EFFECT OF POLYPEPTIDES ISOLATED FROM THE HEART ON THE COURSE OF EXPERIMENTAL MYOCARDIAL INFARCTION

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Drugs currently in use (vasodilators, beta-blockers, calcium antagonists, high-energy phosphates) are effective mainly before the development of an ischemic focus in the myocardium, but not after its formation [6]. Quite successful attempts to treat experimental myocardial infarction (MI) by injecting extracts prepared from the heart into the animal were described almost twenty years ago, but they did not achieve wide popularity. In recent years polypeptides regulating the activity of organs and tissues of animals have been discovered in them (cytomedins) [3]. The discovery of the new class of bioregulators led to a re-evaluation of the results of the study of heart extracts and to the continuation of this research.

The aim of this investigation was to study the action of polypeptides isolated from the calf heart on the course of experimental MI induced in rats by injection of isoproterenol. Isoproterenol necrosis is a model of stress-induced ischemic heart damage [2]. The effectiveness of polypeptides from the heart was compared with that of cytochrome c, also obtained from the bovine heart [1].

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats of both sexes weighing 160-180 g. Myocardial necrosis was produced by two intramuscular injections (at an interval of 24 h) of isoproterenol (Novodrin) in a dose of 80 mg/kg. The control animals received an intramuscular injection of physiological saline in a volume of 0.2 ml 60 min after the first and second injection of isotroterenol, whereas the experimental rats received cytochrome c or the polypeptide preparation from calf heart, obtained by the method of acetic acid extraction in the presence of zinc chloride, followed by precipitation of the substrate with acetone [4] in a dose of 1 mg/kg. The life span of the animals and mortality after 24 h were determined. Activity of total LDH and LDH_1 in the blood serum was measured on a Specord M-40 spectrograph (East Germany), using kits from Boehringer Mannheim (West Germany). The results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that injection of isoproterenol caused the death of 80% of the experimental animals in the course of 24 h. The serum levels of total LDH activity

TABLE 1. Length of Survival and Mortality of Rats with Isoproterenol-Induced Myocardial Necrosis.

Experimental conditions	Number of animals in experiment	Number of animals dying at undermentioned times after 1st injection of isoproterenol				Number of animals dying after 2nd injection of isoproterenol	Total mortality	
		3 h	5 h	8 h	24 h		absolute	%
Isoproterenol + physiological saline	120	28	20	16	—	32	96	80
Isoproterenol + cytochrome c	120	40	8	8	—	36	92	77
Isoproterenol + cardiac polypeptide	120	—	28	12	8	32	80	67

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TABLE 2. Changes in LDH and LDH_1 Activity (in U/liter) in Rat Blood Serum

Experimental conditions	LDH	LDH_1
Intact rats (26)	550±18,3	1,9±0,3
Isoproterenol + physiological saline (24)	629,5±18,7	9,4±1,5
P_1	<0,05	<0,01
Isoproterenol + cytochrome c (20)	656,6±17,1	4,4±0,9
P_1	<0,02	<0,05
P_2	>0,05	<0,05
Isoproterenol + cardiac polypeptide (27)	563,0±27,4	3,0±0,3
P_1	>0,05	>0,05
P_2	<0,05	<0,01

Legend. Number of animals shown in parentheses. P_1) Significance of differences compared with intact rats, P_2) compared with rats receiving physiological saline.

and the cardiac fraction of LDH_1 were considerably increased (Table 2).

Multiple foci of necrosis were found microscopically in the myocardium (mainly in the subvalvular space of the left ventricle), including in animals which survived and were withdrawn from the experiment 24 h after the second injection of isoproterenol.

Injection of cytochrome c reduced the mortality of the animals by 3%. Fewer individuals died 5 and 8 h after the first injection of isoproterenol and cytochrome c (Table 1). Total serum LDH activity was increased more than in the control animals, whereas activity of the LDH_1 isozyme was significantly reduced compared with its level in the group of animals receiving physiological saline (Table 2). The over-all mortality was reduced by 13% in animals receiving the cardiac polypeptides, and their length of survival increased. The rats did not die during the first 3-4 h after injection of the heart preparation (Table 1). Total serum LDH activity was within the limits of the control values, and LDH_1 activity was increased, but not significantly (Table 2).

The preparation, a polypeptide extract from calf heart, can thus be used for the treatment of ischemic heart disease and acute MI. Under the influence of biologically active substances of polypeptide nature contained in the extract, metabolism and growth of cells in the myocardium may perhaps be stimulated [5].

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