Nitrogen Metabolism in Rats with Experimental Diabetes during Acute Alcohol Intoxication

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The concentrations of urea and uric acid increased, while the content of free amino acids decreased in blood serum from rats with alloxan-induced diabetes during acute alcohol intoxication. Activities of glutamate dehydrogenase, AMP deaminase, and tyrosine aminotransferase in the liver of experimental animals increased.

Key Words: *acute alcohol intoxication; experimental diabetes; liver; nitrogen metabolism*

Diabetes mellitus is accompanied by impaired supply of substrates for plastic and energy metabolism, abnormal utilization of these substrates by cells, intensification of protein degradation and consumption of amino acids in gluconeogenesis, activation of ammonia production, and increase in the formation and excretion of urea [1,2]. Alcohol decreases insulin secretion, increases the resistance of cells to this hormone, intensifies protein catabolism, inhibits gluconeogenesis, and contributes to the development of acidosis [8,9,13]. Therefore, alcohol promotes the development of metabolic disturbances that are typical of diabetes mellitus. Alcohol intoxication in subjects with diabetes mellitus (particularly in combination with a change in the dietary pattern) can contribute to the development of acute complications of this disease [3].

This work was designed to study nitrogen metabolism in animals with alloxan-induced diabetes during acute alcohol intoxication (AAI).

MATERIALS AND METHODS

Experiments were performed on male albino rats (n=69) weighing 220-250 g. The solution of alloxan (5%, 135 mg/kg) was injected twice at a 12-day interval to induce experimental diabetes mellitus. The development of diabetes mellitus was verified from blood glucose concentration. AAI was induced by an intraperitoneal injection of 25% ethanol (4 g/kg) to fasting animals. The animals were divided into 3 groups. Group 1 rats (healthy animals) were subjected to AAI. Group 2 animals were examined on day 30 after the first injection of alloxan. AAI in group 3 animals was modeled on day 30 of alloxan-induced diabetes. Intact rats (control) were examined simultaneously with treated animals of each group. Group 1 and 3 animals were decapitated 6 h after alcohol administration. Blood alcohol concentration during this period (measured on a Kristall 5000.2 gas chromatograph) was 10-13 times higher than in the control. The concentrations of glucose, urea, and uric acid and total content of free amino acids were measured in blood serum [4]. Activities of ALT (EC 2.6.1.2), AST (EC 2.6.1.1), glutamate dehydrogenase (GDH, EC 1.4.1.3) [6], tyrosine aminotransferase (TAT, EC 2.6.1.5) [5], AMP deaminase (EC 3.5.4.6), and glutaminase (EC 3.5.1.2) [7] were measured in the liver homogenate. The results were analyzed by Student's t test.

RESULTS

Administration of ethanol to healthy rats and animals with experimental diabetes had little effect on blood glucose concentration (as compared to the baseline). The development of AAI in group 1 animals was accompanied by an increase in serum urea concentration and activities of TAT and GDH. Liver glutaminase

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TABLE 1. Metabolite Concentration in Blood Serum and Enzyme Activity in the Liver of Rats with Alloxan-Induced Diabetes and Acute Alcohol Intoxication (*M*±*m*)

Parameter		Group 1	Group 2	Group 3
Glucose, mmol/liter	control	4.58±0.25	5.63±0.28	5.63±0.28
	treatment	4.71±0.38	12.48±0.52**	12.69±0.16**
Urea, mmol/liter	control	5.34±0.19	4.78±0.31	4.78±0.31
	treatment	7.17±0.64*	10.55±0.61**	9.46±1.40**
Amino acids, mmol/liter	control	4.25±0.21	4.81±0.19	4.81±0.19
	treatment	3.92±0.21	3.85±0.15**	3.54±0.13**
Uric acid, μmol/liter	control	116±14	116±4	116±4
	treatment	129±9	123±2	175±11**
ALT, μmol/g tissue/min	control	22.1±3.1	29.2±2.6	29.2±2.6
	treatment	23.2±2.5	38.0±4.1	34.8±2.1
AST, μmol/g tissue/min	control	24.6±2.8	24.1±1.1	24.1±1.1
	treatment	23.0±1.3	30.0±2.0*	26.3±1.2
GDH, μmol/g tissue/min	control	1.76±0.20	2.05±0.18	2.05±0.18
	treatment	2.50±0.24*	1.43±0.17*	2.75±0.22*
Glutaminase, nmol/g tissue/min	control	634±22	626±53	626±53
	treatment	531±22*	807±74	581±31
TAT, nmol/g tissue/min	control	186±19	156±8	156±8
	treatment	281±16**	126±7**	209±3**
AMP deaminase, nmol/g tissue/min	control	375±15	250±9	250±9
	treatment	326±22	257±16	343±15**

Note. Each group consists of 7-8 animals. *p<0.05 and **p<0.01 compared to the control.

activity was shown to decrease under these conditions (Table 1).

The concentration of urea increased, while the content of free amino acids decreased in blood serum from group 2 and 3 rats. Alcohol administration to animals with experimental diabetes was followed by a significant increase in uric acid concentration in the blood. These changes were statistically significant compared to the control (+51%, p<0.02) and baseline level (+42%, p<0.02).

Activity of AST increased, while activities of TAT and GDH decreased in the liver of rats with experimental diabetes. Activities of AMP deaminase, GDH, and TAT in group 3 rats were elevated 6 h after alcohol administration (compared to the control and group 2 animals). AAI on day 30 of alloxan-induced diabetes was accompanied by a 28% decrease in glutaminase activity (p<0.05 compared to the baseline).

Changes in TAT activity are probably related to variations in glucocorticoid secretion during diabetes mellitus and AAI [2,11]. Significant increase in activities of GDH and AMP deaminase in the liver of group 3 rats was accompanied by a decrease in the content of free amino acids and increase in the concentration of uric acid in the blood. These changes reflect activation of deamination processes and increase in catabolic transformations of purine nucleotides in animals with experimental diabetes mellitus during AAI [14,15]. Simultaneous decrease in glutaminase activity can impair ammonia utilization in the liver. Intensified catabolism of purine nucleotides probably contributes to the increase in the production of hydrogen peroxide in the xanthine oxidase reaction and activation of free radical processes under the influence of alcohol during diabetes mellitus [10,12].

We conclude that AAI during diabetes mellitus increases the severity of disturbances in nitrogen metabolism, which are typical of this disease [1].

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