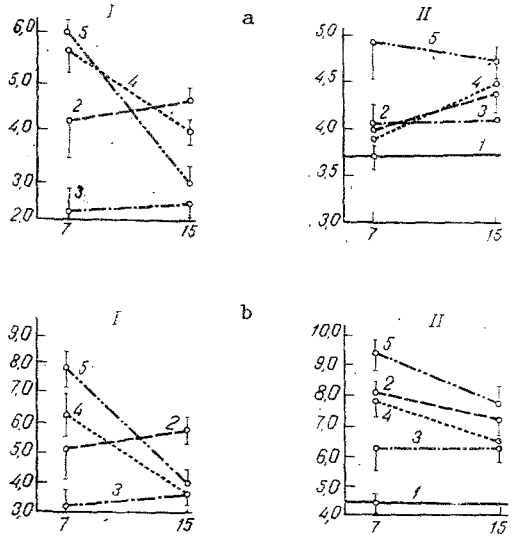

Fig. 1. Changes in relative percentage radioactivity of DNA (a) and RNA (b) in necrotic (I) and perifocal (II) zones of left ventricle of rabbit with experimental myocardial infarction. Abscissa, time after creation of myocardial infarct (in days); ordinate, specific radioactivity of combined DNA and RNA (in cpm/mg/g myocardial tissue). 1) intact animals; 2) infarct (control); 3) infarct + EF; 4) infarct + EF + α-tocopherol; 5) infarct + EF + α-tocopherol + sodium nucleate.

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TABLE 1. Hemodynamic Parameters in Rabbits with Myocardial Infarction Due to Coronary Occlusion, Untreated and Treated at Different Times after Operation

Group of animals	Number of animals	Time after operation, days	MBF, ml/min/100 g	CO, ml/min/kg	CBV, ml/kg	SV, ml
Intact	10		66,3±6,2	179±5,6	107±3,1	0,70±0,026
Myocardial infarct without treatment (control)	10	7	18,5±1,9	139±4,0	128±4,7	0,50±0,020
Myocardial infarct + EF	6	7	28,0±5,3	156±4,1	125±4,5	0,56±0,030
	5	15	26,0±3,1	130±5,2	145±3,6	0,51±0,040*
Myocardial infarct + EF + α-tocopherol	6	7	25,0±2,8	152±5,7*	121±5,3	0,58±0,010
	7	15	29,0±3,1**	163±4,8*	115±6,1*	0,63±0,020*
Myocardial infarct + EF + α-topopherol + sodium nucleate	7	7	31,0±4,1**	167±6,1*	115±4,1*	0,69±0,020
	6	15	39,0±3,9**	176±5,9**	110±3,6**	0,71±0,010**

Legend. MBF) Myocardial tissue blood flow; CO) cardiac output; CBV) circulating blood volume; SV) stroke volume. Significance of differences compared with control: *$p < 0.05$; **$p < 0.01$.

weight; α-tocopherol acetate and sodium nucleate were given in concentrations of 2 and 25 mg/kg body weight respectively. The animals were killed on the 7th and 15th days after the operation under superficial ether anesthesia. RNA and DNA were extracted from myocardial tissue by the usual method [10], followed by spectrophotometric quantitative estimation. To study the intensity of nucleic acid biosynthesis, 2 h before sacrifice the animals were given an injection of the isotope ^{32}P in the form of sodium phosphate in a dose of 0.2 */kg body weight. Radioactivity was measured in a gas-flow counter. The myocardial tissue blood flow was determined by the ^{131}I clearance method in milliliters/min/100 g tissue. The hemodynamic parameters were studied by radiocardiographic obserbations, using ^{131}I-labeled human serum albumin. The numerical results were subjected to statistical analysis by the Fisher – Student test.

EXPERIMENTAL RESULTS

In the course of these investigations the idea was that intramuscular injections of essential phospholipids would regularize the phospholipid content in the damaged myocardium and thereby improve its functional state. However, the results showed that EF not only did not improve nucleic acid biosynthesis in the tissues of the left ventricle (Fig. 1) or improve its hemodynamic parameters (Table 1), but on the contrary it gave rise to several undesirable complications such as a statistically significant fall in the relative percentage radioactivity of RNA and DNA, especially in the necrotic zone of the myocardium. In all probability, administration of exogenous phospholipids in the form of EF creates a favorable basis for further intensification of LPO through a phospholipase mechanism [3]. In turn, high concentrations of lipid peroxides lead to oxidative degradation of phospholipids, and thus to inhibition of activity of enzymes catalyzing nucleic acid biosynthesis [7, 8]. These conclusions were confirmed by the positive results obtained with a combination of EF and α-tocopherol. A marked increase in the intensity of RNA and DNA synthesis and an increase in their content in the damaged myocardium were observed in this case. The changes described in all probability play a leading role in the mechanism of formation of improvements in the pattern of hemodynamic parameters of the damaged heart.

EF had a more demonstrative action when given as one of a combination of three components, another being sodium nucleate. The nature of the enhanced effect of EF in the presence of α-tocopherol and sodium nucleate lies in all probability in the important role of these compounds in maintaining the intact state of membrane lipids. There is no doubt that many intermediate reactions, collectively aimed at maintaining the normal physiological status of this biological system are involved in the achievement of this effect of normalizing cell function as a whole in this pathology.

Reactions of antiradical protection of the cell also play an important role in the intimate processes of activation of DNA and RNA synthesis and of associated systems regularizing hemodynamic criteria. With their high metabolic potential, these reactions perform

*Units omitted in Russian original – Publisher.

an important controlling function on the supply of structural material of lipid nature to membrane structures, creating the essential background of a hydrophobic environment for many membrane proteins, including some membrane-bound phospholipid-dependent enzymes. It can accordingly be concluded that a combined administration of EF with α-tocopherol and sodium nucleate in myocardial infarction of coronary occlusive etiology is an effective way of inhibiting LPO and stimulating the course of biosynthesis in the perifocal zones of the necrotic myocardium.

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BURST DISCHARGES OF A SINGLE NEURON INDUCED BY METRAZOL AND PENICILLIN

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The study of the conditions and mechanisms of formation of generators of pathologically enhanced excitation, which lie at the basis of the development of pathological processes in the nervous system [4], is an urgent task from both theoretical and practical points of view. On its solution depends the solution to the problem of what contribution modifications of relations within the system of neurons and anomalies arising in the neuron itself may make to the development of the pathological process.

The aim of this investigation was to study changes in single unit electrical activity under the influence of convulsants.

EXPERIMENTAL METHOD

Experiments were carried out on the neuron of a slow adapting stretch receptor of a crayfish, isolated from 2-4 abdominal segments. The preparation consisted of a receptor nerve cell with an axon 6-7 mm arising from it and entering the common nerve trunk. Cell dendrites were buried in the receptor muscle, attached to pieces of the shell of two adjacent segments. The receptor cell and muscle of the fast stretch receptor were removed. The preparation was immersed in a bath filled with Harreveld's solution, balanced in its ionic composition with crustacean hemolymph, and maintaining function of the preparation under conditions of complete isolation for a long time. The solution surrounding the cell was changed from a buffer reservoir through a funnel connected to the bath so that this procedure did not give rise to any artefact. Activity was recorded extracellularly by means of a suction

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