ACTIVITY OF ENZYMES OF GLUCONEOGENESIS IN THE RENAL CORTEX OF RATS WITH ACUTE HYPOXIA

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UDC 616-008.922.1.04-036.11-092.9-07:616.61-008.931:577.152.32

Activity of enzymes of gluconeogenesis in the renal cortex was studied in rats after exposure to a reduced atmospheric pressure (200 mm Hg) for 3 h. Hypoxic stress was shown to lead to an increase in the activity of phosphoenolpyruvate carboxykinase and alanine aminotransferase but to have no significant effect on activity of fructose-1,6-diphosphatase, glucose-6-phosphatase, and aspartate aminotransferase. The ratio between glucose-6-phosphate activity and hexokinase activity was increased under these conditions.

KEY WORDS: acute hypoxia; enzymes of gluconeogenesis; renal cortex.

Data on the effect of oxygen deficiency on the rate of glucose synthesis in the renal cortex, which is characterized by high activity of the enzymes of gluconeogenesis [2, 7], are very few in number and contradictory in nature [4, 6, 11].

The object of this investigation was to study the possible effect of acute hypoxia on activity of the key enzymes of gluconeogenesis and glycolysis, controlling the principle stages of glucose formation in the cells of the kidney cortex.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats weighing 180-220 g. Hypoxic conditions were created in a pressure chamber in which the atmospheric air pressure was reduced to 200 mm Hg in the course of 3 h. Activity of the following enzymes was determined in homogenates of the renal cortex: phosphoenolpyruvate carboxykinase (PEPCase)[1; in a modification], fructose-1,6-diphosphatase (FDPase [10], glucose-6-phosphatase (G6Pase) [13], alanine aminotransferase (ALT) and aspartate aminotransferase (AST) [12], hexokinase

TABLE 1. Activity of Some Enzymes of Gluconeogenesis and Glycolysis in the Kidney Cortex of Rats Under Normoxic and Acute Hypoxic Conditions (M±m)

Enzyme	Activity of enzymes, μmoles substrate / mg protein/min			
	number of rats	control	number of rats	con
PEPCase	6	0,051±0,003	5	0,107±0,008*
FDPase	9	0,168±0,012	9	0,181±0,009
G6Pase	9	0,162±0,011	9	0,169±0,008
ALT	14	0,021±0,002	9	0,034±0,003*
AsT	14	0,249±0,027	9	0,242±0,033
HKase	8	0,046±0,002	8	0,028±0,002*
PKase	10	0,313±0,023	10	0,350±0,014

*Differences significant compared with control ($P < 0.05$)

Department of Biochemistry, Khabarovsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. N. Klimov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 4, pp. 415-416, April, 1978. Original article submitted May 24, 1977.

(HKase) [8], and pyruvate kinase (PKase) [3; in a modification]. The protein content in the homogenate was determined by Lowry's method [9]. The results were subjected to statistical analysis by Student's t-test.

EXPERIMENTAL RESULTS

The data in Table 1 show that activation of the enzymes of the initial stages of gluconeogenesis took place in the kidney cortex of rats exposed to acute hypoxia: ALT by 57.8% and PEPCase by 40.1%. However, the activity of the other enzymes of gluconeogenesis (AST, FTPase, and G6Pase) and also the activity of PKase, which competes with PEPCase for cytoplasmic phosphoenolpyruvate, were substantially unchanged. During hypoxia the activity of the key enzyme of glycolysis in the renal cortex fell on average by 37.8 %, in agreement with data [4] obtained by the writers during a study of the activity of this enzyme in the muscles and heart.

Activation of PEPCase, an enzyme limiting the intensity of gluconeogenesis in the liver and kidney cortex [2], it must be emphasized, is of the greatest importance to the increase in the rate of glucose synthesis in the initial stage of exposure to hypoxia. PEPCase activity was found to increase in the liver also of the hypoxic rats from 0.040 ± 0.004 to 0.054 ± 0.003 unit ($P < 0.05$).

Although the activity of enzymes controlling the final stages of gluconeogenesis in the kidney was unchanged under the influence of hypoxia, it was evidently high enough to provide for increased hydrolysis of the synthesized hexose phosphate to liberate glucose. There was a corresponding increase in the ratio of G6Pase to HKase activity – enzymes responsible for the substrate rotation of glucose (glucose⇌glucose-6-phosphate) – on average from 4.6 to 7.8 ($P < 0.01$).

Activation of the enzymes of gluconeogenesis in the kidney during acute hypoxia is in harmony with the increased synthesis of glucose by slices of kidney cortex from pyruvate, alanine, α-ketoglutarate, and glutamate [5], and also with the increase in the blood sugar level of rats under these conditions from 90.3 ± 7.4 to 145.4 ± 11.8 mg % ($P < 0.01$). The increase in PEPCase and ALT activity and inhibition of HKase activity in the kidney cortex were evidently due to the action of glucocorticoids, the secretion of which under conditions of hypoxic stress is intensified, and which change the ratio between the velocities of glycolysis and gluconeogenesis in favor of the latter [2].

The data described above on activity of the enzymes of gluconeogenesis are thus evidence of the more important role of the kidney cortex in the maintenance of glucose homeostasis when the oxygen supply to the body is disturbed.

LITERATURE CITED

1. M. D. Balyabina and M. S. Usatenko, Vopr. Med. Khim., No. 4, 417 (1968).
2. V. S. Il'in and M. S. Usatenko, in: Advances in Biological Chemistry [in Russian], Vol. 7, Moscow (1965), p. 196.
3. K. A. Kozhevnikova and V. S. Il'in, Probl. Éndokrinol., No. 2, 78 (1975).
4. V. V. Postupaev, Vopr. Med. Khim., No. 4, 380 (1963).
5. V. V. Postupaev and É. M. Litonyan, Vopr. Med. Khim. No. 5, 505 (1972).
6. B. F. Burlington and G. J. Klain, Comp. Biochem. Physiol., 20, 275 (1967).
7. H. A. Krebs, Adv. Enzyme Regulat., 1, 385 (1963).
8. C. Long, Biochem. J., 49, 34 (1951).
9. O. H. Lowry, N. J. Rosebrough, et al., J. Biol. Chem., 193, 265 (1951).
10. R. W. McGilvery, in: Fructose-1,6-diphosphatase and Its Role in Gluconeogenesis, Washington (1964), p. 3.
11. L. C. Ou, J. Appl. Physiol., 36, 303 (1974).
12. S. Reitman and S. Frankel, Am. J. Clin. Pathol., 28, 56 (1957).
13. M. A. Swanson, J. Biol. Chem., 184, 647 (1950).