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Review Article

Study of the State of The Endothelium in Rats with Cerebral Ischemia During the Administration of Alcohol

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Abstract

Alcohol intoxication refers to a clinically dangerous condition caused by recent alcohol consumption, when alcohol and its metabolites accumulate in the bloodstream faster than they can be metabolized by the liver. Alcohol has a range of effects on the central nervous system at different doses. Acute disorders include Wernicke encephalopathy, traumatic brain injury, memory loss, convulsions, stroke and hepatic encephalopathy. An increase in stable metabolites [NOx] was found in rats with acute alcohol intoxication (AAI) at doses of 1.5 and 3.5 g/kg and SCI, but less at a concentration of 3.5 g/kg; in rats with AAI at a dose of 1.5 g/kg and SCI, an increase in the degree and rate of platelet aggregation was found in the first 30 seconds. In the group of rats with AAI at a dose of 3.5 g/kg and SCI, no changes in platelet aggregation parameters were detected.

Keywords: endothelium; rats; cerebral ischemia; alcohol

Summary

Alcohol intoxication refers to a clinically dangerous condition caused by recent alcohol consumption, when alcohol and its metabolites accumulate in the bloodstream faster than they can be metabolized by the liver. Alcohol has a range of effects on the central nervous system at different doses. Acute disorders include Wernicke encephalopathy, traumatic brain injury, memory loss, convulsions, stroke and hepatic encephalopathy [1-8].

It is known that during acute alcohol intoxication (AAI), morphological changes occur in the endothelial lining of the microvasculature of brain tissue, that may be a consequence of both the direct cytotoxic effect of ethanol or its metabolites, and the influence of cellular modulators, the release of which leads to increased vascular permeability associated with trophic disorders in the tissue [4-6]. These changes create the basis for the development of dystrophic and necrobiotic processes in the main structural components of the brain. In rats, AAI (1 hour after intraperitoneal injection of ethanol at a dose of 3 g/kg) aggravates the development of hemorrhagic infarction, causes brain edema, disruption of the blood-brain barrier, activation of microglia, oxidative stress and inflammation in the striatum. The cumulative effect of these consequences is the main cause of severe neurological impairment and higher mortality (64%) in rats with AAI and hemorrhagic infarction [9-11].

AAI in healthy male patients causes a temporary decrease in fibrinolytic activity, an increase in the activity of coagulation factor VIII, and a decrease in bleeding time after 12 hours, which explains the susceptibility to cerebral thrombosis of individuals after ethanol intoxication [5]. Acute alcohol intoxication (AAI) was modeled by intraperitoneal injection of a 25% ethanol solution in doses of 1.5 (n=6) and 3.5 g/kg (n=6), which corresponds to mild and severe degrees of alcohol intoxication. The control group of rats was injected with equivolume amounts of saline solution (n=6). Then, subtotal cerebral ischemia (SCI) was modeled in alcoholized rats by ligating both common carotid arteries under intravenous thiopental anesthesia (40-50 mg/kg) for 1 hour. The control group of rats was operated falsely. Stable nitric oxide metabolites and platelet aggregation properties were changed. After a preliminary check for the normality of the distribution of indicators, the obtained data were analyzed by nonparametric statistics using the Statistica 10.0 program for Windows (StatSoft, Inc., USA). The results are presented in the form Me (LQ; UQ), where Me is the median, LQ is the lower quartile value; UQ – upper quartile value. Differences were considered significant at $p<0.05$ [6].

When studying stable metabolites of [NOx] in rats with acute alcohol intoxication (AAI) at a dose of 1.5 g/kg and subtotal cerebral ischemia (SCI), it was found that [NOx] increased by 120.0%, compared with the control group, $p<0.001$ (Table 3.1.3.1), which may be due to the activation of neuronal NO synthase. In rats with AAI at a dose of 3.5 g/kg and SCI, the indicator of stable metabolites [NOx] was increased by 81.9% compared to the control group, $p < 0.001$; and was 17.1% less compared to the group of rats AAI (1.5 g/kg) + SCI, which may be due to the inhibition of arginase in the liver by high concentration alcohol.

Groups	[NO_x], µmol/l
Control (n=6)	30,21 (28,50; 35,9)
AAI (1.5 g/kg) + SCI (n=6)	66,34* (40,34; 81,56)
AAI (3.5 g/kg) + SCI (n=6)	54,97*+ (32,90; 77,49)

Table 3.1.3.1 – Content of stable NO metabolites [NOx] in the blood of rats during acute alcohol intoxication and subtotal cerebral ischemia within an hour, Me (25%; 75%)

Notes:
1 - * - statistically significant differences with the control group p<0.05,
2 - + - statistically significant differences with the AAI group (1.5 g/kg) + SCI, p<0.05,
Study of changes in platelet aggregation properties

When studying platelet aggregation in rats with AAI at a dose of 1.5 g/kg and SCI, an increase in the degree of platelet aggregation was found by 42.2%, p = 0.012, and the rate of platelet aggregation in the first 30 seconds by 97.5%, p = 0.017 (Table 3.1.3.2). In the group of rats with AAI at a dose of 3.5 g/kg and SCI, no changes in platelet aggregation indices were detected compared to the other comparison groups, which may be due to multidirectional changes in platelet aggregation during SCI and exposure to high concentrations of ethanol.

Groups	Aggregation degree, %	Aggregation time, seconds	Aggregation speed (in 30 seconds), %
Control (n=6)	39,8 (38,2; 53,4)	380,0 (360,2; 411,0)	20,4 (13,0; 31,4)
AAI (1.5 g/kg) + SCI (n=6)	56,6* (60,2; 69,5)	367 (287,8; 420,0)	40,3* (33,6; 47,8)
AAI (3.5 g/kg) + SCI (n=6)	46,7 (34,8; 61,8)	342,6 (287,5; 354,9)	37,2 (28,6; 59,8)

Table 3.1.3.2 – Aggregation of rat platelets in rats with acute alcohol intoxication and subtotal cerebral ischemia within an hour, Me (25%; 75%)

Note: - * - statistically significant differences with the control group p<0.05

Thus, an increase in stable metabolites [NOx] was found in rats with AAI at doses of 1.5 and 3.5 g/kg and SCI, but less at a concentration of 3.5 g/kg; in rats with AAI at a dose of 1.5 g/kg and SCI, an increase in the degree and rate of platelet aggregation was found in the first 30 seconds. In the group of rats with AAI at a dose of 3.5 g/kg and SCI, no changes in platelet aggregation parameters were detected.

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