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REDUCTION OF ACUTE ETHANOL TOXICITY BY ZINC SULFATE

A. B. Kampov-Polevoi and A. V. Skal'nyi

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Chronic alcoholization of man and animals leads to the development of symptoms of zinc deficiency, associated with lowering of the Zn^{++} concentration in the blood, liver, and brain [5, 9, 10]. Experimental [5, 6] and clinical [5, 10] investigations have demonstrated positive results from the use of zinc salts to correct disorders induced by chronic alcohol intoxication. The therapeutic effect of zinc salts is usually associated with its effect on activity of certin enzymes (alcohol dehydrogenase, alkaline phosphatase, aminotransferases, etc.), on neurotransmitter metabolism, and on lipid peroxidation. The use of small (from 5 to 50 μg/kg) doses of zinc sulfate and chloride may also antagonize the acute toxic effects of ethanol and increase the survival rate of mice receiving lethal doses of alcohol [6, 8, 13].

The strongest protective effect against acute alcohol intoxication (AAI) has been observed after preliminary administration of fractional doses of zinc preparations [6, 8].

However, although the spectrum of action of zinc preparations includes a marked antialcoholic effect, the possibility that they may have a sobering effect has not hitherto been studied.

The aim of this investigation was to study the possibility of reducing the narcotic and acute toxic action of ethanol by administering zinc sulfate to animals with alcohol intoxication.

EXPERIMENTAL METHOD

Experiments were carried out on 260 noninbred male albino mice weighing 18-24 g, divided into groups with 17-32 animals in each group. The investigations were carried out in accordance with the technical recommendations of the Pharmacological Committee of the USSR [1]. The acute toxicity of ethanol (LD_{50}) was studied first and was shown to be 9.9 g/kg for this population of mice. In the experiments of series I, 30 min after intraperitoneal injection of 25% ethanol solution in a dose of 9.9 g/kg, a solution of analytically pure $ZnSO_4 \cdot 7H_2O$ in doses of 100, 50,

Laboratory for the Search for and Study of Agents for the Prevention and Treatment of Drug Addiction, Research Institute of Pharmacology, Academy of Medical Sciences of the USSR. Department of Rehabilitation of Children with Cerebral Paralysis, V. P. Serbskii All-Union Research Institute of General and Forensic Psychiatry, Ministry of Health of the USSR, Moscow.
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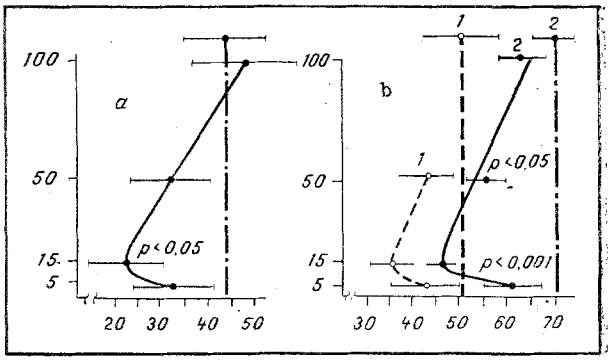

Fig. 1. Changes in mortality (a; in %) and duration of ethanol narcosis (b; in min) in mice with AAI under the influence of biotic doses of zinc sulfate (X ± σ). Ordinate, doses of zinc sulfate, μg/kg. Zinc sulfate injected 15 min (1) and 30 min (2) after narcotic dose of ethanol.

15, and 5 μg/kg or deionized water (control) was injected intraperitoneally into the mice. The number of animals alive and dead was recorded after 24 h. In the experiments of series II, mice were given an intraperitoneal injection of ethanol in a dose of 5.3 g/kg, which as preliminary experiments showed, is the narcotic dose for the given population. The animals were then divided into three groups: animals of group 1 received zinc sulfate in the same doses as in the experiments of series I, 15 min after injection of ethanol, animals of group 2 received zinc sulfate 30 min after ethanol, and mice of group 3 recieved deionized water. The duration of ethanol narcosis was recorded. The results were subjected to statistical analysis with calculation of the coefficient of correlation and Student's t test.

EXPERIMENTAL RESULTS

As Fig. 1 shows, zinc sulfate had a protective effect when administered 30 min after a toxic dose of ethanol, and this effect was dose-dependent. For instance, in a dose of 100 μg/kg body weight zinc sulfate did not affect the survival rate of mice with AAI, whereas in doses of 50, 15, and 5 μg/kg (calculated as the metal) it increased the survival rate of the animals by 11.6, 21.1, and 10.4%, respectively.

Zinc sulfate also affected the duration of the side position after administraiton of a narcotic dose of ethanol. (Fig. 1b), i.e., it had a definite sobering action. For instance, when zinc sulfate was injected in a dose of 15 μg/kg 15 and 30 min after the onset of ethanol narcosis, the duration of narcosis was shortned by 16.2 and 23.7%, respectively. Doses of 100, 50, and 5 μg/kg had no such action.

Thus the positive effect of zinc sulfate is most marked when given in an average physiological dose (15 μg/kg), in agreement with the concept of zonality of the biological action of trace elements (biotics) [2]. According to Venchikov [2], the maximal biological action of trace elements is observed when they are used in physiological (of the order of 10^{-6} mole/kg) and pharmacotoxic (10^{-4}-10^{-3} mole/kg) concentrations, between which there is a so-called "zone of inaction." This observation is confirmed also by our previous data showing that the onset of alcohol motivation can be prevented in rats by zinc sulfate in biological concentrations [4].

In our opinion, the positive effect of zinc sulfate in AAI may be due, besides to changes in ethanol metabolism, to the effect of zinc ions in physiological concentations on GABA synthesis and utilization in the CNS [11, 12].

The ability of zinc sulfate, administered in physiological concentrations during AAI to reduce the mortality among animals, and also shortening of the duration of ethanol narcosis by the action of this compound, demonstrated for the first time, enable the use of physiological (biotic) doses of zinc to be recommended in the combined treatment of acute alcohol poisoning; they also provide a basis for further research aimed at the use of zinc compounds in medical practice.

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