



## EXPERIMENTAL ECHINOCOCCOSIS DURING ADMINISTRATION OF ROLYLAYER LIPOSOMES

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### ABSTRACT

We study the effect of liposomes on the course of hepatic experimental echinococcosis. Intraabdominal administration of liposomes was accompanied by incapsulation just in the first days of the test and by earlier deali maternal echinococcal cyst, absence of colonization nidi in the liver, and in abdominal cavity organs on the 7<sup>th</sup> day of experiment. Liposomes have pronounced hepatoprotection effect that is evidenced by the development of compensatory-adaptive process and absence of dystrophy in hepatocytes cytoplasm. No invasion of cyst parasite into intrahepatic bile ducts in contrast to control ones was observed.

**Key words:** echinococcus of the liver, liposoma, chemotherapy of echinococcus of the liver.

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### INTRODUCTION

The study of carriers of biologically active substances – liposomes in the diagnosis and treatment of various diseases is a new promising direction in medicine [1, 8]. Liposomes are closed bubbles of water surrounded by one or more layers of lipids. The size and shape of liposomes depend on many factors: the acidity of the medium, the presence of salts, etc. Liposomes are very similar to cell membranes and are used to study the effect on cell membranes. Liposomes injected into the body do not cause negative reactions, they are easily destroyed in the body, releasing the delivered substances. Liposomes devoid of antigen properties do not cause protective and allergic reactions of the body [6]. In particular, they can be used for targeted transport of medicinal substances. Liposome-based dosage forms, as a rule, are characterized by lower toxicity, the possibility of targeted drug delivery and a lower risk of adverse reactions [3, 8].

The data in the literature indicate a positive effect of liposomes in the treatment of a number of pathological processes, including inflammatory and oncological diseases (2,4,5,6,7). Targeted delivery of antiparasitic drugs to the lesion site, in particular the echinococcal cyst of the liver, seems to be a very promising way of chemotherapy for echinococcosis, as well as postoperative prevention of relapse of the disease.

### MATERIALS AND METHODS

In this regard, it is of interest to study the effect of empty multilayer liposomes on experimental liver echinococcosis. 2 series of experiments were conducted on Chinchilla rabbits with an initial mass of 2200-3500 g. In the first group, liver echinococcus was modeled according to the method we proposed (patent for invention No. 3441). In the second group, animals with experimental echinococcosis were injected with multilayer liposomes (ML) intravenously and intraperitoneally. Empty multilayer liposomes were prepared according to the method of E.I. Isaev, for which the liver of a ram was used. Lipid extraction was carried out by a modified Folch method. The fractionation of phospholipids was carried out in thin layers of silica gel of the KSK brand

containing 6.5% gypsum, in a system of solvents with chlorophore – methanol – acetic acid – water in ratios of 65:43:1:4. The distribution of labeled liposomes, as well as the kinetics of their inclusion in the liver were studied by dynamic scintigraphy on a gamma camera MV-9100 (VNR), as well as by scanning method.

Echinococcal cysts, their fibrous capsule, liver tissue taken at different distances from the pathological focus were examined. The material was taken on 3-, 7-, 14-, 21-, 28- e day of experience. Intact rabbits were used in the control, a total of 30 rabbits were used. Histological methods of research were used.

## RESULTS AND DISCUSSION

Comparative analysis of morphological changes in the liver during experiments in the control group (untreated) and treated with empty liposomes revealed certain differences. Thus, in experimental echinococcosis of the liver, progressive development of an echinococcal cyst is observed, contamination of the liver and abdominal organs with daughter echinococcal blisters, an increase in dystrophic changes in the liver up to necrosis of hepatocytes. There was also a violation of the functional state of the liver – hyperbilirubinemia, an increase in ALT, AST, and urea enzymes.

Other structural changes were found against the background of the introduction of empty liposomes. When evaluating the results of studies with intraperitoneal administration, more pronounced effects of liposomes were established. On the 3rd day, the liver is of normal size, its surface is smooth at the site of implantation of an echinococcal cyst in the V-VI segment with dimensions of 1.5 × 1.5 cm surrounded by a fibrous capsule. In the circumference of the cyst, there is hyperemia and a focus of hemorrhage. The peritoneum is clean, shiny. Single daughter cysts are observed on the serous membrane of the small intestine, omentum. Microscopic examination of the liver tissue shows enlargement, hyperemia of its vessels and less pronounced dystrophy of hepatocytes. Hypertrophy of Kupfer cells is characteristic.

On the 7th day, an echinococcal cyst is detected only at the site of inoculation. It is reduced in size, the chitinous shell is thickened, compacted. Decayed and deadened scolexes were detected in the echinococcal fluid. Microscopic examination in the circumference of the implant shows hypertrophy of Kupfer cells and accumulation of monocytes, macrophages. In hepatocytes, binucleated cells are determined.

On the 14th day, the echinococcal cyst of the liver is surrounded by a dense fibrous capsule, the chitin shell is dystrophically altered. There is no contamination with parasitic cysts in the abdominal cavity. The hepatic tissue near the focus is microscopically characterized by edema of the interstitial tissue, infiltration by lymphocytes, monocytes, macrophages, hypertrophy. Kupffer cells, cytoplasm of hepatocytes with hypertrophied and hyperchromic nuclei, many dual-core cells.

On the 21st-26th day of the experiment, the condition of the animals improves, their weight increases slightly. There are no foci of insemination in the abdominal cavity. The maternal cyst of the liver is sharply reduced, compacted. Homogenization and disintegration of the contents of the echinococcal bladder is noted. In the circumference of the cyst, hepatic tissue of the usual structure. The chitinous shell is wrinkled. Microscopy reveals turbid swelling of hepatocytes, hypertrophy and hyperchromia of hepatocyte nuclei with the presence of a significant number of double-core cells. Necrosis of hepatocytes observed in untreated animals was not detected.

Thus, macroscopic and microscopic examination of the liver and abdominal organs in echinococcosis against the background of treatment with empty liposomes allows us to draw the following conclusions:

With the introduction of empty liposomes, dystrophic changes in hepatocytes are less pronounced than in experiments without treatment. The activity of ALT and AST enzymes in the treatment with empty liposomes, compared with the group of untreated animals, where the activity of enzymes is high, decreases slightly (from  $1.7 \pm 0.33$  to  $1.4 \pm 0.7$  mmol / l).

The introduction of empty liposomes to experimental animals with liver echinococcus prevents the toxic effect of the parasite on liver tissue by strengthening the walls of blood vessels and sinusoids, as well as increasing the strength of the basement membranes. As a result, toxic changes are less pronounced in the hepatic parenchyma. Macro and microscopic examination of the liver and abdominal organs against the background of treatment with empty liposomes showed that as a result of the membrane-stabilizing, anti-inflammatory and antiparasitic action of liposomes in the inoculation zone, no contamination of parasitic cysts was observed until the end of the experiment. The maternal cyst decreased in size dynamically, thickening, clouding and wrinkling of the chitinous membrane occurred. In the liver tissue adjacent to the cyst, the development of minimal dystrophic changes in the form of small-drop vacuole dystrophy was noted, which is explained by the less pronounced toxic effect of empty liposomes. Confirmation of this is the improvement of bilirubin-pigment metabolism.

## CONCLUSION

Thus, empty liposomes accelerate the formation of refocal inflammation of the fibrous capsule of the echinococcal cyst, and therefore prevents the contamination of the echinococcal process. Liposomes improve the metabolism of phospholipids and lipoproteins that make up the membrane structures of cells and intercellular structures., thereby protecting hepatocytes from dystrophic changes, as well as having a pronounced hepatoprotective effect stimulate the regenerative ability of the liver.

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