Olesova L.D., Matveeva N.P., Mironov G.E., Krivoshapkina Z.N., Okhlopkova ED

Metabolic Changes in Patients with Alcoholism in Yakutia

ABSTRACT

The change of biochemical parameters of blood in patients with alcoholism was investigated. High activity of enzymes, reflecting reserve possibilities of an organism, showed a decrease of adaptation in 50% of patients with alcoholism. A significant change in lipid metabolism is associated with the acceleration of lipid peroxidation. Hypovitaminosis and decreased activity of antioxidant system are the basis for the recommendations to include in the rehabilitation program of higher doses of vitamins and antioxidants.

Keywords: alcoholism, metabolism, adaptation, pro- and anti-oxidants

INTRODUCTION

Human adaptation to extreme climatic factors of the North is accompanied by tension of regulatory mechanisms and manifested as metabolic changes of proteins, fats, carbohydrates, vitamins, macro-and micronutrients. As a result, a polar metabolic type occurs, directing an organism to a new level of homeostasis. Contribution of carbohydrates in energy metabolism becomes lower, whereas fat's (lipids) are higher [5]. Overlaying additional negative factors such as alcohol causes changes in a level of basic biochemical constants (total protein, albumin, glucose, cholesterol, urea, and creatinine), and increases the need for substrates to excessively activated Krebs Cycle (TCA cycle). Work homeostatic system requires regulation and participation of a number of enzymes for supporting an adequate level of the basic substrates . Therefore, the change in the activity of enzymes in blood reflects the nature of metabolic adaptation mechanisms, and each parameter of blood including enzymological aspartate, alanin aminotransferase, gamma glutamyl transpeptidas is a good indicator of the metabolic changes [1,6].

In chronic alcoholism ethanol oxidation is accelerated by 50% due to induction of cytochrome P450. The catalytic activity of the microsomal enzyme associated with the formation of reactive oxygen species - superoxydanionradical and hydrogen peroxide, which may under certain conditions be able to damage the DNA structure. For this reason, in patients suffering from chronic alcoholism, often children are born with genetic malformations. Therefore, the problem of alcoholism remains relevant not only in social terms (growth of disability, mortality, crime), but also in terms of preserving a healthy gene pool.

In this regard, assessment of metabolic changes in chronic alcohol intoxication in the North is not only of theoretical but also practical interest. Elucidation of the mechanism of acute and chronic effects of alcohol on the human body should allow the practice of medicine to solve problems in the diagnosis, prevention and treatment of alcoholism.

The Aim of the Study. To study changes of the basic biochemical parameters and the state of pro- and antioxidant system in chronic alcohol intoxication in the North.

MATERIALS AND METHODS

We examined 60 people with chronic alcoholism at the age of 25 to 67 years. Among them there were 50 men, women - 10. All patients were treated with drug dispensaries. The comparison group consisted of 40 healthy people

who are not alcoholics. Determination of activity glutamyl transferase (GGT), and aspartic alaninovoyaminotransferaz (AST, ALT), alkaline phosphatase (ALP), total protein level (ON), urea, cholesterol, triglycerides (TG), glucose, uric acid in serum were performed on an automatic biochemical analyzer Cobasmiraplus company LaRoche.

Enzymatic antioxidant system (AOS) was evaluated by the activity of superoxide dismutase (SOD), catalase, glutathione reductase (GR), glutathione peroxidase (GP), nonenzymatic AOC - at blood concentrations of ascorbic acid, uric acid and the total content of low molecular weight antioxidants (Lmao). The intensity of lipid peroxidation was assessed by the level of malondialdegide (MDA) end dien conjugates (DC). In addition, we determined a level of thiamine - vitamin B1 blood.

Statistical data processing was performed using the statistical software application package SPSS forWindows 17.0. Standard methods of variation statistics: Calculation of mean values, standard deviations, 95% confidence interval. Data in tables are presented as M ± m, where M - average, m – error of the mean values significance of differences between mean values was assessed using Student's t test and the Kolmogorov-Smirnov test. The probability of the null hypothesis is accepted at $p < 0,05$.

RESULTS AND DISCUSSION

The average concentration of total protein (TP) in patients was equal to 73,9 ± 0,55g / l and ranged from 62.7 to 86,1g / l. Total protein level below 70.0 g / l was found in 13% of patients below the optimal level (75g / l) was found in 71.6% of patients.

Direct correlation of total protein and urea (0,357; $p < 0.01$) shows their coordinated decrease or increase, because they are an objective criterion optimal ratio processes of anabolism and catabolism. The average level of urea amounted to 5,54 ± 0,24 mmol / l. In 53% of patients had higher levels of urea optimum value (5 mmol / L). In 3 patients we found depletion of metabolic reserve: increase in urea (> 9,19mmol / l) and total protein (> 86,1g / l) was accompanied by a non-adaptive hyperenzymemia (ALT> 100ME; AST> 290ME; GGT> 209ME). In fact, all relevant indicators enzymes activity in patients differed from the control values. Thus, the activity of enzymes in patients with chronic alcoholism is significantly higher than in healthy controls: ALT 4.2 times, AST 4.4 times, GGT 5.7 times, alkaline phosphatase 1.6 times (Figure 1). Moreover, the highest rates of enzymes activity are observed in age groups of 30 and 40 years. Moreover, we observed increased activity of AST in the age group up to 70 years, where de Ritis coefficient (the ratio of AST / ALT) is equal to 1.86 at norm of rate 1.3, which indicates strengthening catabolism (Fig. 2). Intensification of the activity of transferases shows pathogenic mechanisms of alcohol metabolic disease. Known as the most sensitive marker of alcohol in the 1 stage the increase in GGT activity under normal ALT and AST defected only 4 people (6.66%) [1,2,7]. Normal GGT activity was detected in 30% of patients. Interim GGT activity was 41-100ME in 35%, higher (from 101-200ME) in 16.7%, and very high (more 200ME) in 18.3% of patients with alcoholism. Amplification GGT activity to maintain glucose at a minimum acceptable level in terms of amino acids deficiency leads to waste first amino acid, and then somatic (skeletal muscle) and visceral (internal organs) pool proteins [6]. During the transition of alcoholism in the 2 stage the increase of AST activity, but not ALT is noted. Cordial relations type AST / ALT (greater than 1.5) was found in 45.6% of patients examined, and only 2 patients (3.5%) the ratio of AST / ALT corresponds to normal values, ie from 1.3 to 1.5. The metabolic change in patients with "cardiac" related AST / ALT is characterized by increased catabolic processes, in particular for the deamination of amino acids by mitochondria activation. Alcohol abuse produces excess of acetyl-CoA with inhibitory effect on glycolysis (via inhibition of pyruvate kinase) and simultaneously indirectly stimulates increase in AST activity (via activation of pyruvate) and the synthesis of fatty

acids. AST increase precedes the simultaneous or delayed increase of ALT, and this is reflected in the change (quantitatively different) coefficient de Ritis from "cardiac" to "hepatic" type in the amplification of anabolism due to activation of the glucose-alanine shunt (GASH). So the remaining 50.8% of the patients had "hepatic" type of de Ritis with a parameter lower than 1.3. Integration of carbohydrate and protein metabolism plays an important role in any adaptive response of the organism [2,4,7].

Long-term alcohol consumption leads profound loss of hepatocytes. Changes in the functional state of hepatocytes leads to disruption of lipid metabolism. The mechanism of occurrence of disease caused by alcohol, on the one hand, the "deposit" of fatty compounds in the liver [2,4], and on the other, - chemical aggressiveness of acetaldehyde, which is manifested in the strengthening of free radical lipid oxidation pathways [8].

Increased level of cholesterol and triglyceride in the blood the surveyed patients as of person suffering from chronic alcoholism, accompanied by an intensification of lipid peroxidation. At the patient examined by us level both the cholesterol and triglycerides in blood was 1.8 times higher than in normal ($p < 0,05$), which increases the chance of developing atherosclerosis. 100% of patients examined the contents of total cholesterol greater than its optimum value (5.0 mmol / l). Increased levels of cholesterol and triglycerides in the blood of persons suffering from chronic alcoholism cause the intensification of lipid peroxidation. In a group of patients the concentration of malonodialdegide (MDA) was 1.6 times (60%) and diene conjugates (DW) in 2 times higher than in healthy individuals, as evidenced by the direct correlation with total cholesterol levels of MDA (0.274; $p < 0.039$) (Figure 3).

Direct high rate of de Ritis with MDA (0.408; $p < 0.002$) and DC (0.554; $p < 0.000$), identified in patients with alcoholism, evidence of the negative impact of the intensification of lipid peroxidation metabolism. A significant increase in MDA level in patients with activation of low molecular weight antioxidants (LMAO). Mid Lmao equal 0,115mkmol / ml and was 2.8 times higher than in healthy individuals. The positive relationship between MDA and LMAO at 0.438 ($p < 0.01$). Shows a negative correlation with the activity of SOD (- 0.282; $p < 0.042$) as well as the activity of SOD, depleting superoksidanionradikal actually did not differ from that in the control group (Figure 3).

A significant increase in the levels of diene conjugates in the survey group target group was accompanied by an increase in the activity of catalase, neutralizing hydrogen peroxide, as compared with a control group ($p < 0,05$).

It is the indirect evidence of activation of microsomal oxidation in a liver due

to induction of P450 cytochrome as catalytic activity of the enzyme is connected with the formation of hydrogen peroxide. Positive correlation Lmao and catalase at 0.468 ($p < 0.01$) shows a parallel activation nhe unit of enzymatic antioxidants at the exprense catalase.

The activity of the low molecular weight main endogenous antioxidant - glutathione reductase (GR) was 1.8 times lower than in healthy persons. GR restores glutathione - the main low molecular weight endogenous antioxidant, which is particularly high concentration in red blood cells and mucous internal organs.

Glutathione peroxide (GP) is an enzyme that breaks down hydrogen peroxide. The activity of the enzyme which is localized in the membrane of the erythrocytes, in patients with alcoholism, there was 1.5-fold higher than in the control group of healthy subjects. Uric acid level (an endogenous antioxidant) in the blood of individuals with chronic alcoholism, was 20% higher.

Long-term consumption of alcohol violates providing the body with vitamins end causes hypovitaminosis [3]. When assessing vitamin organism provision in patients with chronic alcoholism detected very low levels of ascorbic acid and vitamin B1 (lower than in healthy 1.6 times and 1.4 times, respectively) despite the fact that these vitamins are incorporated in rehabilitation. It is known that in the Nord of most of the population is experiencing gipovitaminoz

associated not only with insufficiend receipt food, but with increased requirements for vitamin at low temperatures [5].

Ascorbic acid is a powerful antioxidant. The average content of vitamin C was equal to 0,37 ± 0,02mg%, which is below the normal value. Hypovitaminosis C below 0.4% was detected in 75% of patients. Only 5 patients had an adequate content of ascorbic acid in the body. V1 vitamin deficiencies in patients suffering from chronic alcoholism, can be connected not only to increased utilization of these vitamins in the conversion of glucose in the body, but with malabsorption in the gastrointestinal tract. The glucose level in patients treated with in the control group were administered daily parenteral glucose actually no different from that group and corresponded 4,4±0,7 mmol/l, whereas for healthy persons intravenous glucose significantly increases its concentration in blood. Comparison of this fact with low thiamine levels confirms the well-known fact that long-term alcohol consumption disrupts energy processes related to carbohydrate metabolism.

Constancy of glucose provides catabolism intensive (marker AST), anabolism (marker ALT) level amino acids (marker GGT) and subject to the laws of biochemical homeostasis [1,8].

Thus, long-term toxic effects of ethanol in extreme climatic conditions is a negative factor destabilizing homeostasis. More than half of the surveyed patients there is an increase in blood levels of enzymes (AST, ALT, GGT), reflecting the metabolic adaptation mechanisms and provide for constancy of basic biochemical parameters. In 50% of patients with alcoholism low coefficient de Ritis shows a decline in adaptive reserves. Patients undergo a noticeable change in lipid metabolism and the body's supply of vitamins (vitamin deficiencies). This is probably due to the fact that at high latitudes metabolic adaptation is associated with increased lipid metabolism and endemic vitamin deficiency. Dysregulation of lipid metabolism characterized by hypercholesterolemia and gipertriglitserinemiey. The presence of dyslipidemia contributes to the activation of lipid peroxidation (0.274; $p < 0.039$). The increase in lipid peroxidation products is accompanied by a modification of proteins and peptides: diene conjugates and malon dialdegid can form Schiff bases with amino radicals, damaging the structure of the enzyme, and thus violate the metabolism, as evidenced by the high positive correlation coefficient de Ritis (AST / ALT) with malonaldehyde (0.408; $p < 0.002$) and diene conjugates (0.554; $p < 0.000$). Patients with a higher steady-state levels of lipid peroxidation products, revealed a lack of compensatory activation of the enzymatic antioxidant system. This fact is the basis for recommendation of inclusion of higher doses of vitamins, antioxidants in a rehabilitation program at alcohol intoxication.

References:

1. Biochemistry and Alcoholism (SU): typical clinical and biochemical syndrome in chronic alcohol intoxication / IM Roslyi, SV Abramov, VR Agaronov et al. // Problems of Addiction. - 2004, №5.- S.46-56.

2. Goryushkin I.I. Alcoholism: mechanisms of changes in the activity of gamma-glutamyl transferase and aspartate aminotransferase and the ability to prevent fatty liver /I.I. Goryushkin // Questions Addiction, 2001, № 3.

3. Kirpich IA. Causes and clinical effects of metabolic disorders vitamins in chronic alcoholism / IA Kirpich, PI Sidorov, AG Soloviev. - Questions narkol., 1997, №4. - S. 89-94.1. - pp. 6 -9.

4. Panin L.E. Energetic aspects of adaptation L., 1978.190 p.

5. Olesova L.D. Vitamin C level assessment in an organism of inhabitants of Yakutsk / L.D. Olesova, G.E. Mironova, L.I. Konstantinova // Food and nutrition: problems of safety and correction when forming a healthy lifestile. – SPb, 2012. - P.254-256.

6. The desired VP Mechanisms and clinical manifestations of the toxic effect of alcohol /V.P. Desired / Proc .: Addiction Guide, ed. NN Ivanets. - M .: Medpraktika. - 2002, №1. - S.74-93.

7 . Roslyi, II Alcoholism: The Collapse of protein metabolism //oholismhls.ru/2013/09/21/ alkogolizm-i-izmeneniya-krovi /

8. Lieber, C. S. Role of oxidative stress and antioxidant therapy in alcoholic and nonalcoholic liver diseases / C. S. Lieber //Adv. Pharmacol., 1997, №38.-P.28.

Authors

1. Olesova Luibov Dygynovna, PhD, Head. laboratory biochemical mechanisms of adaptation FGBU "Yakut Scientific Center complex medical problems," 677010, Yakutsk, Sergelyakh highway, 4; 8 (4112) 447857; oles59@mail.ru

2. Matveeva Nurguyana Petrovna, Ph.D., Senior Scientist FGBNU "Yakut Scientific Center of complex medical problems", 677010, Yakutsk, Sergelyakh highway, 4, 8 (4112) 447 857; nyusakha@mail.ru

3. Galina Egorovna Mironov, Ph.D., Professor, Department of Macromolecular Compounds, Organic and Biological Chemistry FGBNOU VPO "North-Eastern Federal University. MK Ammosova. " 89243685610; mirogalin@mail.ru

4. Krivoshapkina Zoya, PhD, Senior Scientist of studying the mechanisms of adaptation FGBU "Yakut Scientific Center of complex medical problems" SB RAMS, 677010, Yakutsk, Sergelyakh highway, 4; 8 (4112) 447857; zoyakriv@mail.ru

5. Okhlopkova Elena Dmitrievna, Head. Laboratory FGBU "Yakut Scientific Center complex medical problems," 677010, Yakutsk, Sergelyakh highway, 4; 8 (4112) 447857;

Fig.1. Indicators enzyme (ME) in the blood of patients with alcoholism

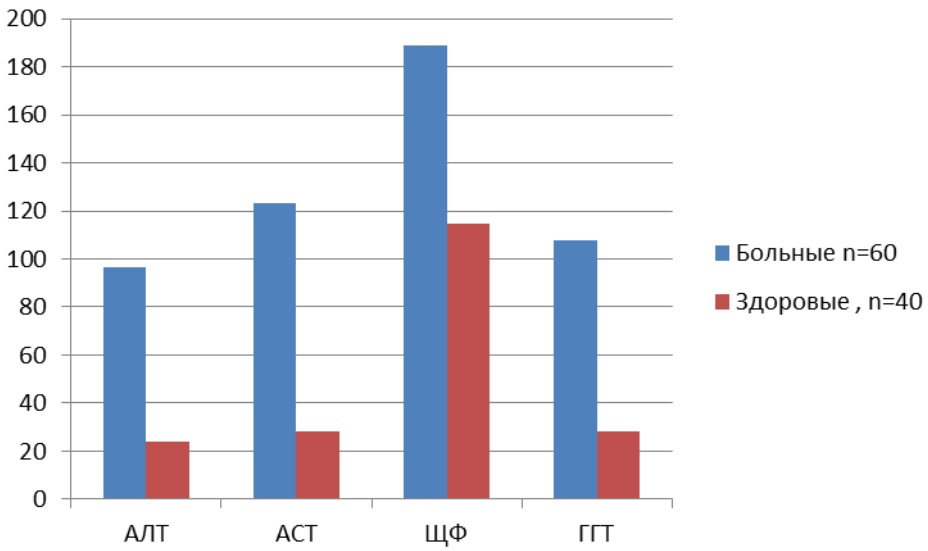

Рис. 2. Показатели активности ферментов (ME) в зависимости от возраста

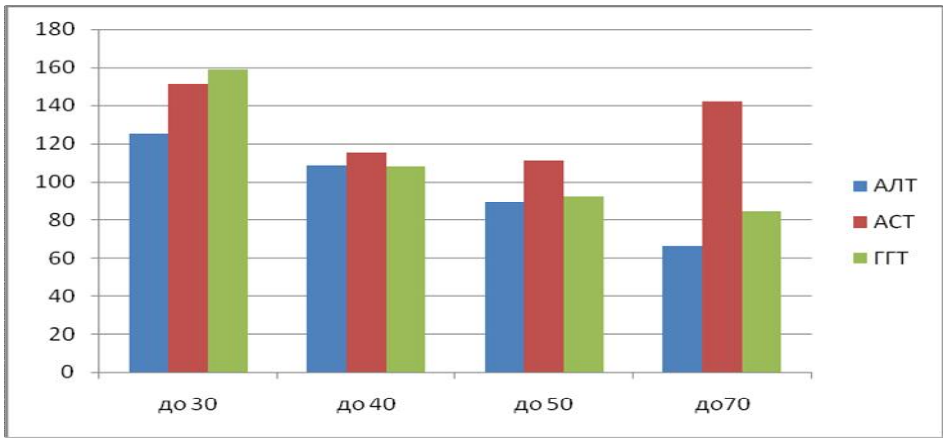

Fig.3 condition lipids and pro-and anti-oxidant system in patients