CHANGES IN THE BLOOD GLUTATHIONE CONCENTRATION IN EXPERIMENTAL MYOCARDIAL INFARCTION IN DOGS

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The integrity of the living organism is maintained by a complex and delicate neuro-humoral regulation of all its biochemical, bio-energetic, oxidation-reduction, and enzymic processes, and also by a series of adaptive, compensatory, and defensive reactions. The study of various aspects of metabolism in many pathological states and, in particular, in myocardial infarction, is of considerable interest.

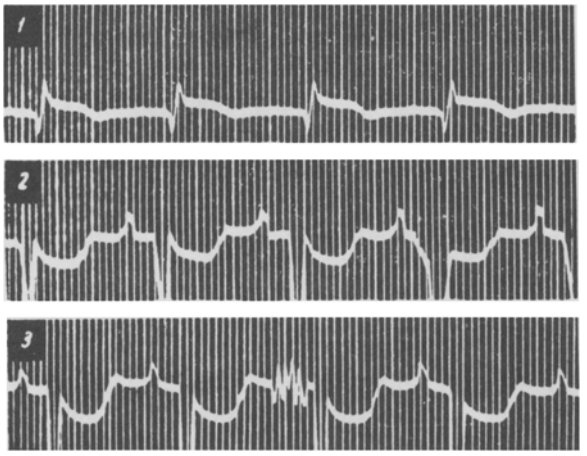

Fig. 1. ECG of dog No. 6 on the 5th day after ligation of the anterior descending coronary artery in its middle third; 1) lead I; 2) lead II; 3) lead III.

One of the links in the complex chain of enzymes and substances determining the course of tissue respiration and proteolysis is glutathione, which was discovered by Hopkins [9]. It is an active donor of sulfhydryl groups in the body, takes part in oxidation-reduction processes, and also plays the role of catalyst in the mechanisms of normal tissue respiration. Also, as a hydrogen acceptor, it facilitates the rapid oxidation and reduction of hemoglobin in the body. After acute disturbance of the arterial blood supply to the myocardium (3.5-4 h after ligation of the coronary arteries) the total glycogen level in the ischemic areas of the myocardium falls by approximately 47% [1] and the oxygen demand of the tissues by 39% [8] compared with the healthy areas. It may be assumed that the concentration of glutathione, which is directly concerned with these processes, in the peripheral blood may be used as an index of the course of reparative processes in the corresponding areas of the myocardium.

Well marked changes in the blood glutathione concentration have been described in the literature in various pathological states: anemias [4], gas gangrene [7], mountain sickness [6], pneumonias [3], diseases of the heart valves [5], disturbance of the pulmonary ventilation [2], etc. In the present paper we describe the results of an investigation of the glutathione dynamics in experimental myocardial infarction. No information regarding the changes in the glutathione concentration in the blood in this disease could be found in the literature, yet this problem is of particular interest in connection with the disturbances of oxidation-reduction processes in myocardial infarction.

EXPERIMENTAL METHOD

Thoractotomy was performed through an incision in the fourth left intercostal space on 9 adult dogs, 2 of which were controls, under intravenous thiopental anesthesia. Controlled respiration was provided by means of a type DP-1 apparatus with a rate of 20-22 respiratory movements per minute. After the pericardium had been opened, the heart was irrigated with 5% novocain solution; the anterior descending coronary artery was ligated together with its venae comitantes. In control experiments the operation of thoracotomy and pericardiotomy was reproduced completely, but the branches of the coronary vessels were not ligated. Systematic studies were made of the electro-cardiographic

Changes in the Blood Glutathione Concentration in Dogs with Experimental Myocardial Infarction

Day after development of infarct	Statistical index	Glutathione (mg%) total	reduced	oxidized
Before infarction	*M*	29	22	7
	m	0,7	2,0	1,0
First	*M*	15	13	2
	m	0,4	0,4	0,1
	P	<0,001	<0,001	<0,001
Mean difference		—14	—9	—5
Second	*M*	14	13	1
	m	0,4	0,3	0,3
	P	<0,001	<0,001	0,001
Mean difference		—15	—9	—6
Third	*M*	17	14	3
	m	0,3	0,3	0,3
	P	<0,001	<0,001	<0,001
Mean difference		—12	—8	—4
Fifth	*M*	21	18	3
	m	0,5	0,4	0,4
	P	<0,001	<0,05	<0,001
Mean difference		—7	—4	—4
Tenth	*M*	60	56	4
	m	2,0	2,0	0,7
	P	<0,001	<0,001	<0,05
Mean difference		+31	+34	—3
Fifteenth	*M*	52	46	6
	m	2,0	2,0	1,0
	P	<0,001	<0,001	0,5
Mean difference		+23	+24	—1
Twentieth	*M*	35	25	10
	m	3,0	2,4	2,0
	P	<0,05	<0,2	<0,2
Twenty-eighth	*M*	29	24	5
		0,5	1,2	1,0
Mean difference		0	+2	—2

indices in 3 standard leads before and after occlusion of the corresponding arteries until they became normalized. The blood glutathione was determined by an iodometric method after different intervals of time. The numerical results were analyzed statistically.

EXPERIMENTAL RESULTS

The most stable and clearly defined indices of insufficiency of the coronary circulation arising after ligation of the anterior descending branch of the coronary artery were the ECG changes characteristic of an infarct of the anterior wall of the left ventricle. During the first 2-3 days, as a rule, considerable changes were observed in the rhythmic activity of the heart in the ECG. These took the form of the appearance of single or multiple extrasystoles, arising mainly from the left ventricle, and well marked tachycardia followed by normalization of the rhythm of the sinus node. Subsequently, marked changes were observed in the ECG of all the experimental animals (reduction of voltage, inversion of the T wave, widening of the Q-T interval and the QRS complex, the appearance of a deep Q_1 wave, and displacement of the S-T segment), reflecting degenerative changes in the myocardium (Fig. 1).

The blood glutathione concentration varied sharply in experimental myocardial infarction depending on the period of development of the pathological process (see the table). On the 1st day after the development of infarction, for instance, the level of the glutathione (expecially the total and reduced) in the animals' blood fell by approximately 50-60% of its initial value, and it continued to fall during the first 3-4 days. In the control animals, on the other hand, only a very slight decrease in the glutathione concentration was observed: the total to 20 mg%, the reduced to 15 mg%, and the oxidized to 5 mg% (normal values 29, 23, and 6 mg% respectively). By the 5th day its level in the blood was close to the initial value (total – 28-30 mg%, reduced – 21-24 mg%, oxidized 6-7 mg%). Meanwhile, in the experimental dogs the blood glutathione concentration was considerably lowered below its preoperative level.

On the 10th-15th day after the development of the myocardial infarct the blood glutathione concentration of the animals began to rise gradually, and this corresponded to the balancing of the changes recorded at this time in the ECG. On the 10th day the concentration of total glutathione had risen by approximately 31%, and on the 15th day by 23% over its initial level. After the 20th day of the disease the blood glutathione level fell again, and on the 27th-28th day it was close to its preoperative values (Fig. 2).

The sharp fall in the blood glutathione level of the experimental dogs during the first few days after myocardial infarction was evidently due to the disturbance of the circulation of the blood, and primarily to the decrease in its mass and minute volume and to the slowing of the blood flow.

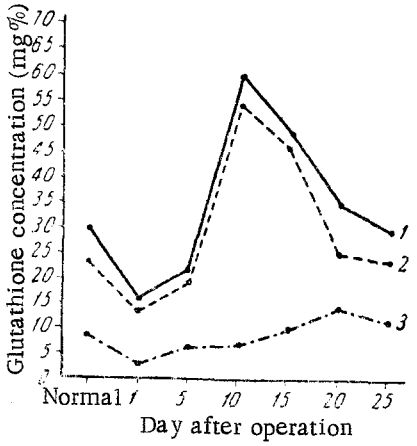

Fig. 2. Changes in the concentration of total (1), reduced (2), and oxidized (3) glutathione in the blood of dogs with experimental myocardial infarction.

The increase in the blood glutathione concentration in the later observations (10-15 days) must be regarded as a manifestation of adaptive, compensatory mechanisms in response to the appearance of the pathological focus in the heart muscle. During cicatrization of the myocardial infarct, the glutathione concentration in the blood of the animals was also normalized. Since glutathione is actively concerned in oxidation-reduction processes [9], the normalization of its blood level in animals with experimental myocardial infarction was evidently accompanied by the balancing of its oxidation-reduction and reparative processes, as was also demonstrated by the changes which we observed in the ECG and the changes in other biochemical blood indices found in this condition.

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