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EFFECT OF LITHIUM NICOTINATE AND TETURAM ON THE COURSE OF SOME BIOCHEMICAL PROCESSES IN "ALCOHOLIC" RATS WITH INFECTIOUS-INFLAMMATORY LESIONS OF THE KIDNEYS

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KEY WORDS: lithium nitrate; teturam; experimental alcoholism; infectious-inflammatory lesions of the kidneys.

Infectious-inflammatory lesions of the kidneys are commonly associated with alcoholism [6, 9, 11]. There are twice as many urologic patients among alcoholics as among patients with any other disease [10]. An important problem which faces psychiatrists and nephrologists is therefore the search for and rational use of remedies which will not only have a marked depressant action, but will also benefit the course of infectious-inflammatory lesions of the kidneys in alcoholism. The writer showed previously that the new antialcoholic agent lithium nitrate (litonit), unlike teturam (disulfiram), increases the immunoglobulin and nonspecific antibody titers, stimulates release of cationic proteins from leukocytes of the blood and urine, and alleviates morphological disturbances in the kidneys.

The object of this investigation was to study the effect of lithium nitrate and teturam on the course of certain biochemical processes in the kidney tissues of infected "alcoholic" albino rats. Biochemical parameters which not only reflect the effectiveness of antialcoholic agents [5], but also characterize the development of inflammation, tissue damage, tissue function, and resistance to the introduced pathogenic microflora, were investigated, namely: activity of sorbitol dehydrogenase and catalase, intensity of lipid peroxidation (LPO) [3, 8, 14].

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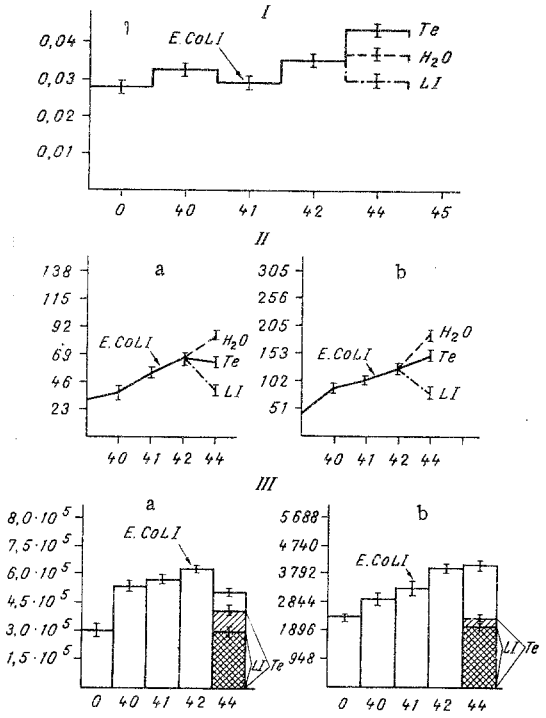

Fig. 1. Dynamics of changes in some biochemical parameters in "alcoholic" (taking alcohol for 40 weeks) rats against the background of infection with E. coli and administration of drugs. Abscissa, duration of experiment (in weeks). I) Sorbitol dehydrogenase activity (in millimoles/mg protein/min); II) catalase activity: a) in kidneys (in micromoles/mg protein/min), b) in blood (in micromoles/mg protein/min); III) intensity of LPO: a) in kidneys (in micromoles/g), b) in blood (in micromoles/liter). Lithium nitrate (Li) and teturam (Te) in injected in a dose of 10 mg/kg daily for 2 weeks.

EXPERIMENTAL METHOD

Experiments were carried out on 250 noninbred albino rats weighing 200-250 g. The "alcoholic" animals, selected by the method in [2], were given free choice of ethanol for 40 weeks. Infectious-inflammatory lesions in the kidneys were produced by a single intravenous injection of a suspension of a 24-hour culture of Escherichia coli (strain O_{III}) in a dose of $3 \cdot 10^9$ bacterial cells into the albino rats ("alcoholics" 10 months old). Sorbitol dehydrogenase and catalase activity and the intensity of LPO were studied in the kidneys and blood before the beginning of alcohol administration, at the 40th week of ethanol consumption, and 7 and 14 days after infection of the "alcoholic" rats, and at the end of a 14-day course of treatment with lithium nitrate and teturam, given in average therapeutic doses. The control group consisted of 10 intact albino rats infected with the same strain of E. coli under similar conditions. The lipid peroxide level was judged by the concentration of malonic dialdehyde (MDA) [15]; sorbitol dehydrogenase activity was investigated by the method in [1] and catalase by the method in [7].

EXPERIMENTAL RESULTS

After alcohol administration for 40 weeks sorbitol dehydrogenase activity of the kidneys was found to be increased (Fig. 1). Activity of the enzyme rose by 18.8% (experiment 0.0329 ± 0.0021 millimole/mg protein/min, control 0.0277 ± 0.0031 millimole/mg protein/min, $P < 0.05$). Catalase activity was increased simultaneously in the kidneys (by 16.9%) as also was the intensity of LPO (by 89.3%). A similar pattern was observed in the blood.

Injection of E. coli into "alcoholic" rats led to a marked change in the parameters studied. For instance, 1 week after infection catalase activity in the kidneys was increased by 77.0% and in the blood by 37.7%. The intensity of free-radical oxidation also increased substantially both in the kidneys and in the blood. Sorbitol dehydrogenase activity in this case was reduced a little (by 10.9%). On the 15th day after infection an even greater increase in catalase activity and in the intensity of lipid peroxidation was observed. By that time sorbitol dehydrogenase activity also showed a significant increase (by 21.9%) and its level was 1.3 times higher than initially (Fig. 1).

Lithium nitrate and teturam, injected into the infected "alcoholic" rats, had opposite actions on the kidneys of the experimental animals. Catalase activity in the kidneys and blood was 1.7 times lower in the animals receiving lithium nitrate than in those not receiving the compound. After injection of teturam no decrease in catalase activity was found in the kidneys, and in the blood it was significantly increased by 17.2%. Under the influence of both drugs the intensity of LPO was reduced, but the change was more marked on account of lithium nitrate (Fig. 1). Sorbitol dehydrogenase activity in the kidneys under the influence of lithium nitrate and teturam showed different changes. Lithium nitrate caused normalization of the activity of the enzyme, whereas teturam caused a further increase. If the sorbitol dehydrogenase activity of the kidneys on the 15th day after injection of E. coli is taken as 100, after administration of lithium nitrate its value fell by 17.8%, whereas after teturam it rose by 17.9%.

Infection of intact rats with E. coli caused no significant biochemical changes.

Alcohol administration to rats for 40 weeks thus caused an increase in sorbitol dehydrogenase and catalase activity and in the intensity of LPO in the experimental animals, which was particularly marked in the kidneys. These parameters reflect the level of renal tissue function and the degree of toxic damage to the organ and, consequently, susceptibility to a pathogenic agent. Activation of the sorbitol-dehydrogenase, catalase, and peroxidase systems is evidently the result of the toxic action of ethanol and its metabolic products on the kidneys, and is evidence that the renal tissue is predisposed to the penetration of infection in alcoholic toxication. This hypothesis is confirmed by the fact that when E. coli is injected into "alcoholic" rats a sharp increase is observed in the intensity of free-radical oxidation in the kidneys, accompanied by increased activity of catalase and sorbitol dehydrogenase [3, 13].

Administration of lithium nitrate to rats with developing infection reduced sorbitol dehydrogenase and catalase activity and the intensity of lipid peroxidation. Since normalization of these parameters is the result of improvement of the course of metabolic processes [8, 12] in the renal tissues, and also is evidence of enhancement of the toxic effect of ethanol and its metabolic products [4], it can be concluded that lithium nitrate has a beneficial effect on the kidneys. On account of this, there is evidently an improvement in the course of the infectious-inflammatory processes in the kidneys during antialcoholic treatment with lithium nitrate. Teturam had no such effect. On the contrary, it led to an increase in the renal sorbitol dehydrogenase and catalase activity. It can be postulated on the basis of these results that teturam potentiates the toxic action of alcohol on the kidneys.

The results of these experiments are evidence of the beneficial effect of lithium nitrate on the kidneys and they show that its use is indicated for the pathogenetic treatment of infectious-inflammatory lesions of the kidneys in alcoholism. Further research in this direction is promising.

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LYMPH FLOW RATE AND PROTEIN-ELECTROLYTE COMPOSITION OF THORACIC DUCT LYMPH IN EXPERIMENTAL ACHOLIA

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Acholia is accompanied by changes in many of the organs and systems of the body [2, 6]. The bile deficiency adversely affects the state of the digestive organs above all. It has also been shown that the composition and quantity of lymph flowing along the thoracic duct (TD) vary by a greater degree than the peripheral blood depending on the metabolic changes taking place in organs of the gastrointestinal tract [5]. In the investigation described below, the state of the blood and lymph circulations and also the protein and electrolyte composition of the lymph in TD were studied in experimental acholia.

EXPERIMENTAL METHOD

Experiments were carried out on 14 cats of both sexes weighing 2.5-3.5 kg. The animals were divided into two groups: 1) control animals (n = 8), 2) cats with experimental acholia (n = 6). A model of acholia was created by introducing a polyethylene tube in the proximal direction into the bile duct. The distal portion of the bile duct was ligated near the point where it enters the duodenum. The end of the tube was exteriorized on the anterior abdominal wall. Lymph was obtained from the experimental animals by cannulation of TD at the point where it enters the mouth of the jugular vein (under thiopental anesthesia). The rate of the lymph flow was determined by measuring the volume of lymph (in ml/kg body weight) escaping from TD through the cannula in 1 min. The central venous pressure (CVP) was determined by means of Waldman's apparatus in the posterior vena cava. Investigations on animals of the experimental group were carried out on the 20th day of production of experimental acholia. The animals were killed by injection of a lethal dose of the anesthetic.

EXPERIMENTAL RESULTS

Acholia was shown to be accompanied by marked changes in the lymp flow and also in the electrolyte and protein composition of the lymph (Table 1). The rate of lymph flow in the animals with acholia was only half of that in the control. Concentrations of protein and K^+ in the lymph were reduced in acholia. Disturbance of the lymph flow rate in acholia was accompanied by marked hemodynamic disturbances: depression of the contractile function of the myocardium (CFM) and hypotension [7], a decrease in cardiac output (CO) and CVP [8]. In animals with acholia, CVP was almost 3 times lower than in the control.

The state of CFM was studied after 20 days of acholia (Table 2). The heart rate of these animals decreased from the 1st to the 10th occlusion of the aorta. A progressive fall of arterial pressure also was observed in animals with acholia, from initial hypotension. The maximal pressure (P_{max}), as an important pa-

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