Assessment of the *In Vivo* Metabolic Effect of Exogenous Lactate Dehydrogenase

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UDC 612.015.3:577.158:599

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 117, № 5, pp. 480-481, May, 1994
Original article submitted August 20, 1993

Active realization of 2-oxoglutarate, malate, and oxaloacetate is observed after administration of lactate dehydrogenase. The levels of transamination and urea formation are within the normal range. By its targeting of oxidative metabolism, lactate dehydrogenase may be regarded as a biogenic factor correcting the glycolytic processes.

Key Words: *lactate dehydrogenase; glycolysis; integral metabolites; transamination; regulation*

The search for agents of a biogenic origin capable of repairing metabolic disorders of various origin is ongoing. From this viewpoint dehydrogenases are interesting objects of investigation, for their functioning provides the optimal ratios of oxidized and reduced forms of nicotinamide coenzymes determining the direction of metabolic flows and the optimal electrical balance of cytosol, and creates the prerequisites for the energy supply of tissues [4,8]. The task of the present research was to elucidate the potential applications of lactate dehydrogenase (LDH), a factor having a specific influence on the oxidative metabolism system.

MATERIALS AND METHODS

Experiments were carried out with 15 outbred gray rabbits weighing 3.7 to 4.1 kg kept in a vivarium on standard diets. Experimental animals were intravenously injected in a dose of 5000 U/kg. LDH enzymatic preparation (EC 1.1.1.27) obtained from mammalian muscles [1]. Blood samples to measure basal values were collected before the infusion and 5, 20 min, and 24 h after it. Activities of malate dehydrogenase, LDH, glutamate dehydrogenase, and glucose-6-phosphate dehydrogenase were measured spectrophotometrically [3,5-7], and of serum glutamic-pyruvic and glutamic-oxaloacetic transaminases by standard Lachema kits. Levels of oxaloacetate, malate, glycerophosphate, dioxyacetone phosphate, lactate, pyruvate, glutamate, and 2-oxoglutarate were measured in protein-free blood extract by a specific enzymatic method [2], while glucose and urea concentrations were assessed using Lachema kits.

RESULTS

LDH infusion into experimental animal's blood is attended by an increase of its activity (Fig. 1). A characteristic feature is a hyperbolic type of enzyme activity in the course of 24 h. The peak is observed at 20 min, and after 24 h the activity remains quite high. No lactate acidosis is observed (Table 1), this indicating the possibility of using lactate as an energy precursor in, among other things, myocardial metabolism, as well as a substrate in gluconeogenesis. The content of the oxidized component of the LDH redox system, pyruvate, remains virtually unchanged. When assessing glycolysis intensity one cannot overlook an increased aldolase activity concomitant with LDH. The concentration of the forming dioxyacetone

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0007-4888/94/0005-0476$12.50

phosphate has a tendency to decrease. In the same period an increased level of α-glycerophosphate, a metabolite concentrating in its structure the reduced equivalents, is observed. This permits its use as a hydrogen donor in reoxidation reactions with subsequent NADH realization in energy metabolism and reduction synthesis. Active realization of the reduced and oxidized metabolite occurs in the malate dehydrogenase redox system, this reflecting a high intensity of aerobic metabolism in the tissues. A specific feature is an increased glucose concentration, gradually growing to 6.3 mmol/liter by the 20th min after the enzyme infusion. This is apparently a homeostatic mechanism directed toward maintaining a constant osmotic concentration under conditions of intensive realization of unified substrates. The absence of glutamate and glucose-6-phosphate dehydrogenases in the blood sera of experimental rabbits indicates the integrity of the membrane structures.

No changes in the activity of serum glutamic-pyruvic and glutamic-oxaloacetic transaminases were seen over the course of the experiments. Fluctuations in blood urea concentrations within the normal range of values indicate stability of the processes involved in protein metabolism, specifically, in amino acid transformation and decontamination of nitrous metabolism products.

Hence, exogenous LDH is actively involved in metabolic processes in the body and may exert a goal-directed predominant influence on anaerobic carbohydrate catabolism. LDH infusion provides for coordinated functioning of glycolytic enzymes without causing the accumulation of intermediate and final decomposition products. Such a feature of the metabolic effect may be used when choosing means for enzymotherapeutic correction of metabolic disturbances.

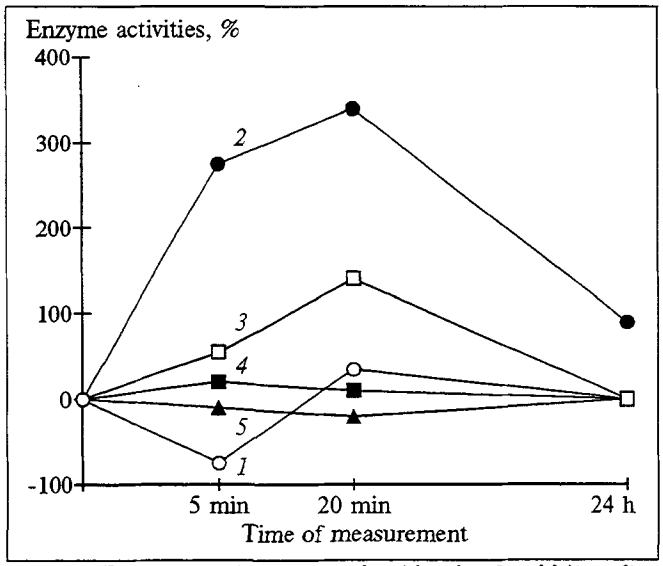

Fig. 1. Enzyme activities in the blood of rabbits after intravenous LDH. *1*) malate dehydrogenase; *2*) LDH; *3*) aldolase; *4*) glutamic–pyruvic transaminase; *5*) glutamic–oxaloacetic transaminase.

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TABLE 1. Metabolite Levels in the Blood of Rabbits (in μmole/ml) after Intravenous LDH Infusion ($M \pm m$)

Parameter	Control	Experiment	
		5 min after infusion	20 min after infusion
Malate	0.462±0.041	0.311±0.039*	0.286±0.027
Oxaloacetate	0.208±0.015	0.242±0.016	0.141±0.013*
Lactate	4.091±0.176	3.510±0.180*	3.396±0.143
Pyruvate	0.147±0.007	0.117±0.005*	0.090±0.009*
α–glycerophosphate	0.584±0.022	0.570±0.030	0.692±0.040
Dioxyacetone phosphate	0.156±0.006	0.140±0.010	0.118±0.004*
Glutamate	0.237±0.020	0.336±0.026*	0.237±0.027*
2–oxoglutarate	0.086±0.004	0.090±0.007	0.072±0.010
Urea, mmole/liter	3.230±0.434	3.953±0.380*	3.910±0.430
Glucose, mmole/liter	4.024±0.188	4.821±0.282*	6.282±0.394*

Note. Asterisk shows statistically reliable data ($p<0.01$).