This fact was matched by a considerable (by almost 65%) increase in SOD activity in the liver of animals adapted to anoxia, and a smaller decrease (by not more than 27%) in SOD activity after exposure to EPS. Adaptation to anoxia did not lead to any change in the level of glutathione-S-transferase activity; the level of activity of this enzyme, moreover, remained constant after EPS also. Nevertheless, glutathione peroxidase activity in rats adapted to anoxia was depressed (by 3.7 times), although it was unchanged after exposure to EPS.

The results of this investigation do not contradict ideas on the important role of LPO in the mechanism of liver damage associated with EPS and the possibility of protecting the liver by adaptation to anoxia.

Thus although the mechanism of prevention of the dyslipoproteinemia developing under the influence of EPS by adapting the animals to anoxia probably involves inhibition of LPO in the liver, the disturbance of lipid metabolism in the liver associated with EPS may be due to the action of other factors.

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EFFECT OF PROSTAGLANDIN E_2 ON DEVELOPMENT OF ADRENALIN-INDUCED MYOCARDIAL DYSTROPHY

E. A. Markova, I. R. Misula, and Yu. M. Tsyapa

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KEY WORDS: adrenalin-induced myocardial dystrophy; prostaglandin E_2; lipid peroxidation.

One of the most important steps in the pathogenesis of heart damage following injection of large doses of catecholamines (CA) [1, 5, 9] or their synthetic analogs [8], and also during emotional–painful stress, is over-activation of lipid peroxidation (LPO) [3]. Lipid hydroperoxides damage membranes of the sarcoplasmic reticulum and mitochondria, as a result of which the Ca^{++} concentration in the sarcoplasm of the cardiomyocytes increases; an excess of Ca^{++} gives rise to a combination of changes known as the calcium triad, which leads ultimately to irreversible contracture of the myofibrils and to the development of foci of necrosis [4]. There are indications that potentiation of adrenergic influences on various organs and increased noradrenalin secretion in them lead to activation of synthesis and secretion of prostaglandins (PG) of the E group, which may limit the action of CA by a feedback mechanism [11, 12].

The aim of this investigation was to study the effect of PGE_2 on LPO activity during the development of adrenalin-induced myocardial dystrophy.

Department of Pathological Physiology, Ternopol' Medical Institute.

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TABLE 1. Effect of PGE_2 on Survival Rate of Rats with Adrenalin-Induced Myocardial Dystrophy

Experimental conditions	Number of rats			Mortality, %
	initially	dying during first hour	dying during 24 h	
Adrenalin	25	8	3	44
PGE_2 + adrenalin	25	—	—	—

EXPERIMENTAL METHOD

Experiments were carried out on 60 noninbred male albino rats. Tests were carried out on 10 control animals and also on experimental animals 1 and 24 h after intramuscular injection of 0.1% adrenalin hydrochloride solution in a dose of 1.5 mg/kg body weight (25 animals). PGE_2 was injected intramuscularly 15 min before adrenalin, in a dose of 0.8 mg/kg (25 animals). A soviet preparation of PGE_2 was used, namely prostenon, synthesized in the Pure Substance Sector, Academy of Sciences of the Estonian SSR (Professor J. E. Lille). Levels of diene conjugates (DC) and malonic dialdehyde (MDA) in the myocardium were determined by the method in [10]. Hearts weighing 0.5 g were cut up with scissors, treated with 4.5 ml of cold physiological saline, and homogenized in a refrigerated Potter–Elvehjem homogenizer. To determine the DC concentration 0.2 ml of homogenate was treated with 1.8 ml of an extracting mixture of heptane with isopropyl alcohol (1:1). After 10 min the sample was centrifuged at 6000g (15 min) on a TsUM-1 centrifuge. The supernatant fraction was transferred into graduated test tubes, to which one-tenth of the volume of distilled water was added; the contents were shaken twice, the heptane phase was withdrawn, and ethyl alcohol was added in the ratio of 1:5 by volume. The optical density of the samples was measured on an SF-4A spectrophotometer at 233 nm. To determine the MDA concentration 0.5 ml of homogenate was treated with 3.5 ml of distilled water, 0.2 ml of 5M HCl, and 1 ml of 17% TCA. The sample was centrifuged for 20 min at 4000g. The supernatant was treated with 1 ml of a 0.8% solution of 2-thiobarbituric acid and the tubes were immersed for 15 min in a boiling waterbath. The optical density of the samples was measured on the SF-4A spectrophotometer at 532 nm. The concentrations of DC and MDA in the samples were calculated from the molar extinction coefficients: for DC 2.20×10^5 $cm^{-1} \times M^{-1}$ at 233 nm and for MDA 1.56×10^5 $cm^{-1} \cdot M^{-1}$ at 532 nm [6, 7].

EXPERIMENTAL RESULTS

The DC and MDA levels in the myocardium of the experimental rats 1 h after injection of adrenalin showed significant increases by 2.3 and 5.5 times respectively.

After 24 h the concentrations of the test products in the myocardium of the rats still remained higher than in the control: DC twice as high, MDA 5 times higher.

Injection of PGE_2 into the animals before injection of adrenalin had a well marked action on LPO activation. The DC concentration in the myocardium of the rats 1 h after injection of PGE_2 and adrenalin was increased by 1.3 times ($p < 0.01$), a smaller increase than in rats receiving adrenalin alone. The MDA concentration in these animals was increased by 1.7 times ($p < 0.01$). This also was lower than in rats receiving adrenalin.

A similar pattern of the time course of DC and MDA concentrations was observed 24 h after injection of PGE_2 and adrenalin. Although these parameters were higher than in the control, by 1.25 times ($p < 0.01$) and 1.8 times ($p < 0.01$), they were lower than in rats receiving adrenalin alone (by 1.7 and 3.2 times respectively).

Thus preliminary injection of PGE_2 prevents excessive adrenalin-induced LPO activation and reduces damage to the myocardium, as shown by the reduced mortality of the animals (Table 1).

Synthetic PGE_2 (prostenon) differs from natural PG by being long-acting [2], and it thus creates favorable conditions for exhibition of its cardioprotective effect.

According to data in the literature [11, 12] the modulating action of PG on the effect of CA is realized through two principal types of feedback mechanism: 1) PG reduce noradrenalin

release from sympathetic terminals through their action on the Ca-dependent mechanism of mediator secretion in the membrane of the nerve ending; 2) PG limit the direct action of CA on effector cells by inhibiting cAMP formation. Considering that extrinsic CA were injected, the second of these mechanisms was evidently predominant in the experimental animals.

It can be concluded from these results that PG, like other stress-limiting systems of the body [4], are factors limiting myocardial damage in adrenalin-induced myocardial dystrophy.

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QUANTITATIVE EVALUATION OF BLOOD SUPPLY OF A FOCUS OF MYOCARDIAL ISCHEMIA IN DOGS IN EXPERIMENTAL PHARMACOLOGY

D. D. Matsievskii, V. V. Lyskovtsev, E. K. Grigor'eva, E. A. Zbrizher, and G. G. Chichkanov

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To assess the anti-ischemic action of drugs it is very important to have data on their effect not only on the total blood supply to the heart muscle, but also on the blood supply to the actual focus of myocardial ischemia. The reason is that whereas many antianginal drugs do not increase the total blood flow into the heart, and may even reduct it, they redistribute the blood flow in favor of the ischemic zone [9] and, in that way, they improve its functional state.

Most existing methods of evaluating the local and collateral blood flow in a region of myocardial ischemia involve the use of labeled microspheres [10], or measurement of clearance of radioactive isotopes [11] and other substances [1], they are discrete, and some of them do not allow the parameter studied to be assessed quantitatively [8]. Determination of the coronary blood flow in a focus of myocardial ischemia by recording the outflow of venous blood from the ischemic zone involves disturbance of the integrity of the coronary artery or of the vein draining blood from the ischemic focus [5, 12].

Bioengineering Laboratory, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR. Laboratory of Pharmacology of Antianginal Agents, Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR G. N. Kryzhanovskii.)

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