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STRUCTURAL AND FUNCTIONAL CHARACTERISTICS OF RAT LIVER WHEN MODELING MAGNESIUM DEFICIENCY STATES AND THEIR CORRECTION BY A NATURAL HEALING FACTOR WITH AN INCREASED MAGNESIUM CONTENT

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Abstract

In an experiment on 50 white Wistar rats of auto bread dilution, the authors evaluated the structural and functional changes in the liver parenchyma in magnesium deficiency and the possibility of their correction by exogenous administration of magnesium in the form of 5% solution of "magnesium oil".

Studies have shown that the development of magnesium deficiency is accompanied by coarsening of connective tissue pre-layers in the liver, dystrophic changes in the cytoplasm of hepatocytes, and spasm of a part of the vessels. At the same time, the detoxification and bile-forming function of the liver decreased and the activity of redox enzymes and ATP-ases in liver cells weakened.

The use of a 5% solution of "magnesium oil" improved, but did not restore the impaired liver function to normal, increased the activity of redox enzymes and ATPases. In this case, the structural damage to the liver was eliminated. The authors believe that changes in the structure of the liver are connected, with magnesium-deficient states, by inhibition of energy supply processes, which depend on the activating action of the magnesium ion. The introduction of exogenous magnesium, improving the processes of energy supply, helps to restore the structure of the liver and improve its function.

Key words: *magnesium oil, structural and functional organization of the liver, magnesium deficiency states*

Introduction

According to contemporary views, magnesium is one of the most important elements that plays the role of a regulating factor in the life of the body and is included in the first four of the 12 basic chemical elements of the body [1-4]. The total amount of magnesium in the body ranges from 850 mmol / L to 1160 mmol / L. Although the largest amount of magnesium is found in the bones, significant amounts are found in the tissues of muscles, liver, kidneys, and blood [5, 6]. The main role of magnesium is to activate enzymes: cholinesterase, phosphoglumutase, pyrophosphatase, arginase, carboxylase, cellular dipeptirase, etc. In addition, it activates enzymes that regulate the functions of cell membranes (their stabilization, cell adisia, transmembrane electron flow). It should be emphasized that magnesium is involved in the regulation of the balance within the cellular potassium, since it maintains the activity of the Wa+-K+-ATPase membrane canos, due to the activation of Na+-K+-ATPase [7]. Magnesium is necessary for the synthesis of acetylcholine, synthesis, and catabolism of the immune status [8, 9]. In general, it is believed that the level of magnesium in the human body is a constant that controls human health [5, 16, 17].

Studies of the correlation between the development of pathological processes in the body and the content of magnesium have demonstrated the presence of chronic magnesium deficiency in the body with cardiovascular diseases, arterial hypertension, bronchial asthma, obesity, type II diabetes mellitus, states of prolonged distress [10, 11]. In general, the problem of magnesium deficiency is complex, topical, and requiring an urgent solution, since magnesia contributes to damage to the cardiovascular, hepatobiliary, nervous, and endocrine systems [12]. Based on the foregoing, the study of morphofunctional changes in the heart, liver, kidneys and nervous system with magnesium deficiency is an important task of medical science.

The aim of the work was to assess the structural and functional changes in the liver with a deficiency of magnesium in the body and the possibility of correcting these changes with a natural magnesium-containing therapeutic factor - "magnesium oil".

Methods

The material of the work was the data obtained in the study of 50 white rats of the Cistar line of auto bread breeding weighing 180-200 g. The maintenance and work with the animals were carried out in accordance with the recommendations of the Directive of the European Parliament and Council (2010/63 / EU) and the order of the Ministry of Education and Science, youth and sports of Ukraine from 01.03.2012. №249 "About the hardening of the order of scientific installations of research and experiments on animals" [13, 14].

In accordance with the objectives of the work, the animals were ranked into 3 groups:

Group I (10 animals) - intact animals, data from which served as control.

Group II (20 animals) - rats that were exposed to magnesium deficiency.

Group III (20 animals) - rats, who received a solution of "Magnesium oil" against the background of magnesium deficiency.

Magnesium deficiency was created in rats by long-term consumption of a special diet. This diet consisted of a mixture of 30% casein: 40% potato starch, 10% corn oil, and 20% white rusks as the only food. The mixture was prepared in distilled water, the same water was used as drinking water, at the same time the feeding regime was changed, and the daylight hours were lengthened. The experiment lasted 70 days. In the case of using "Magnesium oil", its 5% solution began to be injected from the 50th day of the experiment, intragastrically with a soft probe with an active one, in a volume of 1% of body weight.

At the end of the experiment (70 days), the animals were removed from it by decapitation under general anesthesia (ether), pieces of the liver with a volume of 0.5 cm3 each were removed, and 5 ml of blood were collected.

Selected pieces of liver were separated. One was fixed in a 4% solution of paraformaldehyde for 24 hours, then passed through alcohols of increasing concentration and poured into celloidin. From the obtained blocks, histological sections with a thickness of 7-9 μm were made, which were stained with hematoxylin-eosin. The resulting products were examined using a light microscope. The second piece was frozen with dry carbon dioxide (-7C °) from which cryostat sections were made, on which, according to the instructions of Z. Loyd's

manual, they were determined by histochemical lactate dehydrogenase (LDH).

The remains of a frozen piece of liver were used to obtain a homogenate in which the activity of Mg^{+2}/Ca^{+2}- ATPase was determined.

In a taken blood sample, biochemical methods were used to determine the activity of Alanine aminotransferase (AnAT) and aspartate amino transaminase (AcAT); the content of total bilirubin and its fractions. Determination methods according to the instructions "Experimental and preclinical studies" [15].

The obtained data were subjected to standard statistical processing and tabulated.

Results

Macroscopic examination of the liver of rats with a magnesium deficiency model did not reveal any special differences from the control ones. The surface of the liver is smooth, shiny, it is not visually enlarged, the anterior edge is sharp, the tissue is brown, which makes it different from the norm, in which the tissue is brown - crimson.

Microscopic examination of the lobular structure of the liver parenchyma is preserved.

Interlobular layers are thickened due to coarsening of connective tissue fibers. The vessels of the triads with somewhat thickened walls are moderately congested and partly spasmodic. The central vein is full-blooded. Hepatocytes are uniformly medium in size, collected in beams. Hepatocytes are mainly with one nucleus, although there are quite numerous cells with two nuclei. The nuclei are richly colored, their content is homogeneous. The cytoplasm of hepatocytes is lumpy, weakly basophilic; vacuoles are determined in individual hepatocytes. LDH activity in hepatocytes is 5.0 ± 0.534 units: LDH activity - 6.0 ± 0.514 units.

In general, we can talk about a change in the properties of connective tissue and a decrease in the functional activity of hepatocytes.

The results of assessing the metabolic activity in the liver are shown in Table 1.

According to the data presented in Table 1, the development of a magnesium deficiency state is accompanied by a decrease in the activity of Al AT and Ac AT, while the decrease in their activity takes place in various degrees. It can be assumed that there is not only a weakening of the processes of persamination in the liver but also an imbalance in the components of this process. The content of total bilirubin also increases, which may indicate a weakening of bile formation in the liver, and since the ratio of bilirubin fractions also changes, we can talk about a weakening of the detoxification activity of the hepatic parenchyma.

As for the magnesium-dependent ATP-ases, according to the data in Table 1, their activity weakens. The studied ATP-ases belong to the group of enzymes that provide transmembrane transport, therefore, the weakening of their activity is reflected in the liver of many metabolic processes, including those associated with the detoxification system. Obviously, the change in the activity of ATP-ases is caused by the above-described violations of the hepatic functions and changes in the structural and functional organization of the parenchyma.

A study of the liver of rats with magnesium deficiency treated with a solution of magnesium oil revealed the following. Macroscopically, the liver is indistinguishable from that of control rats. The surface is smooth, shiny, the front edge is sharp, the fabric is brown - crimson.

On microscopic examination, the lobular organization of the liver is preserved. Interlobular septa are dense, thin. The vessels of the triads are moderately full-blooded, the same central veins. The walls of the vessels are thin, of the usual appearance.

Hepatocytes are mainly of medium size, collected in beams. Interbeam spaces are slit-like, Kupffer cells with flattened nuclei. Binuclear hepatocytes are rare.

Basically, the mass of hepatocytes is medium-sized nuclei, richly colored. The cytoplasm in them is homogeneous, eosinophilic. Hepatocytes with vacuoles were not found. The LDH activity in hepatocytes is 6.0 ± 0.24 units, the LDH activity is 7.0 ± 0.384 units. Thus, the doses of magnesium oil received by the rats prevented the development of changes in the structural and functional organization of the liver, which is characteristic of magnesium deficiency states.

Assessment of the state of metabolism in rats of this experimental group revealed the following.

According to the data in table 1. the activity of Al AT was lower than in the control group but higher than in the case of uncorrected magnesium deficiency. Ac AT activity had a stable tendency to increase and practically did not differ from the control. However, the ratio of the activities of Al AT and Ac AT is somewhat changed, compared with the control, this suggests that the activity of the processes of persamination in the liver is quite high, although their structure has not completely recovered.

Also, the content of total bilirubin approaches the control data, decreasing in relation to the data of uncorrected magnesium deficiency, that is, the function of bile formation in the liver of rats of this group is activated. It should be noted that the ratio of bilirubin fractions remains at the level of uncorrected magnesium deficiency, which is obviously associated with incomplete restoration of the detoxification function.

As for the activity of ATP-ases, according to the data in Table 1, the activity of these enzymes has a tendency to increase in relation to uncorrected magnesium deficiency, but these changes are not reliable. At the same time, the ratio of the activity of these enzymes, while slightly decreasing, remains higher than in the control, that is, there is no full-fledged energy supply of transmembrane transport. Under these conditions, an improvement in metabolism takes place, but it is incomplete, although these changes are sufficient to restore the structural and functional organization of the liver parenchyma.

Conclusions

The results of our research have shown that a long-term magnesium deficiency state is accompanied by structural and functional changes in the liver. These changes are manifested by a thickening of interlobular layers, spasms of some vessels, the appearance of a significant number of binuclear hepatocytes, and degenerative changes in their cytoplasm.

Changes in the structural and functional organization of the liver parenchyma are associated with the observed decrease in the detoxification function of the liver and, apparently, depending on the weakening of the activity of redox enzymes in hepatocytes and the decrease and imbalance of ATP-ases, which provide transmembrane transport in cells.

Taking a solution of "magnesium oil" by experimental animals improves biliary and detoxification functions. This occurs against the background of an increase in the activity of redox enzymes and ATP-ases in liver cells. Perhaps due to these metabolic transformations under the influence of high doses of exogenous magnesium, the structural and functional organization of the liver parenchyma is restored.

Acknowledgments

The authors declare that there are no conflicts of interest.

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Table 1. Features of metabolic parameters in rats with magnesium deficiency and its correction with "magnesium oil"

Group / Indicator	Control	Magnesium deficiency	Magnesium deficiency + mag. oil	P1	P2
Al AT unit / l	133,09 ± 4,68	55,71 ± 1,29	105,9 ± 5,46	< 0,01	< 0,01
As AT unit / l	278,84 ± 6,57	255,16 ± 8,17	287,73 ± 11,20	< 0,05	> 0,5
Total bilirubin MC mol / L	5,79 ± 0,81	8,45 ± 0,35	4,99 ± 0,44	< 0,05	< 0,05
Bilirubin direct MC mol / L	1,98 ± 0,32	3,87 ± 0,17	2,03 ± 0,19	< 0,05	< 0,05
Bilirubin indirect MC mol / L	3,81 ± 0,51	4,58 ± 0,18	2,96 ± 0,11	> 0,5	> 0,5
Mg+2-Ca+2-ATP-ase mg R / g tissue	9,11 ± 0,93	7,22 ± 0,54	7,82 ± 0,11	> 0,5	> 0,5
Mg+2-Na+ / K+-ATP-ase mg R / g tissue	6,40 ± 0,62	3,11 ± 0,14	3,50 ± 0,16	< 0,01	> 0,5

P1 - magnesium deficiency to control;

P2 - magnesium deficiency + magnesium oil and magnesium deficiency