TYROSINE AND TRYPTOPHAN METABOLISM IN THE LIVER OF ALBINO RATS AFTER TRAUMA

Nguen Ngok Lan and Zh. I. Akopyan

UDC 617-001-092.9-07:616.36-008.939.65-074

Oxidation of tyrosine and tryptophan in the liver of albino rats with traumatic shock was investigated. The tyrosine-ketoglutarate aminotransferase activity was increased by 50% 5 min after trauma compared with the control and reached a maximum 6 h after appearance of definite signs of shock. Tryptophan-pyrrolase activity was also increased and was highest 25 min after trauma.

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Metabolism of tyrosine, phenylalanine, tryptophan, and certain other amino acids in the human and animal body in various pathological states has recently attracted the attention of biochemists and clinicians. Interest in metabolism of these amino acids is due to the fact that in some diseases the oxidation of these amino acids undergoes profound changes. Data can be found in the literature concerning the effect of certain nonspecific enzymes on tyrosine metabolism, but so far as the effect of experimental traumatic shock on this process is concerned, no such information could be found.

Because of the practical importance of this problem we decided to investigate tyrosine and tryptophan metabolism after trauma.

EXPERIMENTAL METHOD

Experiments were carried out on female albino rats weighing 150-180 g kept on a standard diet with 18% protein.

Traumatic shock was produced by crushing the soft tissues of the thigh. The onset of shock was judged from a fall in body temperature of the animals by 1.5-2.5° below normal and from external clinical signs. The animals were used in the experiment at various times after trauma and in various phases of shock. The intensity of tyrosine oxidation was estimated from the increase in p-hydroxyphenylpyruvic acid, which was determined by the method of Cannellakis and Cohen [5] with certain modifications. The incubation medium consisted of 1.65 μmole l-tyrosine, 100 μg α-ketoglutaric acid, and 50 μg pyridoxal phosphate. The enzyme source was 1 ml of a 10% liver homogenate in 0.2 M phosphate buffer, pH 7.4. The total volume of the samples was 4 ml. Incubation was carried out at 37° for 1 h with shaking in an atmosphere of air. Oxidation of tryptophan was estimated from the increase in kynurenin, determined by Knox's method [6]. The incubation medium consisted of 1 μmole L-tryptophan. The enzyme source was 1 ml 10% liver homogenate in 0.2 M phosphate buffer, pH 6.9. The conditions of incubation were the same as for tyrosine estimation.

EXPERIMENTAL RESULTS

In the experiments of series I the effect of experimental shock on tyrosine metabolism in the rat liver was studied. The results of the corresponding experiments are shown in Fig. 1. It will be seen that 5 min after trauma the activity of tyrosine-ketoglutarate aminotransferase was increased by 50%. Highest activity was observed 6 h after trauma. Later the activity of the enzyme fell gradually.

When discussing the mechanism of the increase in intensity of tyrosine oxidation, we associate it with fluctuations in secretion of corticosteroids and their discharge into the blood stream. Many experimental investigations have shown that in shock of different etiology the level of 17-hydroxycorticosteroids and ACTH rises sharply in the first 40 min after the onset of phase I of shock (the erectile phase) [2-4]. During

Institute of Biological and Medical Chemistry, Academy of Medical Sciences of the USSR, Moscow (Presented by Active Member of the Academy of Medical Sciences of the USSR V. N. Orekhovich). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 66, No. 7, pp. 59-61, July, 1968. Original article submitted December 29, 1966.

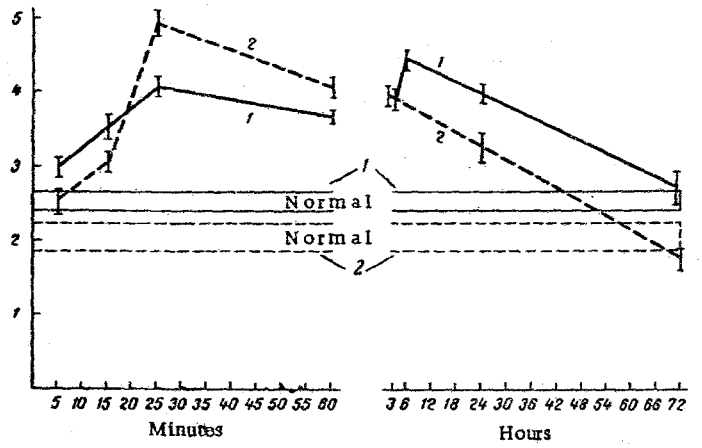

Fig. 1. Effect of traumatic shock on oxidation of tyrosine and tryptophan in the liver of albino rats. Ordinate: increase (in μmoles/g fresh tissue) per hour; abscissa: time after trauma. 1) p-Hydroxyphenylpyruvic acid; 2) kynurenin.

this period, however, the regulatory mechanisms are still capable of restraining excessive secretion of these hormones and their discharge into the blood stream. After 25 min, therefore, we found no excessive increase in intensity of tyrosine oxidation. It must also be borne in mind that in this phase of shock not only the adrenals, but other hormonal systems, especially the thyroid, undergo changes. In this phase considerable thyroid hyperfunction and the production of excessive amounts of thyroxin are observed. According to published data [7], thyroid hormones definitely depress the activity of tyrosine-ketoglutarate aminotransferase. The relatively smaller increase in activity of this enzyme in the erectile phase may perhaps be partly attributable to the inhibitory action of thyroxin. A definite functional antagonism is thus observed between the adrenal cortical hormones and the thyroid hormones in the reaction to trauma. It would also be a mistake to ignore certain other factors influencing biochemical processes in the body during shock.

As mentioned above, following a decrease in intensity of oxidation of tyrosine, an increase in the tyrosine-ketoglutarate aminotransferase activity was observed (by almost 200% compared with the control level). This increase was observed 6 h after trauma, corresponding to phase II (the torpid phase) of shock. According to published data, in this phase of shock the blood corticosteroid level gradually rises to a maximum. This increase depends not only on the conditions of their secretion, but also on their slower breakdown as a result of changes in metabolism. A definite parallel thus exists between the increase in activity of tyrosine-ketoglutarate aminotransferase and the blood corticosteroid level. The increase in the blood corticosteroid level is the main cause of the high level of tyrosine oxidation. In the torpid phase of shock thyroid function is considerably depressed, and this, in turn, causes a marked increase in intensity of tyrosine oxidation [1].

In the experiments of series II the effect of trauma on intensity of tryptophan oxidation in the liver was studied in rats at various times after injury. The corresponding results are shown in Fig. 1. The tryptophan-pyrrolase activity increased, but not at the same rate as in the case of tyrosine, and after 5 min its activity was almost at its original level. After 15 min the activity of the enzyme was appreciably higher and reached a maximum 25 min after trauma (more than 200% compared with the control level). This was followed by a decrease in intensity of tryptophan oxidation. The tryptophan-pyrrolase activity reached a maximum after 25 min, whereas the activity of tyrosine-ketoglutarate aminotransferase reached a maximum 60 min after trauma. This difference may perhaps be explained by the different mechanism of induction of these two enzymes.

Trauma to the soft tissue of the thigh and shock arising as a result of this trauma thus leads to considerable changes in tyrosine and tryptophan metabolism, which are the direct result of disturbance of synthesis of certain regulatory hormones and of their entry into the blood stream.

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