ENDOGENOUS POISONING ARISING IN ACUTE MYOCARDIAL INFARCTION WITH LYMPHATIC STIMULATION

G. Sh. Garaev, Ya. D. Mamedov, Z. D. Ismailova, and F. I. Mirzabekova

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An important role in the pathogenesis of acute myocardial infarction (AMI) is ascribed to the toxic factor, and special importance in resorption of endotoxins under these circumstances is attached to the lymphatic system [2, 3, 5, 10]. Stimulation of the lymphatic drainage of the myocardium has been shown to prevent and eliminate endotoxicosis at the organ and tissue level, and to improve repair processes after AMI [5, 7, 9]. With this in mind, it was decided to study the toxicity of blood and lymph in the course of development of AMI and under the influence of drugs with a lymphagogue action, namely heparin, rheogluman, and propranolol.

EXPERIMENTAL METHOD

Experiments were carried out on 32 mongrel dogs weighing 12-22 kg. The drugs were injected immediately after ligation of the anterior interventricular artery, and twice a day for the next 3 days, in the following doses: propranolol 0.1 mg/kg, heparin 150 U/kg, rheogluman 5 ml/kg. The toxicity of the blood and lymph was estimated on the basis of the results of the *Paramoecium* test [7]. Lymph was obtained from the drained thoracic duct and blood from the femoral artery.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that the toxicity of the lymph in the initial state was greater than that of the blood, in agreement with data obtained by other workers [1, 4, 6]. However, 15 min after ligation of the coronary artery values of toxicity of the blood and lymph were different. For instance, the time of death of *Paramoecium* in the blood, which in the initial state was 14.15 ± 0.65 min, decreased to 13.11 ± 0.74 min, and in the lymph it fluctuated within wider limits: 15.87 ± 0.52 min in the initial state and 9.52 ± 0.25 min after 15 min. Thus the time of death of *Paramoecium* in the blood was increased by 7%, compared with 40% in the lymph. After 1 h the time of death of *Paramoecium* was 9.32 ± 0.25 min ($p < 0.05$) and 6.55 ± 0.69 min in the lymph ($p < 0.05$). The shortest time of death of *Paramoecium* in the body fluids was observed 3 h after cessation of the coronary blood flow. On this occasion the time of death of *Paramoecium* in the blood and lymph showed a statistically significant reduction by 44 and 64% compared with the initial background value.

Starting with 24 h, the time of death of *Paramoecium* increased and approached its initial value 3 days after formation of the model. It will be clear from Table 1 that injection of drugs with a lymphagogue action led to a decrease in the toxicity of both blood and lymph. It was found that the effect was almost identical after injection of propranolol and rheogluman. Just as in the control series, in series with administration of these substances in the early period the time of death of the *Paramoecium* (TDP) was less than initially. However, 1 h after administration of rheogluman, TDP in the blood was 11.2% longer than in the control. The difference was even greater after 3 h. After 24 h TDP fluctuated between the values for intact animals, and reached this level on the 3rd day after administration of propranolol and rheogluman. Roughly the same dynamics also was observed after administration of heparin. The difference in this case was that until the end of the investigations TDP did not reach the level recorded in the intact state. The dynamics of changes in toxicity in the lymph was similar in direction to that in the blood,

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TABLE 1. Changes in Toxicity of Blood and Lymph under the Influence of Propranolol, Rheogluman, and Heparin in Dogs with AMI

Experimental conditions	Toxicity							
	before ligation	time after ligation and injection of preparations						
		15 min	30 min	60 min	120 min	3 h	24 h	72 h
Control	14,15±0,65	13,11±0,71**	10,71±0,82**	9,32±0,25*	8,63±0,53*	7,97±0,59**	9,52±0,41*	13,4±0,55**
	15,87±0,52	9,52±0,25**	7,67±0,35*	6,55±0,69*	6,1±0,47**	5,69±0,65**	9,37±0,65**	12,3±0,44*
Propranolol	14,15±0,65	13,55±0,78	11,43±0,84**	10,76±0,72**	9,85±0,47**	9,31±0,83**	10,83±0,31**	14,3±0,51
	15,87±0,52	7,67±0,37**	6,32±0,41**	7,47±0,52*	8,92±0,49*	9,36±0,63**	11,63±0,59**	14,54±0,49**
	14,15±0,65	13,48±0,71**	11,57±0,82**	10,93±0,67**	10,02±0,61**	9,72±0,72*	11,05±0,43*	14,36±0,57
Rheogluman	1,87±0,52	7,42±0,41*	6,55±0,32**	6,69±0,51**	8,73±0,45**	8,75±0,57*	10,27±0,65**	13,63±0,59**
	14,15±0,65	12,47±0,37**	10,67±0,76**	9,88±0,52**	8,93±0,43*	9,05±0,57*	10,65±0,48**	13,90±0,41
Heparin	15,87±0,52	8,35±0,51*	7,02±0,31*	6,31±0,43**	7,23±0,61**	8,63±0,41*	10,05±0,58**	12,57±0,63**

Legend. Numerator indicates blood, denominator — lymph; $*p < 0.05$, $**p < 0.01$.

but the changes were more marked. For instance, whereas 1 h after injection of rheogluman TDP in the blood was 10.76 ± 0.72 min, in the lymph it was 6.69 ± 0.51 min. On average, after injection of propranolol, heparin, and rheogluman the toxicity of the lymph rose to its highest level of 2.2-2.5 times compared with initially.

Improvement of the lymphatic drainage led to a shift of the peak of toxicity of the lymph to earlier times. For instance, whereas in the control series of experiments the lymph was most toxic 3 h after production of AMI, after injection of propranolol and rheogluman the peak of toxicity was observed after 30 min, and 60 min after injection of heparin. These data are evidence that stimulation of lymph formation is not accompanied by dilution of the toxins in the lymph, and that this activation of lymph formation and lymphatic drainage assist with the "clearing" of the tissues from toxic substances that have accumulated in them. This effect is evidently based on improvement of the lymphatic microcirculation in individual organs and tissues. The load on the lymphatic system as a drainage system increases, incompletely oxidized metabolic products and harmful metabolites are directed from the tissue interspaces into lymphatic capillaries. This may explain the fact that after administration of lymphagogue substances the toxic properties of the lymph initially increase sharply. Later, however, administration of drugs with a lymphagogue action reduced the toxic properties of the lymph of the experimental animals, possibly due to the "clearance" of toxins from the tissues. For instance, whereas in the control series of experiments the toxicity of the lymph increased by 2.8 times after 3 h, it increased by 1.6 times after administration propranolol and 1.8 times after administration of rheogluman and heparin.

The results of this investigation thus showed that in AMI, as a result of destructive changes in the cardiomyocytes toxic substances are formed, and they are mainly transported through the lymphatic system. Stimulation of lymphatic drainage with the aid of lymphagogue agents facilitates rapid flushing to toxic products from heart tissue, and for that reason the level of toxicity of the lymph is initially higher than in the blood.

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