INDICATIONS FOR THE USE OF LITONIT IN COMBINATION TREATMENT OF COLIGENIC NEPHRITIS IN ALCOHOLISM

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The development of rational methods of treatment of infectious inflammatory conditions of the urinary tract when renal pathology is associated with chronic alcoholism is a little studied aspect of modern urology and nephrology [5, 9, 10]. The tactics of combination treatment of infectious inflammatory lesions of the kidneys, as they now exist, based on the use of antibacterial and anti-inflammatory drugs, have little effect in such cases. This is due primarily to the fact that alcohol itself, and also the antialcoholic agents commonly used (aversion and sensitizing therapy) considerably depress the immunologic protective and reactive processes and also depress function of the kidney and its resistance to inflammation.

The aim of this investigation was an experimental study of the possibility of using litonit (lithium nicotinate), which has marked depressant properties and has a corrective effect on tissue metabolism [2], in the combination treatment of alcohol-induced coligenic inflammation of the kidneys.

EXPERIMENTAL METHOD

The state of the immunologic protective properties of the body and renal function was judged by determining the absolute and relative concentrations of oxidized and reduced forms of nicotinamide coenzymes and levels of immunoglobulins of the A, G, and M classes. Experiments were carried out on 250 noninbred male albino rats weighing initially 180-200 g. "Alcoholic" animals, selected by the usual methods, were given ethanol for 10 months (40 weeks) under free choice conditions. Infectious inflammation of the kidneys was induced by giving a single intravenous injection of a suspension of a 24-h culture of *Escherichia coli* (Serotype OIII) in a dose of $3 \cdot 10^9$ bacterial cells to the "alcoholic" animals. Concentrations of oxidized and reduced forms of nicotinamide coenzymes and also the ratio betwen them were studied in the kidneys and blood before the beginning of alcoholization, at the 40th week of ethanol consumption, 7 and 14 days after infection of the "alcoholic" rats, and at the end of a 14-day course of treatment by the method in [12]. Litonit was injected in a dose of 10 mg/kg. Serum concentrations of IgA, IgG, and IgM were determined at the same times of the investigation. The control group consisted of 10 intact rats, infected with the same strain of *E. coli* under similar conditions. The immunoglobulin levels were estimated by the method in [13].

EXPERIMENTAL RESULTS

Chronic alcohol consumption caused an increase in the concentrations of oxidized forms of nicotinamide coenzymes in the blood, but the level of reduced forms remained unchanged. Prolonged ethanol consumption led to an increase mainly of reduced forms of $NADP^+$ in the kidneys, accompanied by a significant fall in the $NADP^+/NADPH$ ratio under these circumstances.

A different picture was observed after infection of the "alcoholic" animals with the strain of *E. coli*. Addition of infection caused a marked decrease in the concentrations of oxidized and reduced forms of nicotinamide coenzymes and of the ratio between them. The greatest changes in these parameters were observed on the 14th day after injection of the pathogen. The $NADP^+$ concentration in the blood, for example, was lower than in the control by 25 and

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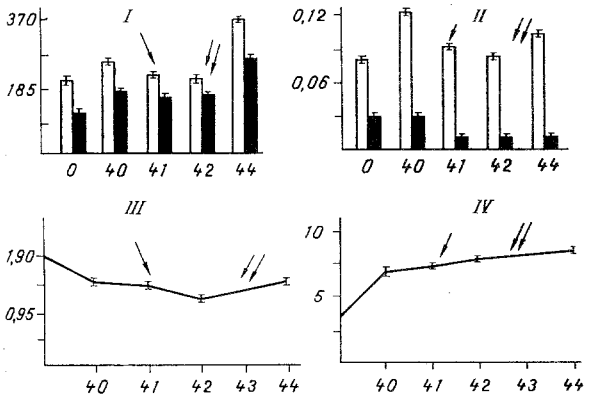

Fig. 1. Changes in absolute (I, II) and relative (III, IV) concentrations of nicotinamide coenzymes in kidneys (I, III) and blood (II, IV) of "alcoholic" albino rats infected with *E. coli*, under the influence of litonit treatment. I, II) abscissa, period of alcohol consumption (in weeks); ordinate, concentrations of nicotinamide coenzymes (in μg/g tissue or /liter blood). Unshaded columns — $NAD^+ + NADP^+$, shaded columns — NADH + NADPH; III, IV) abscissa, period of alcohol consumption (in weeks); ordinate, ratio $(NAD^+ + NADP^+)/(NADP + NADPH)$. Here and in Fig. 2, single arrow indicates infection with *E. coli*, two arrows indicate injection of litonit.

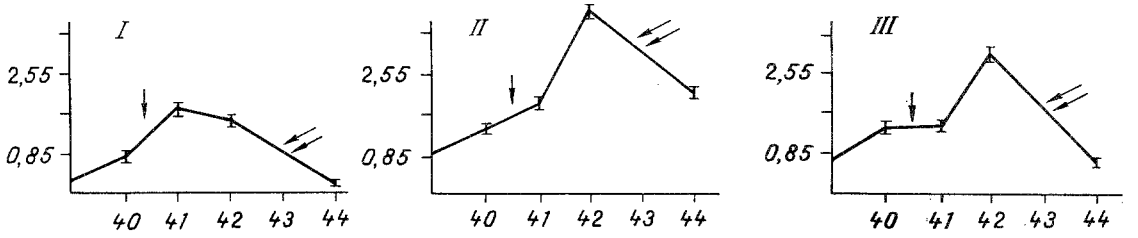

Fig. 2. Changes in serum IgA (I), IgG (II), and IgM (III) levels in "alcoholic" albino rats infected with *E. coli*, under the influence of litonit treatment. Abscissa, duration of alcohol consumption (in weeks); ordinate, immunoglobulin concentrations (in g/liter of blood serum).

33% on the 7th and 14th days of the investigation, respectively, ($P < 0.01$) whereas in the kidneys it was lower by 14 and 20% ($P < 0.05$). The total concentration of $NADP^+ + NADPH$ in the blood was lowered by 1.5 and 1.7 times, respectively, and in the kidneys by 1.2 times (Fig. 1).

A course of injections of litonit in a dose of 10 mg/kg into the "alcoholic" animals infected with *E. coli* caused a significant change in the biochemical parameters studied. On the 14th day of administration of litonit the concentration of oxidized forms of coenzymes in the kidneys rose from 200.0 ± 10.1 to 368.0 ± 35.1 μg/g ($P < 0.001$), and the concentration of reduced forms rose from 160.0 ± 13.3 to 258.0 ± 27.1 μg/g ($P < 0.01$). The total concentration of the coenzymes in this case was increased by 70%. A same trend was discovered in the blood.

The results also are evidence that prolonged ethanol consumption not only disturbs processes of tissue respiration, but also changes the state of the animals' humoral immunity. After alcoholization for 40 weeks an increase in the concentrations of IgA, IgG, and IgM was observed in the blood serum, with the greatest increase found in the IgA level (Fig. 2). Infection of the "alcoholic" rats was accompanied by an increase in the immunoglobulin concentrations. However, whereas the IgA level was highest on the 7th day of injection of *E. coli*, concentrations of IgG and IgM showed their greatest increases by the 14th day after infection. If concentrations of IgA, IgG, and IgM in intact rats are taken as 100, by the 40th week of alcoholization these parameters were raised by 21, 78, and 106%, respectively ($P < 0.05$); on the 7th and 14th days of injection of the pathogen, the IgA, IgG, and IgM levels were higher by 662, 139, and 110% and by 535, 393, and 339%, respectively ($P < 0.01$).

A course of litonit treatment restored the normal immunoglobulin concentrations. On the 14th day of its administration a significant fall was observed in concentrations of immunoglobulins of all classes. The greatest decrease was found in the IgA and IgM concentrations. Administration of litonit to the infected "alcoholic" rats lowered the serum IgA level by 87.1% ($P < 0.001$), the IgG level by 89.8% ($P < 0.05$), and the IgM level by 40.2% ($P < 0.01$).

The experimental results thus show that prolonged alcoholization depresses renal function and the resistance of the kidneys to inflammation. This is shown by the marked decrease in the ratio between oxidized and reduced forms of nicotinamide coenzymes in the kidney tissue. Considering the great importance of this parameter in the assessment of the energy metabolism and functional capacity of the kidney tissue [6, 8], it can be tentatively suggested that chronic alcohol consumption inhibits metabolic processes and leads to hypoxia in the affected kidney. The addition of secondary infection against this background leads to even more severe biochemical disturbances. The increase in concentrations of immunoglobulins of all classes in the blood serum suggests that in chronic alcoholism serious immunologic disturbances are present, and according to many workers [5, 3, 11], this plays an extremely important role in the mechanism of alcohol damage to the kidneys and the development of infection and inflammation in them. Treatment with litonit, besides increasing the concentrations of oxidized and reduced forms of nicotinamide coenzymes in the kidneys and blood, restores the normal serum immunoglobulin levels. The results are evidence that under the influence of litonit definite functional and immunologic changes take place in renal activity. The increase in the concentration of nicotinamide coenzymes, together with normalization of activity of renal sorbitol dehydrogenase and catalase, and a fall in the intensity of free-radical lipid oxidation, which the writer demonstrated previously, is evidence of activation of metabolism in the affected kidney. The course of inflammation in the kidneys is also known to depend on the level of nonspecific immune defense of the organism. Normalization of the serum immunoglobulin levels after administration of litonit reflects strengthening of the defenses of the body and its resistance to the action of the pathogenic microflora. A fall in the IgA, IgG, and IgM levels can also be regarded as a sign of resolution of inflammation in the kidney tissue [1, 7].

During administration of litonit to "alcoholic" rats infected with *E. coli* the biochemical and immunologic disturbances in the kidneys thus disappear. During treatment of alcohol-induced infectious inflammation in the kidneys, besides the use of agents of pathogenetic and etiotropic therapy, it is rational also to use litonit, which not only possesses antialcoholic properties, but also stimulates renal function and increases the resistance of the kidneys to inflammation.

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