EXPERIMENTAL BIOLOGY

Metabolic Types of Regulation of Lactate Dehydrogenase and Alcohol Dehydrogenase Activity in the Liver of Intact Animals

Yu. V. Zimin

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A possible relationship between metabolic types of regulation of liver oxidative enzymes (lactate dehydrogenase and alcohol dehydrogenase) and the blood level of cortisol and insulin in intact animals is explored. The liver enzyme activity is found to depend on the initial physiological state of the organism.

Key Words: *lactate dehydrogenase; alcohol dehydrogenase, liver*

There is now a large body of data providing evidence for differences in the nature of enzyme activity changes in acute and chronic liver disorders, primarily those connected with the disturbance of the structural-functional integrity of the cell membranes and organelles [1,3]. However, we still have much to learn about the mechanisms of natural resistance of the liver, which are largely governed by specific patterns of enzyme activity regulation in liver cells. In particular, little is known about the metabolic types of liver reactions in intact animals, which are responsible for the natural level of resistance and for the capacity of the liver to adapt to various environmental factors.

The goal of the present work was to study the metabolic regulation of liver oxidative enzymes in connection with changes of the serum cortisol and insulin level in intact animals.

MATERIALS AND METHODS

Experiments were carried out on 20 male outbred dogs. The liver was extracted under thiopental anesthesia. The direct and inverse reaction of lactate dehydrogenase (LDH) and alcohol dehydrogenase (ADH) were examined using a 10% liver homogenate [4]. Enzyme activity was expressed in nM NADH per min per mg protein. Serum insulin and cortisol levels were recorded in radioimmunoassay [5]. The results were statistically processed.

Department of Experimental Enzymology, State Medical Academy, Nizhnii Novgorod. (Presented by Yu. A. Romanov, Member of the Russian Academy of Medical Sciences)

RESULTS

Experimental animals exhibited 3 different types of LDH inverse: LDH direct (LDH_i/LDH_d) reaction ratio. The first type was characterized by an LDH_i/LDH_d ratio of less than 0.5, and the second type by a ratio>1.5. The LDH_i/LDH_d ratio of the third type was between 0.5 and 1.5.

It was established that the first type of liver metabolic regulation is associated with the lowest LDH and ADH_i activity and the minimal concentration of serum cortisol. ADH_d activity and the insulin concentration exceeded those in the groups with the second and third types of regulation (Table 1). LDH binding to mitochondrial membranes leads to a more pronounced reduction of inverse enzyme activity as compared to the direct activity [8]. This creates conditions for lactate-to-

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Table 1. LDH and ADH Activity in Liver Homogenate and Serum Content of Cortisol and Insulin in Intact Animals ($M \pm m$; $n = 20$)

Type	LDH_d	LDH_i	ADH_d	ADH_i	Cortisol, nmol/liter	Insulin, μU/ml
	nmol NADH per min per mg protein					
1	205.34±24.62	54.73±3.22	84.82±8.50	37.33±4.48	33.70±7.95	21.66±6.35
2	257.54±19.92	953.77±114.78*	40.85±4.88*	273.45±22.82*	101.39±28.96*	8.61±1.29*
3	340.73±26.74*	414.86±53.22*	41.01±5.65*	137.54±25.74*	75.48±16.20*	18.38±7.11

Note. n: number of animals; *: reliable difference as compared with first type.

pyruvate transformation, the latter product being recruited in the Krebs' cycle under aerobic conditions. Unlike LDH, ADH under aerobic conditions resides mostly in the microsomal fraction, a fact which is confirmed by the increased utilization for energetic purposes under such conditions [6]. Evidently, the first type of metabolic regulation involves the activation of bioenergetic hepatocyte function and an anabolic trend of liver metabolism against the background of an increased serum insulin content.

The intrinsic features of the second type of liver metabolic regulation include an increased LDH activity in both the direct and inverse reactions, by 20% and 94%, respectively. The serum cortisol concentration exceeds that with the first type by 67%. ADH_i activity is also considerably increased (by 86%). On the other hand, ADH_d activity is reduced by 44%. The serum insulin concentration is decreased by 60% (Table 1). It appears that cortisol causes a redistribution of LDH/ADH activity in the mitochondrial and microsomal fractions of the liver cell. This results in the binding of LDH to microsomal membranes, thereupon increasing the activity of the inverse enzyme reaction and promoting an increase in the lactate concentration [7]. At the same time, mitochondria-bound ADH activates the inverse reaction directed at the utilization of aldehydes, the content of which rises under anaerobic conditions. Thus, the second type of liver enzyme metabolic regulation is characterized by a marked trend toward catabolic reactions and the activation of aldehyde biotransformation.

The third type exhibits intermediate properties as compared to the first and second; however, judging from the direction of biochemical changes it is closer to the second type. LDH_d and LDH_i exceed those of the first type by 39.7% and 86.8%, respectively. Moreover, ADH_i is increased by 72.9%, and serum cortisol by 55.4%. ADH_d activity is reduced by 51.6%, but the insulin level drops only 15%. It follows from these data that this intermediate metabolic type expresses mostly a catabolic direction of liver metabolic reactions.

The investigations made it possible to identify three types of metabolic regulation of oxidative enzyme activity in intact animals. This points to differences in the initial level of individual liver resistance. Apparently, the manifestation of one or another metabolic type is connected with the hormone-induced redistribution of LDH, ADH, and other enzymes between the mitochondrial and microsomal fractions of the cell.

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