LACTATE DEHYDROGENASE ISOENZYMES OF THE HEART, LIVER, AND KIDNEYS IN EXPERIMENTAL ISCHEMIC STATES

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The effect of hypoxia of varied etiology (myocardial infarction, acute blood loss, thermal burns) on the activity of lactate dehydrogenase isoenzymes (LDH; 1. 1. 27) was studied in various tissues. Irrespective of the causes of the hypoxia in the animal's tissues, the LDH isoenzymes responded by an increase in the activity of the M-type. These changes were most marked in the liver.

The study of the general principles governing development of pathological processes in the body is an important problem in modern medicine. One such process is tissue hypoxia developing under the influence of several pathological agents. From this point of view the investigation of the response of organs to hypoxia of different pathogenesis is of considerable interest.

It was accordingly decided to study the isoenzymes of lactate dehydrogenase (LDH; 1. 1. 27) in various organs in ischemic states due to myocardial infarction, acute blood loss, and thermal burns.

EXPERIMENTAL METHOD

Circulatory and mixed circulatory and ischemic hypoxia were used as the models of ischemia. Circulatory hypoxia was produced in eight rabbits by ligation of the descending branch of the left coronary artery, while circulatory-ischemic hypoxia was produced by acute blood loss (2% of the body weight), for which 12 albino rats were used.

Thermal burns of the third degree were inflicted on 18 albino rats by application of a hot cotton-wool swab, soaked in alcohol, for 50 sec to the animal's previously epilated back. The area of the burn was 25-30% of the body surface.

The isoenzymes were investigated in the necrotic zone of the heart and in the liver of the animals with experimental myocardial infarction and in the liver and kidneys of the animals with burns and blood loss.

The LDH isoenzymes were isolated by vertical electrophoresis in polyacrylamide gel. LDH activity was determined spectrophotometrically by the method of Hill and Levi [1] and expressed as the change in the $NAD \cdot H_2$ concentration in moles/min/g tissue. The activity of each isoenzyme fraction was expressed as a percentage of the total activity of all the isoenzymes.

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TABLE 1. LDH Isoenzymes in Various Ischemic States (relative percentages of activity of LDH isoenzymes)

Isoenzymes	Myocardial infarction				Acute blood loss			
	heart		liver		liver			
	N	E	N	E	N	6 h	24 h	96 h
H_4	100	31,0±5,0	22,0±1,9	16,0±4,8	10,0±2,0	29,3±6,2	18,0±2,7	н. в.
P		<0,05		>0,05		<0,5	<0,05	
H_3M	—	17,0±5,0	30,0±2,5	9,0±1,3	12,0±1,1	14,9±1,8	11,5±4,7	н. в.
P				<0,05		>0,05	>0,05	
H_2M_2	—	16,0±2,5	27,0±3,4	21,0±3,2	15,0±2,0	12,4±1,1	19,6±1,7	30,8±3,6
P				>0,05		>0,05	>0,05	<0,05
HM_3	—	14,0±2,0				12,4±1,1	31,3±6,9	22,2±1,5
P								
M_4	—	22,0±2,1	20,0±1,7	53,0±6,5	62,0±4,0	30,9±2,4	21,1±1,8	51,5±5
P				<0,05		<0,05	<0,05	>0,05

Isoenzymes	Acute blood loss				Thermal burns					
	kidney				liver			kidney		
	N	6 h	24 h	96 h	3 days	6 days	12 days	3 days	6 days	12 days
H_4	10,0±3,0	62,8±12,0	25,3±2,08	47,7±14,0	N	N	15,0±3,2	10,0±1,2	14,0±3,7	11,0±2,45
P		<0,05	<0,05	<0,05			>0,05	>0,05	>0,05	>0,05
H_3M	60,0±4,0	19,4±11,0	24,1±2,2	9,9±2,5	N	N		51,0±3,6	61,0±2,0	50,0±2,7
P		<0,05	<0,05	<0,05	—	—	—	>0,05	>0,05	>0,05
H_2M_2	12,0±2,7	6,6±1,6	15,4±3,8	15,05±6,0	N	N	N	16,0±2,3	9,0±3,5	16,0±2,3
P		>0,05	>0,05	>0,05	—	—	—	>0,05	>0,05	>0,05
HM_3	8,0±2,2	5,7±1,3	19,0±3,9	12,3±3,3	34,0±4,4	33,0±4,2	24,0±3,0	11,0±1,7	7,0±0,6	12,0±1,0
P		>0,05	<0,05	>0,05				>0,05	>0,05	>0,05
M_4	8,0±1,8	5,36±2,1	16,4±1,8	14,9±6,4	66,0±4,4	67,0±4,2	60,0±6,5	10,0±2,0	7,0±1,1	10,0±2,0
P		>0,05	<0,05	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05

Note. N) normal; E) experiment; P calculated relative to normal.

EXPERIMENTAL RESULTS AND DISCUSSION

Activity of the LDH isoenzymes responsible for anaerobic metabolism (M-isoenzymes) was well-marked in the necrotic zone in the animals with myocardial infarction, whereas activity of the aerobic fraction of LDH (H_4) was simultaneously reduced. Activation of isoenzymes of the M-type also was observed in the liver, with a decrease in the activity of the H_3M fraction LDH (Table 1).

Marked changes in isoenzyme activity were found during the first few hours after acute blood loss. In the liver, for instance 6 and 24 h after blood loss activation of the aerobic H_4 fraction of LDH and inhibition of activity of the anaerobic N_4 isoenzyme were observed. A sharp decrease in activity of the aerobic fractions of LDH and an increase in the activity of the H_2M_2 isoenzyme, characteristic of tissues with an embryonic type of metabolism, were observed 96 h after blood loss. The reaction of the LDH isoenzymes in the kidney in this group of animals was less marked and was limited to a redistribution of activity of the aerobic H_4 and H_3M isoenzymes, although 24 h after blood loss activation of the anaerobic M_4 LDH isoenzyme was observed.

An even more marked response of the liver was found in the animals after thermal burns, in which only the activity of the anaerobic LDH isoenzymes (HM_3 and M_4) could be detected. A partial return of the isoenzyme spectrum to normal in the liver of this group of animals was observed on the 12th day after burning. So far as the isoenzymes of the kidneys are concerned, until the 12th day only very slight fluctuations in their activity could be observed.

These experiments thus show that, irrespective of the character of the ischemic states, changes of similar type were observed not only in the total LDH activity, but also in the activity of its individual molecular forms. Activity of the anaerobic LDH fractions of the M-type, which are known to function in high concentrations of lactic acid [2], was increased. These changes correspond completely to the character of the pathological process, during which lactic acid accumulates in the tissues. The reaction observed can thus be regarded as a mechanism for maintaining the supply of energy to the tissues during the development of ischemia.

LITERATURE CITED

1. B. R. Hill and C. Levi, Cancer Res., 14, 513 (1954).
2. E. S. Vessell, Nature, 210, 421 (1966).