LYMPHATIC AND BLOOD TRANSFERASE LEVELS DURING THE FEBRILE REACTION

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UDC 616.428-092:612.57]-076-092.9

KEY WORDS: febrile reaction; lymph; transferases.

Transferases perform an important role in homeostasis, namely the synthesis and degradation of amino acids, which accounts for the great interest of research workers in their study in the tissues and body fluids in various forms of pathology. As a rule, the changing enzyme profile is studied in peripheral blood, whereas the character and direction of their changes in the lymph have not yet found reflection in the literature.

It was accordingly decided to compare levels of alanine and aspartate aminotransferases (AlAT and AsAT) and of their isozymes, and of indicator enzymes of the liver, namely leucine aminotransferase (LAT) and γ-glutamyl transferase (GGT) and its isozymes in lymph flowing from different regions of the body, and in the blood serum or rabbits during the febrile reaction (R).

EXPERIMENTAL METHOD

Experiments were carried out 63 chinchilla rabbits weighing from 2.5 to 4.2 kg. FR was induced by intravenous injection of pyrogenal, by the method described previously [10]. Lymph was obtained from the thoracic duct (TD) at the point where it drains into the venous angle, the hepatic lymph duct draining the lymph nodes of the liver, and the intestinal lymphatic trunk; blood for investigation was taken from the femoral vein. Concentrations of AlAT and AsAT [7, 15] and their isozymes [4, 13], of LAT, GGT [8, 14], and its isozymes [12], in the blood and lymph were determined in the course of FR of varied duration. The animals were killed by injection of a lethal dose of general anesthetic.

EXPERIMENTAL RESULTS

As Table 1 shows, concentrations of AsAT, LAT, and GGT in the lymph were lower than in the blood serum. Meanwhile, the AlAT level in hepatic and intestinal lymph was close to that in venous blood.

FR was accompanied by enzyme levels many times higher in the body fluids, and the degree of this increase and its duration were greater in lymph than in blood. In the course of FR the enzyme levels rose proportionally to the number of injections of the lipopolysaccharide. In lymph flowing from the liver and PED, changes in the GGT level were greater in degree and in duration. During a short FR the increase in the cytoplasmic (thermostable) and microsomal (thermolabile) fractions of GGT in the blood and lymph was identical in degree, whereas during prolonged fever, the increase in content of the enzyme took place on account of its microsomal fraction.

A study of the increase in AsAT and AlAT levels in the body fluids (the latter was greater in the case of prolonged fever) showed that during FR lasting 1, 3, and 5 days their content increased in the fractions of mitochondria and cytosol. After 10 injections of pyrogenal the combined level of the enzymes rose purely on account of isozymes of cytoplasmic origin.

Kazan' Medical Institute. (Presented by Academician of the Russian Academy of Medical Sciences A. D. Ado.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 113, No. 6, pp. 584-586, June, 1992. Original article submitted November 18, 1991.

 0007-4888/92/0006-0778$12.50

TABLE 1. Content of Transferases (in μmoles/liter·sec) in Lymph and Blood Serum during Febrile Reaction (M ± m)

Name of enzyme	Control animals	Injection of pyrogenal							
		once		3 times			5 times		10 times
		after 2.5-3 h	after 5-5.5 h	4th day	6th day	10th day	6th day	10th day	11th day
AsAT	0,10±0,02	0,18±0,02	0,55±0,07*	0,60±0,06*	0,10±0,02	0,09±0,02	0,68±0,06*	0,61±0,08*	0,68±0,08*
AlAT	0,13±0,02	0,21±0,03*	0,34±0,05*	0,56±0,05*	0,09±0,02	0,14±0,03	0,93±0,08*	0,77±0,06*	0,89±0,10*
LAT	0,05±0,01	0,27±0,03*	0,27±0,03*	0,79±0,06*	0,33±0,03*	0,08±0,01	0,48±0,03*	0,32±0,03*	0,50±0,04*
GGT	0,46±0,05	0,74±0,11*	1,27±0,25*	1,83±0,16*	2,34±0,33*	0,84±0,08*	2,96±0,25*	3,16±0,21*	3,92±0,31*
AsAT	0,09±0,02	0,22±0,03*	0,51±0,07*	0,58±0,06*	0,13±0,03	0,13±0,04	0,62±0,09*	0,64±0,07*	0,75±0,04*
AlAT	0,17±0,02	0,24±0,02*	0,41±0,06*	0,74±0,08*	0,08±0,01*	0,12±0,04	0,98±0,10*	0,78±0,07*	1,01±0,08*
LAT	0,05±0,01	0,25±0,02*	0,25±0,02*	0,72±0,04*	0,31±0,03*	0,07±0,02	0,56±0,03*	0,29±0,02*	0,53±0,08*
GGT	0,52±0,06	0,83±0,18*	1,04±0,18	1,70±0,19*	2,80±0,40*	0,92±0,18*	3,13±0,35*	3,13±0,25*	3,26±0,29*
AsAT	0,11±0,02	0,23±0,02*	0,58±0,07*	0,53±0,05*	0,08±0,01	0,14±0,03	0,47±0,05*	0,62±0,06*	0,61±0,0.
AlAT	0,17±0,02	0,20±0,02	0,28±0,03*	0,67±0,08*	0,14±0,02	0,11±0,03	0,66±0,06*	0,61±0,06*	0,75±0,06*
LAT	0,05±0,01	0,30±0,03*	0,28±0,04*	0,67±0,06*	0,23±0,02*	0,06±0,01	0,57±0,03*	0,25±0,02*	0,61±0,09*
GGT	0,69±0,11	0,72±0,07	0,85±0,15	2,42±0,23*	2,17±0,20*	0,93±0,17	2,51±0,32*	2,24±0,28*	2,83±0,31*
AsAT	0,26±0,04	0,39±0,05*	0,48±0,03*	0,53±0,06*	0,21±0,03	0,19±0,03	0,59±0,06*	0,59±0,05*	0,88±0,11*
AlAT	0,18±0,02	0,33±0,04*	0,36±0,03*	0,50±0,03*	0,17±0,02	0,26±0,02	0,56±0,04*	0,50±0,04*	0,75±0,13*
LAT	0,12±0,02	0,42±0,05*	0,19±0,03*	0,63±0,11*	0,21±0,02*	0,08±0,01	0,64±0,05*	0,12±0,02	0,45±0,05*
GGT	0,95±0,22	1,49±0,13*	1,45±0,20*	2,17±0,22*	2,52±0,24*	1,21±0,19	3,13±0,38*	2,58±0,31*	3,35±0,31*

Legend. *$p < 0.05$.

Normally the level of an enzyme in the lymph depends on the structure of the capillary barriers and the molecular weight of the enzyme, but mainly it reflects its concentration in the blood plasma. A lower level, for most of the enzymes studied, in the lymph of the control animals can evidently be explained by the absence of conditions favoring their accumulation.

The results of these experiments thus showed that the frequency and duration of changes in lymphatic and blood transferase levels during FR did not correlate. As a rule, their changes in the lymph (especially in lymph from TD and the liver) were more marked and lasted longer after the period of fever, evidence that their blood level during FR is definitely lymphogenic in origin.

The causes of the increase in transferase content under pathological conditions have been interpreted differently. Some workers consider that high blood enzyme levels are the result of entry of enzymes into the blood following destructive and necrotic changes in the tissues [16]. Others regard this increase as an indication of cell damage and of disturbance of permeability of the cell membranes of organs which have a high intracellular content of a particular enzyme [11]. The 3rd group regard raised blood enzyme levels as a nonspecific adaptive reaction as a result of exposure of the body to any kind of powerful stimulus [2].

Adrenocortical hormones have been shown to be the principal regulators of transferase levels in the liver, and elevation of their level during injury is linked with increased secretion of corticosteroids [6]. Meanwhile, corticosteroids induce activation of GGT through a type of specific induction of biosynthesis of enzyme protein [5]. In experiments in which hydrocortisone was injected into intact animals a sharp increase in transferase activity of TD lymph was found, due to potentiation of the transport function of the lymphatic system [9]. On the other hand, FR is accompanied by activation of adrenocortical function and an increase in the blood corticosteroid concentration [1].

The level, as we know, has a high content of transaminases, especially AlAT and LAT, and it can therefore be postulated that the greatest rise of the enzyme levels in the lymph and blood during FR is due to increased permeability of the cellular and intracellular membranes of the hepatocytes as a result of the developing hypoxia and retention of blood in the liver.

Next, when discussing the dynamics of AlAT and AsAT isozyme levels, it has to be pointed out that a fall of the mitochondrial isozyme levels in the body fluids is evidence of a functional block in the mitochondria of the hepatocytes [4]. This danger first appeared in our investigations after 10 injections of pyrogenal.

The results of this investigation thus show that the transferases released during FR are resorbed into the lymphatic network, and that their levels in the blood serum are largely determined by the transport function of the lymphatic system. Meanwhile, the increase in concentration of transferases in the lymph and blood during FR is evidently a useful homeostatic reaction, aimed at preventing more profound disturbances of nitrogen equilibrium.

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