**Activity of Na+, K+-ATPase of the rats liver and brain cell plasmatic membranes in chronic alcohol intoxication and after administration of zinc acetate**

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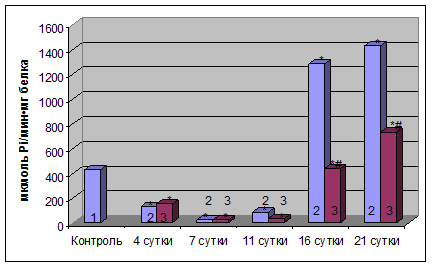
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**Introduction**. Development of alcoholism is based on deep changes of the structure and functions of plasmatic membranes of various cells, leading to the functional disorder of membrane-bound enzymes. Such enzymes may act as biological targets, which, on the one hand stipulate the ethanol`s deleterious effect, and on the other hand – adaptation of the organism to alcoholization.

Development of alcohol intoxication is known today to be accompanied by Zinc deficit in a number of organs in humans and animals. For zinc deficit correction, its salts are used, among which zinc acetate is characterized by the lowest toxicity [8]. That is why the object of our work was to determine the influence of zinc acetate to activity of Na+,K+-АTPase in the rats liver and brain cell plasmatic membranes in chronic alcohol intoxication.

**Materials and methods.** The tests were conducted in white outbred male rats of 180-200 g body weight, fed with the standard food ration of the vivarium with a free access to water. 40° ethyl alcohol was administered orally by 2 ml per 100 g of the animal body weight per day. The animals were divided into 3 groups. The 1-st group – control animals; the 2-nd group – rats with a chronic alcohol intoxication, caused according to the method of M. Kh. Khalilov and Sh. A. Zakikhordzhaev [7]; the 3-d group – rats with a chronic alcohol intoxication, additionally administered zinc acetate in the dose of 2 mg per 100 g of the animal body weight [8]. The animals were decapitated on the 4, 7, 11, 16 and 21 days. The total fraction of hepatocytes in rats was obtained according to the modified method [5]. Obtaining of the fractions of the rats liver and brain cell plasmatic membranes, as well as determining activity of Na+,К+-АТPase was conducted according to [6]. The protein concentration was determined according to method [9]. Statistical processing of the obtained data was performed by the generally accepted methods of the variational statistics subject to 7—12 repeats (M±m, n=7–12) [1].

**Results**. In the course of investigation of ethanol influence on the activity of Na+, K+-AТPase of plasmatic membranes of the rats hepatocytes, we registered its increase on the 4-th (by 25%) and 7-th day (by 50%), decrease on the 11-th day (by 36.4%) and repeated increase of the enzyme activity for the 16-th day (in 2.5 times) and 21-st day (in 5 times) of the experiment in comparison with the control (Fig. 1).



***Fig. 1. Activity of Na+, К+–АТPase of plasmatic membranes of the rats hepatocytes in the chronic alcohol intoxication and administration of zinc acetate (1 – control; 2 – ethanol; 3 – ethanol + zinc).***

\* – Р≤0.05 in comparison with the control

#– Р≤0.05 in comparison with the experimental model

µmol PI/min-mg of protein

Control

The 4-th day

The 7-th day

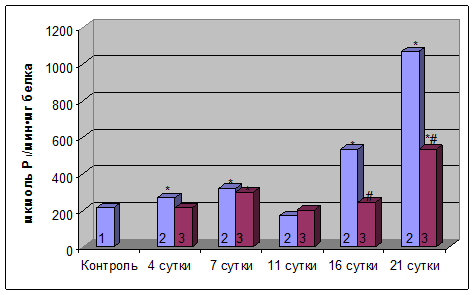
The 11-th day

The 16-th day

The 21-st day

Administration of zinc acetate in the chronic alcohol intoxication led to increase of activity of the given enzyme of the plasmatic membranes of the rats hepatocytes on the 7-th (by 40%) and 16-th day (by 15%) in comparison with the control values, whereas on the 4-th and 11-th day such value did not differ from the control one. During the last stage of the investigation (the 21-st day) activity of Na+, К+-АТPase was 2.5 times higher in comparison with the control (Fig. 1).

Thus, zinc acetate leads to decrease of ethanol influence on Na+, К+-АТPase of plasmatic membranes of the rats hepatocytes, decreasing such enzyme activity. In administration of zinc acetate there is a decrease of activity of Na+,К+-АТPase in comparison with the respective stages in the conditions of alcohol intoxication at the initial stages (on the 4-th and 7-th day – by 20% and 7%, respectively), as well as at the later stages of the experiment (on the 16-th and 21-st day – by 54% and 50%, respectively), whereas on the 11-th day of the experiment there is an insignificant increase of the enzyme activity.



***Fig. 1. Activity of Na+, К+–АТPase of plasmatic membranes of the rats hepatocytes in the chronic alcohol intoxication and administration of zinc acetate (1 – control; 2 – ethanol; 3 – ethanol + zinc).***

\* – Р≤0.05 in comparison with the control

#– Р≤0.05 in comparison with the experimental model

µmol PI/min-mg of protein

Control

The 4-th day

The 7-th day

The 11-th day

The 16-th day

The 21-st day

Unlike hepatocytes, in the brain cells in the chronic alcoholization we detected a decrease of activity of Na+,K+-AТPase of the plasmatic membranes at the earlier stages of investigation on the 4-tg, 7-th and 11-th day (in 3, 16 and 5 раз, respectively) in comparison with the control. Then there was a fast growth of the enzyme activity on the 16-th and 21-st day of the experiment (in 3 and 3.3 раза, respectively) in comparison with the control (Fig. 2).

In the chronic alcohol intoxication administration of zinc acetate led to a decrease of activity of the investigated enzyme of the rats brain cells plasmatic membranes on the 4-th, 7-th and 11-th of the experiment in comparison with the control (in 3, 20 and 15 раз, respectively). On the 21-st day the activity of Na+,K+-AТPase increased by 1.8 times in relation to the control values. In comparison with the respective terms of the ethanol activity, the enzyme activity on the 11-th, 16-th and 21-st was respectively lower in 3, 2.8 and 1.8 times lower.

Na+, K+-AТPase (АТP-phosphohydrolase, EC 3.6.1.37) is an integral protein of the cells plasmatic membranes, implementing the energy-dependent oppositely directed transfer of ions of Na+ and K+. Na+, K+-AТPase is involved in many cell functions and processes, related to the existence of ionic gradients, in particular, in provision of the electrical excitability of the nerve and muscle tissues [12]. At the same time it has been shown that in various pathologic conditions there is its inactivation [10]. Its reason may be either direct action on the enzyme or structural changes in the membrane (for example, as a result of free-radical processes in cerebral ischemia, sublethal ionizing irradiation), or multi-level disorders of the tissue-specific cell activity regulation mechanisms and expression of isoenzymes of Na+,K+-AТPase in various chronic pathologic conditions [3].

Ethanol is known to cause a decrease of membrane fluidity. According to the data of a number of authors it is accompanied by intensification of the active transmembrane transportation of Na+ as a result of increase of the number of carriers and their similarity growth to such an ion, as well as stabilization of intra- and extra-cellular exchange of Ca2+.

The data available today in relation to ethanol influence on activity of Na+, K+-AТPase are contradictive. Thus, while studying a direct ethanol action on Na+, K+-AТPase in the *in vitro* experiments, inhibition of the enzyme activity has been shown [11]. Sensitivity of Na+, K+-АТPase to ethanol activity *in vitro* depends on the integrity of the protein-lipid complex of the enzyme in membrane [4]. Besides, on its phospholipid surrounding, in particular acid phospholipids, ensuring formation of the negative charge on the membrane surfaces, which stipulates repulsion between the latter ones and attraction of polycationic proteins [2]. The data we received on the contents of phospholipids in the ethanol influence and their correction in administration of zinc acetate may be one of the factors of the enzyme activity changes shown by us.

**Conclusions**. Thus, we have shown the increase of activity of Na+, K+-AТPase of the rats liver and brain cells plasmatic membranes in the chronic alcohol intoxication development dynamics. Administration of zinc acetate led to a decrease of activity of Na+, K+-ATPase. Subject to the obtained results, it is possible to conclude on the perspective of its further studying for the purpose of its use for correction of metabolic disorders, which can be a basis for developing new medical anti-alcohol products.

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