STIMULATION OF LYMPHATIC DRAINAGE OF THE HEART BY PROPRANOLOL, HEPARIN, AND RHEOGLUMAN IN ACUTE MYOCARDIAL ISCHEMIA

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Recently discovered facts have shown the pathogenetic importance of disturbances of lymph formation and transport in the development and course of myocardial infarction [1, 3, 4], and therapeutic agents, aimed at restoring the lymphatic drainage of the heart, have demonstrated an encouraging therapeutic effect [2, 5-7]. The state of affairs described above motivated studies of the effect of drugs widely used in clinical cardiology at the present time, namely propranolol, heparin, and rheogluman, on the lymphatic drainage of the myocardium in acute myocardial ischemia (AMI).

EXPERIMENTAL METHOD

Experiments were carried out on male and female dogs weighing 13-20 kg, anethetized with pentobarbital (40 mg/kg). The state of the drainage function of the lymphatic system of the heart was determined by the method in [8]. The time from the moment of injection of Evans' blue dye into the epicardium at the apex of the left ventricle until the appearance of the dye in the epicardial lymphatic trunk (stage I of "clearance" of the lymphotropic dye from the heart) and the time after injection of Evans' blue dye until the final cessation of its elimination from the heart (stage II of clearance of the dye). Evans' blue was injected twice into each dog: 15-30 min and 90-120 min after creation of experimental AMI, by ligation of the anterior interventricular artery. To avoid mechanical injury to the lymphatics, the branches of the left coronary artery were dissected very carefully and ligatures were applied accurately. Control inspection showed that observance of these conditions guaranteed integrity of the normal passage of lymph. There were three series of experiments. In series 1, the rate of clearance of the lymphotropic dye from the heart muscle was determined in 5 dogs with an intact coronary artery (control 1). In series 2 the same parameter was recorded in 35 animals with experimental AMI (control 2). In series 3 (18 dogs) the myocardial lymphatic drainage was determined in animals with ligation of the coronary artery, and receiving injections of drugs stimulating lymph formation and lymph drainage. There were three groups of observations in this series: A) animals receiving heparin (150 U/kg body weight); B) animals receiving rheogluman (5 mg/kg); C) animals receiving propanolol (0.1 mg/kg). The therapeutic preparations were injected intravenously 3-5 min after ligation of the coronary artery.

EXPERIMENTAL RESULTS

The experiments showed that the first stage of excretion of Evans' blue dye through the myocardial lymphatic ystem in animals with an intact blood supply to the heart, and not receiving any treatment (control 1) was 4.2 ± 0.8 min, and in stage II it was 31.9 ± 3.5 min. The absence of any significant correlation between the duration of stages I and II will be noted. On repeated determination of the myocardial lymphatic drainage (after 90-120 min) very slight lengthening of both stages was observed (Table 1). In the experiments of series 2 (control 2) ligation of a branch of the left coronary artery led to marked changes in both stage I and stage II of clearance of the dye from the myocardium, a characteristic feature of the phenomenon of lymphatic stasis, developing 90-120 min after occlusion of the branch of the coronary artery. After determination of the dye elimination time during the first 15-30 min after ligation (stage I) it was noted that this stage was lengthened (compared with animals with an intact myocardium) by about 3-4 times. It was lengthened even more in stage II.

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TABLE 1. Time of Elimination of Evans' Blue Dye from Dog Heart in Control and after Administration of Drugs ($p < 0.05$)

Stages of elimination of Evans' blue	Intact myocardium (control 1)				Creation of experimental myocardial infarction (control 2)			
	time after procedure (min)							
	15–30		90–120		15–30		90–120	
	absolute	%	absolute	%	absolute	%	absolute	%
I	4,2±0,8	100	4,5±0,6	100	12,5±1,7	298±12,9	18,3±1,9	406±35,8
II	31,9±3,5	100	33,6±2,7	100	123±7,6	386±14,6	130*	436

Legend. Asterisk indicates time of observation during which the dye continued to be eliminated from the myocardium.

TABLE 2. Experimental Model of Myocardial Infarction and Administration of Drugs

Stages of elimination of Evans' blue	Heparin						Rheogluman		
	time after procedure (min)								
	15–30			90–120			15–30		
	absolute	% of control 1	% of control 2	absolute	% of control 1	% of control 2	absolute	% of control 1	% of control 2
I	9,9±0,7	235±11,7	79,2±8,7	10,3±0,9	229±14,5	56,2±4,7	5,5±0,54	131±10,6	44±5,7
II	81,8±4,3	256±10,9	71,5±7,7	83,4±3,6	248±12,5	—	50,5±6,7	158,3±9,9	41±6,3

Stages of elimination of Evans' blue	Rheogluman			Propranolol					
	time after procedure (min)								
	90–120			15–30			90–120		
	absolute	% of control 1	% of control 2	absolute	% of control 1	% of control 2	absolute	% of control 1	% of control 2
I	5,7±0,6	127±11,6	45,6±3,6	6,2±0,6	148±13	49,6±8,5	6,8±0,5	151±11,6	37±2,9
II	53,5±7,5	159,2±9,6		58,3±2,7	183±14,2	47,3±7,6	60,7±4,2	181±13,5	—

In the course of the ischemic process, depression of lymphatic drainage of the heart progressed. This was shown by a test carried out 90-120 min after the creation of myocardial ischemia. Stage I and, in particular, stage II were more prolonged than in tests carried out immediately after ligation of the branch of the coronary artery. Stage II deserves particular attention. Throughout the time of observation (2-2.5 h) the dye does not leave the lymphatic system of the heart of any single animal. These observations demonstrate convincingly that occlusion of the branch of the coronary artery caused a disturbance of lymphatic drainage not only in the immediate zone of injury to the myocardium, but also in parts of it distinct from the focus of developing necrosis and ischemia. Naturally, this was bound to be reflected in the metabolism and function of the "sound" part of the myocardium, and to cause autointoxication of parts of the heart not damaged by ischemia.

After injection of heparin the lymphatic drainage of the heart with occlusion of the coronary artery was improved compared with animals not receiving heparin (control 2). Whereas in the control 2 series the duration of stage I was lengthened by 3-4 times, in animals receiving heparin it was lengthened on average by 2-2.5 times. The duration of stage II also was shorter, for in the control 2 series (in the first 15-30 min after occlusion) it was increased by 5 times, and in animals receiving heparin, by 1.8 times. The improvement of stage II will be particularly noted: the complete elimination time of the dye from the myocardium 90-120 min after occlusion of the coronary artery. Without heparin it reflected complete or almost complete blocking of the lymphatic drainage of the heart, as shown by the continued presence of the dye in the efferent lymphatic vessel throughout the period of observation. After injection of heparin this time was longer than in animals with an intact myocardium but shorter than in animals "untreated" with heparin.

Injection of rheogluman led to marked improvement of the lymphatic drainage of the myocardium. It greatly accelerated the clearance of the lymphotropic dye from the myocardium (which was slowed as a result of ligation of the branch of the coronary artery). Comparison of stage I of clearance of the injected dye from the myocardium in dogs with a ligated coronary artery, but not receiving rheogluman, with dogs also undergoing ligation of the coronary artery, but receiving rheogluman, revealed a marked difference: in the first case this time was lengthened by 248%, but in the second case by only 131%. Stage II of clearance of the dye from the heart, just as in stage I, was greatly lengthened after ligation of the coronary

artery, but in dogs receiving rheogluman it was shortened by 4 times ($p < 0.05$) compared with dogs of control group II.

Injection of propranolol had an action on both stage I and stage II of elimination of the dye. The initial value in stage I was 4.2 ± 0.8 min, but after ligation of the coronary artery and injection of propranolol it was increased to 6.2 ± 0.6 min (140%) after 15 min and to 6.8 ± 0.5 min (151%) after 90-120 min. The values for stage II were: 31.9 ± 3.5 min before ligation of the branch of the coronary artery, increasing to 58.3 ± 1.7 min (183%) 15 min, and to 60.7 ± 4.2 min (181%) 90-120 min after ligation and injection of propranolol.

It can be concluded from these results that acute focal ischemia leads to marked inhibition of the lymphatic drainage of the heart, detectable as early as during the first 30 min after ligation of the branch of the coronary artery, and progressing in the case of prolonged ischemia. The therapeutic substances tested (heparin, rheogluman, propranolol) have the ability to selectively stimulate the drainage function of the lymphatic system in the myocardium.

LITERATURE CITED

1. S. P. Il'inskii, Current Problems in Hemostasis [in Russian], Moscow (1988), p. 213.
2. A. A. Kedik, Problems in Functional Lymphology. Abstracts of Proceedings [in Russian], Novosibirsk (1982), p. 99.
3. Yu. M. Levin, Principles of Thereapeutic Lymphology [in Russian], Moscow (1986), p. 288.
4. Ya. D. Mamedov, Myocardial Infarction [in Russian], Moscow (1989).
5. V. N. Orlov, A. E. Radzevich, and N. M. Shilova, Clinical Lymphology. Abstracts of Proceedings [in Russian], Moscow–Podolsk (1985), p. 213.
6. A. E. Radzevich and N. A. Shilova, Problems in Functional Lymphology. Abstracts of Proceedings [in Russian], Novosibirsk (1982), p. 161.
7. N. A. Shilova, A. E. Radzevich, I. A. Libov, et al., Current Problems in Cardiovascular Pathology [in Russian], Moscow (1982), p. 89.
8. M. Feola, Pathophysiology and Therapeutics of Myocardial Ischemia (1977), p. 337.

BLOOD PLASMA DIENE CONJUGATES IN UNCOMPLICATED AND COMPLICATED FORMS OF HEALING OF AN EXPERIMENTAL MYOCARDIAL INFARCT

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Physical and social rehabilitation of patients with myocardial infarction are largely determined by the results of healing of the infarcted zone. The causes of early disability of these patients are disturbances of healing with the development of postinfarct aneurysm of the heart and its sequelae in the form of acute and chronic circulatory failure [2, 4, 5].

It has been shown [9] that uncomplicated healing of a myocardial infarct (MI) is based on changes in reactivity appropriate for the severity of the disease, with complete synchronization of necrotic and repair processes. If reactivity is disturbed, these processes are desynchronized, with the result that the heart wall is weakened in the zone of the infarct and hemodynamic factors form a postinfarct cardia aneurysm or, in more severe cases, cause the wall to rupture [8].

In the course of necrotic and repair processes in the zone of the infarct, the kinetics of cellular reactions with activation of the lipid peroxidation system (LPO) assumes great importance. It is claimed that injury to the cardiomyocytes and other structures of the

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