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COMPARATIVE CHARACTERISTICS OF MORPHOFUNCTIONAL CHANGES IN THE MECHANISMS OF ADAPTATION AND COMPENSATION OF GRID, MEMBRANE DIGESTION AND ABSORPTION IN ACUTE AND CHRONIC FORMS OF TOXIC HEPATITIS

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Abstract

The study of the morphofunctional state of various parts of the digestive-transport conveyor in liver pathology, which is now so widespread in various countries of the world, has not only theoretical, but also applied significance. The liver, being a multifunctional organ, directly and indirectly interacts with various parts of the gastrointestinal tract. A detailed study of this interaction seems important, first of all, from the point of view of fundamental aspects of biomedical problems. This functional connection has been studied in sufficient detail in normal conditions. For example, the bile-forming and bile-excretory activity of the liver, in addition to the activation of digestive hydrolases in the intestinal cavity, is directly involved in the implementation of membrane digestion, renewal of the glycocalyx and a number of other vital functional functions of the body. This is why the slightest disturbance in the activity

of the liver leads to serious morpho-functional changes in a number of organs and systems and, above all, the digestive system.

Keywords: Toxic hepatitis, transporters, digestive enzymes.

Introduction:

The liver, being a multifunctional organ, directly and indirectly interacts with various parts of the gastrointestinal tract.

It is known that the bile-forming and bile-excretory activity of the liver, in addition to the activation of digestive hydrolases in the intestinal cavity, is directly involved in the implementation of membrane digestion, renewal of the glycocalyx and a number of other vital functional functions of the body. This is why the slightest disturbance in the activity of the liver leads to serious morpho-functional changes in a number of organs and systems and, above all, the digestive system.

Indeed, available clinical and experimental data indicate that various forms of acute and chronic liver pathology are accompanied by obligatory changes in the secretory, motor-evacuation activity of the digestive organs. He believes that by changes in the enzyme spectrum of the gastrointestinal tract, that is, by the isoenzyme status of digestive hydrolases, one can judge the severity of liver disease. At the same time, in the literature there is still no detailed description of the state of cavity digestion, membrane digestion and absorption in any form of liver pathology.

The available data obtained on people with liver disease, despite their invaluable significance for the clinic, are scattered and relate either to the activity of gastric and pancreatic enzymes in the contents of the gastrointestinal tract, or enteral enzymes in biopsies taken mainly from the initial parts of the small intestine, and therefore not allow us to judge possible shifts in the ratio of the rates of various stages of digestion in liver pathology. Meanwhile, according to modern concepts of trophology, the characteristics of the mechanisms of assimilation of nutrients in a healthy and sick organism in certain conditions should be built taking into account, at least, the state of cavity and membrane digestion.

Purpose of the Study:

To study the influence of various forms of toxic hepatitis on the state of morpho-functional indicators of digestive enzymes and, based on the data obtained, to assess the violations of the physiological relationships between the process of cavity, membrane digestion and absorption of nutrients.

Materials and Methods:

The experiments were carried out on adult male Wistar rats with approximately the same body weight of 350±30 g. The animals were kept in a well-ventilated, bright room in wooden cages measuring 50 x 30 x 28 cm, six individuals in each, with free access to food and water. The room temperature ranged from 20 to 26.4°C. In order to eliminate the possible influence of the elemental factor on the studied parameters, animals in both the control and experimental groups were given a standard balanced diet. It included wheat bread, fish, oats, yeast, red carrots, barley, mixed feed, cottonseed oil, table salt, as well as basic vitamins and minerals.

A total of 2 series of experiments were carried out. The first is devoted to studying the effect of a single injection of a large dose (25 mg/per 100 g body weight, subcutaneously) of the hepatotoxic alkaloid heliotrine in rats - acute toxic hepatitis. The second series was a study of the effect of long-term administration in small doses (5 mg/100 g body weight) of the same drug - chronic toxic hepatitis. In both cases, the effect of a toxic alkaloid on the activity of pancreatic and enteral enzymes on the functions of carbohydrate hydrolysis was studied. Throughout the experiments, the general condition of the animals was systematically monitored: body weight, daily food and water consumption were recorded. All manipulations with animals were always carried out at the same time of day (10 a.m.).

Technique for reproducing an experimental model of acute and chronic toxic hepatitis in rats.

Acute and chronic heliotrine intoxication of the liver was caused according to a previously tested method (b, 91). In case of acute poisoning, rats were injected subcutaneously with a solution of heliotrine acidified with hydrochloric acid (pH 7.0), at the rate of 25 mg per 100 g of body weight in a volume of 0.25 ml once.

When creating chronic intoxication, rats were subcutaneously injected with 5 mg of heliotrine per 100 g of body weight in the same volume of solvent for 42 days, once a week.

In both cases, rats in the control group were injected subcutaneously with a similar amount of solvent at the same time.

Animal slaughter and techniques for preparing various enzymatically active preparations.

Animal slaughter.

The animals were killed by decapitation 16 - 18 hours after the last poisoning, at the same time of day (9.30-10.00). At the same time, 6 individuals were killed simultaneously from both the control and experimental groups, 1 - 3, 7, 10. 30th. 60th

and 90th days after a single injection of heliotrine and on the 3rd, 18th and 72nd days after stopping repeated injections, i.e. on 45th. 60th and 120th days of experience.

After decapitation of the animal, the abdominal cavity was opened along the midline of the abdomen, and inspections of the abdominal organs were quickly performed with a description of the macroscopic picture of the digestive organs. Next, the pancreas, liver and small intestine were separated from other organs of the digestive tract, thoroughly cleaned of calamus and connective tissue, the length of the small intestine was measured, washed with cooled Ringer's solution (pH 7.4) and then each organ was weighed separately.

In experiments studying the spatial distribution of enteral enzymes along the length of the intestinal tube, the small intestine, after separation of the duodenum from it, was divided into 3 equal sections, conventionally called the proximal, medial and distal sections. Then all sections of the small intestine were placed on an ice-cooled glass surface and, after a longitudinal cut with the edge of a glass slide, the mucous membrane was carefully scraped off from them, after which the mucous and serous membrane of each section were weighed separately. Next, the mucous tissue of each section of the thin nod as well as the pancreas and liver were placed in separate plastic bags, tags were attached to them and frozen in liquid nitrogen.

Technique for preparing homogenates of the pancreas and small intestinal mucosa.

To determine enzymatic activities, pancreas samples were thawed at room temperature, then weighed, transferred to a glass homogenizer placed in a polyethylene glass with pieces of ice and homogenized with an iteflon pestle driven by an electric motor at 200 - 300 rpm.

Ringer's solution (pH 7.4) was added to the homogenate at the rate of 1 ml per 100 mg of tissue mass. The homogenate thus obtained, after appropriate dilution, was used as an enzymatically active material.

To prepare homogenates from frozen samples of the mucous membrane of the small intestine or its various parts, the same manipulations were carried out and in the same sequence as with the pancreas. The duration of homogenization in all cases did not exceed 45.

Incubation conditions for enzymatically active drugs and substrates.

For the normal course of enzymatic hydrolysis, a certain optimum temperature, pH, substrate concentration and good contact of the substrate with the enzyme are required. (Under natural conditions, mixing of the chyme and its movement in the aboral direction, contact of nutrients with the surface of the small intestine is ensured by the motor activity of the intestine. In experiments in vitro, improving the contact of the substrate with the enzyme and the waste of hydrolysis products into the depth

of the phase was achieved by continuous stirring. For this purpose, preparations of the pancreas and small intestine were placed in test tubes with the corresponding 3-substrates (starch, sucrose, maltose) and incubated in a specially designed Warburg apparatus at automatic swinging (60 cycles per minute) and a temperature of 37 - 38°C. In all cases, the substrate solutions were preheated to 37 - 38°C.

Biochemical methods for determining the enzymatic activities of the digestive organs. When determining pancreatic and intestinal enzymatic activities in the tissues of these organs, biochemical methods were used, widely used in modern experimental gastroenterology (17, 81, 195). α-amylase activity in pancreatic homogenates, the contents of the thin nod and blood was determined by the Smith-Roy method (349) modified by A.M. Ugolev (219).

The principle of the method is to quantify the starch remaining after enzymatic hydrolysis and forming a blue complex compound in the presence of iodine.

The latter can be measured colorimetrically. Enzyme activity was expressed in milligrams of substrate digested in 1 min and calculated as per 1 g of raw tissue. 1 ml of chyme or blood (specific activity), and for the total mass of the organ (total activity). From the intestinal enzymes themselves, we determined the activity of maltase. sucrase and -amylase. The activities of maltase and sucrase were determined using the glucose oxidase method of Dahlquist (287) and ɤ-amylase by the method of Aurichio and Rubino (274).

The method is based on the quantitative determination of glucose released from the corresponding substrates after enzymatic hydrolysis. Glucose is oxidized by molecular oxygen in the presence of D-glucose oxidase to form hydrogen peroxide, which, in the presence of peroxidase present in the incubation mixture, is split into water and atomic oxygen. The latter leads to the conversion of O-dianisidine to form a yellow compound that can be measured colorometrically. The intensity of the color is directly dependent on the amount of oxidized glucose. In the mucous membrane of the thin nodule under natural conditions there is always a certain amount of adsorbed α-amylase of pancreatic origin, which can distort the results when determining the true α-amylolytic activity of the intestine. Therefore, it is necessary to get rid of α-amylase. In the method of Aurichio and Rubino. which we used to determine ɤ-amylase, provides for preliminary inhibition of α-amylase. To do this, the enzymatically active material (mucous homogenate) was preliminarily incubated in a maleate buffer (pH 5.8) at a temperature of 37-38°C in the presence of trypsin (4 mol/ml) and EDTA (1 mg/ml) for 30 minutes. Enzyme activities were calculated per 1 g of raw tissue (specific activity) and per tissue weight (total activity).

Determination of protein content

Protein in pancreatic homogenates and small intestinal mucosa was determined by the method of Lowry et al. (336). This method is based on the color reaction of the Folin-Ciocalteu phenolic reagent with protein.

Conclusions

1. When simultaneously determining the activity of pancreatic α-amylase and enteral α-amylase, maltase and sucrase in rats subjected to single or repeated injections of heliotrine solution, it was found that in toxic hepatitis, the chemical digestion of carbohydrates is inhibited at the level of integration of the mechanisms of cavity and membrane hydrolysis. Inhibition of the rate of membrane hydrolysis during acute heliotrine intoxication occurs against the background of constancy or activation of cavity digestion, and in conditions of chronic intoxication it is accompanied by a simultaneous decrease in the rate of cavity hydrolysis.
2. A single injection of heliotrine in rats leads to an increase in –α-amylase activity of the contents of the small intestine and blood, with its relative constancy in the pancreatic tissue. It follows that; a) the rate of cavity hydrolysis of polysaccharides in this liver pathology remains at a relatively constant level or, at least, does not decrease; b) when assessing the activity of the pancreas, it is not enough to judge only by the results of determining the enzymatic activity of duodenal contents or blood serum; for this, it is necessary to take into account the functional state of the mechanisms that implement the biosynthesis, exocretion and incretion of digestive hydrolases.
3. Acute heliotrine intoxication leads to a significant decrease in the specific activity of intestinal carbohydrates, maximally grown for sucrase. slightly less for maltase and even less for amylase. These data, together with the results regarding the greater resistance of the mechanisms of cavity hydrolysis of polysaccharides to the influence of heliotrine, can serve as a theoretical basis for choosing a rational ratio of various carbohydrates in the diet for heliotrine hepatitis, and, possibly, other forms of liver disease.
4. Heliotrine hepatitis unequally changes the activity of kyme carbohydrates in different parts of the small intestine. The inhibitory effect of heliotrine is greater in the proximal-medial parts of the small intestine and significantly less in the duodenum and the distal part of the jejunum.

Consequently, assessment of the functional state of membrane digestion based on the results of determining the enzymatic activities of the mucous membrane of any one section of the thin lining can lead to the same conclusions.

5. When comparing indicators of the functional state of the submammary gland and small intestine after a single or repeated injection of heliotrine, it was demonstrated that both acute and chronic intoxication of the liver significantly reduces the rate of the final stage of carbohydrate hydrolysis. However, the function of the small intestine in acute intoxication is restored to the control level, and in chronic intoxication it remains reduced throughout the 4-month observation period.
6. Acute and chronic intoxication with heliotrine leads to hypotrophy and/or hypoplasia of the pancreas and mucosa of the thin chyme. which manifests itself in a decrease in the mass of the digestive organs at the beginning of the development of the pathological process. Further, this decrease is replaced by an increase in the mass of the pancreas and small intestinal mucosa, which is due to increased swelling of their tissue, as evidenced by data on low tissue protein content throughout the experiment.

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