Effect of Chorionic Gonadotropin on Lactate Dehydrogenase and Alcohol Dehydrogenase Activity in the Pathologically Altered Liver

Yu. V. Zimin and I. M. Solopaeva

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Chorionic gonadotropin is shown to alter lactate dehydrogenase and alcohol dehydrogenase activity in the pathologically altered liver and to exert a regulatory effect on the catalytic properties of these enzymes.

Key Words: *chorionic gonadotropin; lactate dehydrogenase; alcohol dehydrogenase; liver*

One approach to the management of chronic hepatitis and of cirrhosis consists in the use of agents that stimulate regeneration of the liver. It has been shown that chorionic gonadotropin (CG) stimulates liver regeneration and the reversal of pathological changes, with the result that the structure and function of this organ return toward normal [6]. CG promotes enhanced RNA synthesis and lowers the activity of lysosomal enzymes by elevating the activity of organ-specific enzymes (urokinase, fructose-1-phosphatase) [1,5]. Preliminary studies have indicated that CG has a direct effect on the catalytic properties of lactate dehydrogenase (LDH) *in vitro* [3], which suggests that this hormone may act as a nonspecific regulator of enzyme activity in the cell.

The purpose of the present study was to examine how CG might affect the regulation of LDH and alcohol dehydrogenase (ADH) activity in the pathologically altered liver.

MATERIALS AND METHODS

The effect of CG on LDH and ADH activity in the pathologically altered liver was studied on a model of toxic hepatitis produced in randomly bred male rats by administering them subcutaneously a 66% solution of carbon tetrachloride (CCl_4) in a dose of 0.3 ml 4 times per week over a 3-month period. After the discontinuation of CCl_4 injections, some of the rats were treated with CG and some were left untreated. CG was injected subcutaneously in a dose of 75 units per 100 g body weight. The animals were killed by decapitation 2 and 30 days after the start of hormone therapy. The control group consisted of intact rats. Activities of the direct and reverse LDH and ADH reactions were measured in liver homogenates and expressed in nmol NADH/min per mg protein [4].

RESULTS

As shown in Table 1, the activity of the oxidative enzymes LDH and ADH was altered in the homogenates of livers from rats with toxic hepatitis. Thus, the activity of the direct LDH reaction was higher by 69% and that of the reverse LDH reaction lower by 40% than in the control group of intact rats. The activity of the direct and reverse ADH reactions was lower in both cases, by 51% and 55%, respectively. The reduced capacity of the liver to effect biotransformation of alcohols and aldehydes and the predominantly aerobic type

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

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TABLE 1. Effect of Chorionic Gonadotropin (CG) on LDH and ADH Activity in Liver Homogenates (Expressed in nmol NADH/min per mg Protein) in Rats with Toxic Hepatitis ($M \pm m$, $n = 10$)

Group	LDH, direct	LDH, reverse	ADH, direct	ADH, reverse
1st	435.67±4.73	553.19±16.22	70.89±6.23	87.17±2.59
2nd	740.91±7.76*	330.21±9.41*	34.83±2.58*	39.23±1.49*
3rd	431.11±16.67	1036.56±41.08*	9.64±0.26*	102.10±3.17*
4th	606.39±10.80*	1223.47±27.88*	38.29±1.16*	101.30±2.95*
5th	701.08±9.77*	1158.77±41.87*	25.28±0.63*	141.02±4.03*
6th	798.76±19.45*	1645.09±36.99*	35.02±1.06*	333.27±9.32*

Note. Group 1, intact rats; group 2, rats with toxic hepatitis; group 3, rats with toxic hepatitis killed on day 2; group 4, rats with toxic hepatitis killed on day 30; groups 5 and 6, rats with toxic hepatitis killed on day 2 and day 30, respectively, after the start of CG treatment. An asterisk denotes $p<0.05$ vs. the control group.

of LDH reaction observed in toxic hepatitis are indications that the metabolic changes that occur in the liver in this condition make liver metabolism similar to that shown by embryonal tissue and poorly differentiated hepatomas [7]. Two days after the discontinuation of exposure to CCl_4, we observed a 88% increase in the activity of the reverse LDH reaction, as compared to the control values, and that of the direct ADH reaction virtually reverted to the control level. Thirty days after the discontinuation of CCl_4 injections, the activities of the direct and reverse LDH reactions were 38% and 121% higher, respectively. The activity of the direct ADH reaction amounted to only 53% of the control level (Table 1).

After two days of CG treatment, the activities of the direct and reverse LDH reactions were 60% and 110% higher, respectively, than in the control group, the activity of the direct ADH was 65% lower, while that of the reverse ADH reaction was 62% higher (Table 1). Short-term CG treatment of animals with toxic hepatitis appears to activate substantially anaerobic metabolism in the liver and the biotransformation of highly toxic aldehydes there, which may be an important factor in the regulation of the regenerative process.

After the 30-day treatment with CG, LDH activity remained high in both the direct and the reverse reactions, exceeding the control level by 82% and 198%, respectively. In contrast, the activity of the direct ADH reaction was 51% lower whereas that of the reverse ADH reaction was 283% higher.

The results of this study indicate that discontinuation of exposure to CCl_4 led to spontaneous regeneration of the liver. This was accompanied by alterations in the activity of oxidative enzymes (LDH and ADH) and by metabolic reactions of a catabolic nature in the liver, which weakened the regenerative process. CG, by stimulating substantially the regeneration of the pathologically altered liver, elevated LDH and ADH activities and increased the bioenergetic potential and biotransforming resistance of hepatocytes. On the one hand, these changes are associated with the induction by this hormone of *de novo* enzyme synthesis in the cell. On the other, there is evidence that endogenous CG can be synthesized in liver cells [2] and may also alter enzyme activity there [3]. CG probably exerts multiple effects on hepatocytes by affecting intracellular mechanisms that regulate catalytic properties of enzymes and by activating anabolic reactions, thus providing a basis for enhanced regeneration of the diseased liver.

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