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The impact of alcohol intoxication complicated by toxic hepatitis on the state of the autonomic nervous system and cognitive functions

Akalaev R.N., Stopnitskiy A.A., Khodjiev Kh.Sh., Saidova M.K.
Republican Research Center of Emergency Medicine (RRCEM)
(2, Kichik HalqaYoli Street, 100115, Tashkent, Uzbekistan),
Tashkent Institute of Postgraduate Medical Education
51, Parkent, M. Ulugbek district
Tashkent, Uzbekistan

Authors: Akalaev R.N. – DSc, professor, Head of Scientific and Clinical Toxicology Department of the RRCEM
(ORCID 0000-0002-3628-1313).
Stopnitskiy A.A. – doctoral student of Scientific and Clinical Toxicology Department of the RRCEM, PhD
(ORCID 0000-0001-8087-7416)
Khodjiev Kh.Sh. – Deputy chief physician of the RRCEM for medical work
(ORCID 0000-0002-7048-4472)
Saidova M.K. - doctoral student of Scientific and Clinical Toxicology Department of the RRCEM
(ORCID 0000-0002-1962-8354)

Abstract: The aim of the study: to study the parameters of the autonomic nervous system and cognitive functions in patients with acute alcohol poisoning complicated by toxic hepatitis of varying severity.

Material and Methods

This study included 312 patients with acute alcohol poisoning at the age from 28 to 55 years who were admitted to the Department of Toxicology and Toxicological Reanimation of the RRCEM against the background of chronic alcohol consumption in 2015-2019.

Results and discussion

It follows from the data obtained that in case of mild poisoning, against the background of a short binge, the biochemical parameters were either within the normal range, or showed a slight tendency to increase. All indicators were several times higher than the upper limit of the reference values in patients with moderate and severe poisoning.

Conclusions.

1. In patients with alcohol intoxication, there is a decrease in cognitive functions in proportion to the severity of intoxication and the level of lactate, free ammonia.

2. Patients with a severe degree of alcohol intoxication develop pronounced intellectual impairments that require medical correction, with subsequent mandatory psychological rehabilitation.

3. For acute alcohol poisoning against the background of binge drinking, the development of hypersympathicotonia, caused by an increase in the tone of the sympathetic division of the autonomic nervous system, is characteristic.

4. Indicators of cardiointervalography can be used to diagnose the severity of alcohol intoxication and as predictors of alcoholic delirium.

Keywords: patients, alcohol intoxication, autonomic nervous system, cognitive functions.

Acute alcohol intoxication is poisoning with ethyl alcohol products accompanied by the development of a comatose state [1, 2, 3]. In medical textbooks and manuals, alcohol poisoning is distinguished of mild (at an ethanol level of 0.5 to 1.5 g/l), moderate (at an ethanol level of 1.5 to 2.5 g/l) and acute alcohol intoxication itself manifested by toxic encephalopathy in the form of alcoholic coma of I, II and III degrees [3]. This classification is suitable for practical use, but only in the case of admission of patients who have once abused ethyl alcohol products.

In Uzbekistan, as well as in other CIS countries, patients with acute alcohol poisoning are admitted to the toxicology departments. In the majority of hospitalized patients with this pathology, the deterioration of the condition is not associated with a single alcohol consumption, but with the previous long-term chronic abuse of alcoholic beverages. This situation creates certain difficulties both in terms of diagnosing the severity of poisoning and tactics of intensive therapy. it happens because the traditional orientation of doctors to the level of consciousness and the concentration of alcohol in the blood is losing its significance [1, 2].

During chronic binge drinking, in addition to the direct effect of the next dose of ethyl alcohol on the body, the mechanism of the mediated toxic effect of ethanol begins to act, which is determined by a cascade of metabolic disorders arising from its oxidation, as well as the toxic effects of acetaldehyde and its metabolic products [1, 2, 4, 5, 6]. Acute alcohol intoxication against the background of long-term alcohol consumption is almost inevitably accompanied by the development of post-intoxication alcohol syndrome [5, 6, 7].

One of the most dangerous complications of ethanol intoxication is toxic-hypoxic encephalopathy (THE), which occurs as a result of the development of both specific and nonspecific mechanisms of brain damage [8, 9]. The main manifestations and severity of THE are determined, first of all, by the nonspecific effect of ethanol on the membranes of the cells of the central nervous system. Of the mediated mechanisms of toxic effects, two have recently been distinguished. The first is the development of tissue hypoxia and metabolic acidosis due to the accumulation of ethyl alcohol metabolism products [1, 2, 8, 9]. The second is a violation of the detoxifying function of the liver against the background of prolonged abuse of alcoholic beverages and a sharp increase in the level of free ammonia [7, 8, 10, 11]. Studies carried out in the Scientific and Clinical Department of Toxicology of the RRCEM have shown the enormous importance of this metabolite in the diagnosis of the severity of alcohol intoxication against the background of chronic abuse of ethanol products [2, 11]. We have found a clear correlation between the level of concentration of free ammonia in the blood and the degree of impairment of cognitive functions, as well as the autonomic nervous system of the body [4].

For adequate treatment and diagnostic tactics, we offered to allocate patients coming as a result of drinking alcohol against a background of binge drinking in a separate nosological group: "Acute alcohol poisoning against a background of chronic alcohol intoxication." This category of patients is also divided into mild, moderate and severe degrees of poisoning, while basic randomization is based on the following criteria: duration of binge drinking, level of consciousness, level of ethanol in the blood, level of free ammonia in the blood, blood lactate, liver enzymes (ALT, ACT , LDH) in the blood, the concentration of medium molecules in the blood [7, 13].

Many authors have noted that in patients during binge drinking, in almost 100% of cases, there are signs of cardiac dysfunction, primarily in the form of pronounced excitation of the autonomic nervous system (ANS). Almost all patients have episodes of sinus tachycardia during this period. In 25–30% of patients, atrial fibrillation is detected and in 10–15% - the phenomenon of depression of the contractile function of the left ventricle of the heart, up to the development of acute heart failure [7, 14]. The mechanism of alcoholic damage to the heart is associated with increased production during binge drinking and toxic effects on the myocardium of catecholamines. Excitation of the ANS in patients with alcohol intoxication is always correlated with arousal of the central nervous system (CNS) and is accompanied by such clinical symptoms as vomiting, fear of death, sweating, tremors of the extremities, aggressive behavior of patients, therefore ANS indices can also serve as predictors of complications from the central nervous system [7, 14].

Among the large number of methods for studying the ANS, attention is drawn to the mathematical analysis of the heart rhythm - cardiointervalography (CIG). In this case, the sinus node acts as a sensitive indicator of all changes in the control loops. This technique was developed and proposed by academician R.M. Baevsky et al., Which is based on the change in the variability of cardiointervals. The used mathematical and statistical indicators of the heart rate make it possible to judge the state of the sympathetic and parasympathetic parts of the autonomic nervous system. In this regard, cardiointervalography is considered as a universal method of functional research [15].

In recent years, a large number of studies related to the use of CIG in acute poisoning with psychopharmacological agents, carbon monoxide, cauterizing poisons have been published, which prompted us to study the role of this method in diagnosing the severity of alcohol intoxication [7].

The aim of the study: to study the parameters of the autonomic nervous system and cognitive functions in patients with acute alcohol poisoning of varying severity.

Material and Methods: This study included 312 patients with acute alcohol poisoning at the age from 28 to 55 years who were admitted to the Department of Toxicology and Toxicological Reanimation of the RRCEM against the background of chronic alcohol consumption in 2015-2019.

All patients underwent a comprehensive examination on the 1st, 2nd, 3rd day. We studied clinical and anamnestic data, the duration of binge drinking, the results of the analysis of ethanol in the blood, biochemical blood tests - ALT, AST, LDH, the level of free ammonia, lactate, medium molecules.

The classification offered by R.N Akalaev et al. (2019) was used as the basic criteria for the distribution of patients by severity, according to which the subjects were divided into 3 groups:

Group I consisted of 78 patients with severe alcohol intoxication.

Group II consisted of 166 patients with an average degree of alcohol intoxication.

Group III consisted of 68 patients with mild alcohol intoxication.

Patients with concomitant chronic diseases of the liver, heart, kidneys and central nervous system were excluded from the study [2].

Patients received a standard intensive care regimen, which included infusion therapy, vitamin therapy, sedation with benzodiazepines and antipsychotics.

In order to analyze the ANS, the following studies were carried out:

Study of hemodynamic function: heart rate, systolic and diastolic blood pressure (SBP and DBP), Kerdo's autonomic index (VI) according to the formula VI = (1 - D/P), where D is diastolic blood pressure, P - pulse rate per minute. The study of the heart rhythm analysis of cardiointervalography method (CIG) according to R.M. Baevsky (1986). For this purpose , we recorded cardiointervalograms at 100 intervals in lead II and manually calculated the indicators using the aforementioned method, and in 2019 similar calculations were performed automatically using the Cardiometer-MT apparatus (Mikard-Lana, Russia) in online mode. In this case, the following parameters were studied: Mo (mode), AMo (amplitude of the mode), SI (stress index) - in arbitrary units. All parameters were also studied on the 1st day from the date of admission.

The assessment of the severity of intellectual disabilities was studied using the MMSE scale for 10 positions, the FAB scale for 6 positions and the Reitan test on the 1st day.

Data processing was performed using Microsoft software and Excel spreadsheets.

Results and discussion. Baseline indicators in all examined patients indicate serious disorders of the homeostasis system resulting from alcohol abuse. At the same time, we noted that the severity of the patients' condition did not practically depend on the concentration of ethanol in the blood (Table 1). On the contrary, it was in patients with severe alcohol intoxication that the alcohol level was 1.5 and 1.35 times lower than in groups II and III (Table 1). This is apparently due to the suppression of the liver's ability to metabolize the next dose of alcoholic beverages during prolonged chronic abuse, which leads to a gradual decrease in their consumption.

Table 1. Ethanol concentration in blood in patients with alcohol poisoning (at admission), n = 312 (M ± m)

Analysis rate (normal)	I group n=78	II group n=166	III group n=68
Blood ethanol level (0-0.5 g/ l)	1,4±0,3	2,1±0,2*	1,9±0,3*

Note. * - p <0.01 compared with the group of severe patients

In the study of biochemical parameters, on the contrary, significant changes were noted in each group, which were most evident in the group with severe alcohol intoxication (table 2).

Table 2. Biochemical parameters in patients with alcohol intoxication (n = 312)

Indicator, units, norm	I group n=78	II group n=166	III group n=68
ALT, u/l, 0-42	246,2±41,2	184,2±23,4*	97,5±11,3*
AST, u/l, 0-37	195,7±32,1	137,5±16,5*	80,4±11,2*
LDH, u/l, 313-618	1242,6±79,6	889,1±75,2*	642,3±34,8*
Total bilirubin, μmol / l,, 8,55-20,5	37,0±3,2	24,2±3,7*	20,2±0,8*
Free ammonia, mcmol / l, 18-33	186,2±9,5*	99,4±11,5*	51,7±6,2*
Venous blood lactate, mmol / L, 0,9-1,6	5,2±0,5	3,3±0,2*	2,3±0,3*
Middle molecules (MM), optical density units 0,068-0,182	0,664±0,078	0,382±0,066*	0,230±0,022*

Note: * - p <0.05 compared with the group of severe patients.

Our observations showed that all patients with severe poisoning showed signs of toxic hepatitis, which was manifested by a significant increase in liver enzymes ALT, AST, LDH and bilirubin, exceeding the normal limit values in 5.4, 5.4, 1.8 and 1.7 times, respectively. In patients with an average degree of poisoning, we observed a moderate increase in the enzymes ALT, AST, LDH by 3.5, 3.0 and 1.4 times, respectively, and the level of bilirubin remained within the upper limits of the norm. In patients of group III, with a short binge drinking, we observed only a slight increase in ALT and AST (table 2).

The most interesting results were obtained in the study of the level of free ammonia and blood lactate (table 2). At the same time, the concentration of ammonia in the blood in severe patients exceeded the norm by 5.6 times, in patients with moderate intoxication by 3.0 times, even in those admitted with a mild degree by 1.5 times, which indicated a pronounced inhibition of the detoxifying function of the liver. The level of lactic acid showed the presence of tissue hypoxia in all patients with alcohol intoxication, in proportion to the duration of alcohol abuse, which was manifested by an increase in the level of lactate in group I patients 3.2 times higher than normal, in groups II and III by 2.0 and 1.4 times, respectively (table 2).

As for the medium molecules, in patients with severe poisoning, an increase of more than 0.6 density units was noted, which reflected the presence of severe endogenous intoxication (table 2).

In patients admitted with moderate poisoning, the changes in MM were much less evident, but, nevertheless, exceeded the upper limits of the norm by 1.7 times, respectively. In patients with mild poisoning, we observed a slight excess of this indicator.

Thus, from the data obtained, it follows that in case of mild poisoning, against the background of a short binge drinking, biochemical parameters were either within normal values, or showed a slight tendency to increase. In patients with moderate and severe poisoning, all indicators were several times higher than the upper limit of the reference values.

The study of ANS indices in three groups of patients (with severe, moderate and mild alcohol intoxication) revealed the development of hypersympathicotonia caused by an increase in the tone of the sympathetic part of the autonomic nervous system in proportion to the severity of intoxication (Table 3). This was characterized by an increase in the values of the parameters of the amplitude of the mode (AMo), stress index (SI).

Table 3. Indicators of the vegetative status of the organism in patients with acute alcohol intoxication (M ± M, n = 312)

Indicator, units, norm	I group n=78	II group n=166	III group n=68
SBP (120-130)	165,5±21,9	132,5±12,1*	125,5±11,8*
DBP (70-80)	102,1±9,1	91,2±7,9*	84±6,3*
Heart rate (65-90)	128,2±11,2	104,5±9,9*	96±6,8*
VI (0-0,1)	0,25±0,07	0,18±0,03*	0,12±0,0*4
Mo, sec (0,7-0,8)	0,57±0,03	0,584±0,02*	0,63±0,03*
AMo, % (25-30)	41,75±2,87	42,65±3,20*	36,31±2,3*
SI (stress index), units (30-60)	64,2±7,7	95,5 ±11,2*	167,8±14,5*

Note: * - p <0.05 compared with the group of severe patients.

At the same time, in patients with a severe degree of alcohol intoxication, such hemodynamic parameters as DBP, SBP, heart rate, Kerdo index exceeded the limit of normal values by 1.3, 1.2, 1.6, 2.5 times, and CIG indicators - Mo and AMo were 1.2 and 1.3 times lower, respectively, which indicated a pronounced tension of the compensatory mechanisms of the organism.

The study of cognitive functions on admission showed their depression in proportion to the severity of the patient's condition (Table 4). According to the screening of the level of intelligence on the MMSE scale, patients of groups III and II at admission were noted for mild and moderate cognitive impairments - 25.8 ± 2.1 and 23.31 ± 1.8 points, in dynamics the cognitive deficit was quickly practically stopped. As for the patients of group I, the MMSE scale indices for all positions were 1.4, 1.5 times lower than in groups II and III (Table 4).

Table 4. Indicators of cognitive functions in patients with acute alcohol intoxication of various severity degrees upon admission (n = 312)

Indicator units, norm	I group n=78	II group n=166	III group n=68
MMSE scale (points) (norm 28-30 points)	19,3±2,2	23,31±1,8	25,8±2,1*
FAB scale (points) (norm 16-18 points)	9,6±2,8	11,4±2,1	14,1±1,8*
Reitan test (norm up to 100 sec.)	Not determined	122,7±11	98,6±6*

Note: * - p <0.05 compared with the group of severe patients.

The analysis of intelligence on the FAB scale in patients with severe intoxication revealed violations of conceptualization and dynamic praxis. The total test result in patients of group III did not exceed, on average, 9.6 ± 2.8 points, which is 1.1 times lower than in group II and 1.2 times lower than in group I (Table 4).

As for the marker of hepatic encephalopathy - the Reitan test, according to this indicator, the best result was found in patients of group III who performed the test within the normal range - for 98.6 ± 6 seconds, patients of group II performed it somewhat longer - 1.2 worse than in group III. Patients with severe alcohol intoxication could not perform this test due to inadequate condition.

Thus, we observed a clear correlation between the level of free ammonia, lactate and the degree of inhibition of cognitive functions in alcohol poisoning against the background of chronic alcohol intoxication, which proves the important role of these metabolites in the development of alcoholic encephalopathy.

Subsequently, in 63 (80.7%) patients with a severe degree of alcohol intoxication, the development of alcoholic delirium was noted, while in patients with a moderate degree, this complication was observed only in 11 (6.5%), in patients with a mild degree degree of alcohol intoxication, delirium was not observed.

Conclusions.

1. In patients with alcohol intoxication, there is a decrease in cognitive functions in proportion to the severity of intoxication and the level of lactate, free ammonia.

2. Patients with a severe degree of alcohol intoxication develop pronounced intellectual impairments that require medical correction, with subsequent mandatory psychological rehabilitation.

3. For acute alcohol poisoning against the background of binge drinking, the development of hypersympathicotonia, caused by an increase in the tone of the sympathetic division of the autonomic nervous system, is characteristic.

4. Indicators of cardiointervalography can be used to diagnose the severity of alcohol intoxication and as predictors of alcoholic delirium.

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