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INFLUENCE OF THE COORDINATIVE PREPARATION OF BISMUTH (III) WITH HISTIDINE ON THE MORPHOLOGICAL PICTURE OF INTERNAL ORGANS

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ABSTRACT

In this article, the remedy named Vigitryl based on bismuth (III) was administered to the laboratory rats with a weight of 160-180 g in 30 days. Then, the internal organs were separated and the morphological appearance was examined at the end of the experiment. The histological picture of the internal organs of the experimental group, which was injected with vigril 25 mg/kg, showed that long-term administration of the drug Vigitril in the structure of the studied internal organs does not cause changes.

KEYWORDS: Vigitryl, bismuth (III), toxicity, histomorphology, internal organs.

INTRODUCTION

The body is a holistic, interconnected system. In the case of the occurrence of pathological processes in any particular organ, other organ systems begin to respond to varying degrees of normal balance. Many morphological studies are devoted to changes in tissues and organs under the influence of the external environment. This practical orientation appeared due to the great interest in the deterioration of the ecological situation, the emergence of a variety of adverse factors in the working environment and in everyday life. It is known that even in small doses that do not cause pronounced toxic effects, xenobiotics (heavy metals, rare earth elements, etc.) can have an effect, leading to disadaptation of the body.[3,4]

Under the influence of toxic substances in the organs, pathological processes occur, accompanied by morphological changes in the tissues forming them. Disruption of the structure of one of them is reflected in the functional and structural properties of other tissue systems, which leads to certain disruptions in interstitial interactions. The elucidation of the biological mechanisms of the action of toxic substances at the intercellular and interstitial levels is of great importance for understanding the pathogenesis of various diseases.

One of the aspects of studying the intercellular and interstitial relationships is the identification of interactions between tissues when exposed to harmful substances on the human body, since the relationships between tissues and their cellular elements help identify the mechanisms of interstitial regulation in the body. Consequently, cells of different origin take part in the intertissue interaction reactions.[2]

Bismuth compounds have been used in medicine for more than 200 years to treat various diseases, including syphilis, hypertension, infections, skin diseases, and gastrointestinal disorders. The detection of the bacterium Helicobacter pylori (H. pylori), which is responsible for the occurrence of gastritis, with subsequent complications, such as gastric and duodenal ulcers, has led to studies of the antimicrobial potential of bismuth preparations. The antimicrobial properties of bismuth preparations are well studied, they have been used to eradicate H. pylori long ago, and in the era of increasing antibiotic resistance, preparations based on bismuth tri-potassium dicitrate took priority in eradication therapy regimens.

Over the past few years, tremendous progress has been made in understanding structures, as well as the mechanism of action of bismuth preparations. Recent advances in biophysics and molecular biology have provided invaluable tools needed to study the bioorganic chemistry of bismuth. For example, inductively coupled plasma mass spectrometry with a time resolution makes it possible to track the presence of bismuth drug in single H. pylori cells (approximately 1.0×10^6 Bi atoms/cell). The absorption of bismuth by H. pylori bacteria is slowed down by ferric ion (Fe^{3+}), indicating that bismuth drugs can use certain ways to transfer iron in the pathogen. A number of bismuth protein targets present in H. pylori have been identified by the metall-metall proteome approach. Various bismuth-containing complexes have been synthesized that exhibit in vitro activities, including antifungal, antiviral, or even anti-tumor effects. These studies served as an impetus for the development of new bismuth preparations, including the development of bismuth-containing nanostructures (BiCNs). Recently, comprehensive reviews of the chemistry and biological chemistry of bismuth, as well as its medical use, have been published.[7]

Recent studies have shown that the use of bismuth preparations can also reduce the toxic effect of anticancer chemotherapy and, possibly, such drugs may also be effective in the treatment of AIDS. In this regard, bismuth preparations have a great interest in medical practice, and this problem becomes not only medical, but also the most important social.[5]

It is mandatory to evaluate the structure of internal organs using histological and histochemical methods. In the absence of deviations from the physiological norm of the indicators of the functional state of organs in experimental animals, when assessing the toxicity of potential drugs, the main test that determines the effect of the drug on the body is histological studies.[1]

Based on the above, we decided to study the effect of the new bismuth (III) coordination compound with histidine on the morphology of the internal organs.

MATERIALS AND RESEARCH METHODS

The chronic toxicity of bismuth (III) with histidine (vigitril) was studied in 40 white outbred rats of both sexes, weighing 160-180 g. The animals were divided into 4 groups.

The 1st group of the control group received distilled water in the appropriate volume. The 2nd, 3rd and 4th group experienced, received the drug, respectively, in a dose of 10 mg/kg, 25 mg/kg and 30 mg/kg. The drug was administered daily orally for 30 days. Observation of the behavior of animals was carried out for 30 experimental days and another 30 days of the recovery period. At the end of the experiment, animals were decapitated under ether anesthesia and they took pieces of internal organs (lungs, heart, liver, spleen, adrenal gland, kidneys, stomach, duodenum, colon and rectum). They were placed in 12% formalin solution. Part of the animals of the experimental group left for further observations.[3]

RESULTS AND DISCUSSION

The histological picture of the internal organs of the experimental group, which was injected with vigril 25 mg / kg.

Kidney. On the preparation of the cross section of the kidney. At the periphery of the cut, the cortical substance surrounds the medulla arcuate, and the latter has a pyramid-like shape. Cortical substance is represented by proximal and distal nephron, as well as renal corpuscles. The proximal section is formed by tubular formations, the lumen of which is lined with low cylindrical epithelium. According to the degree of staining of the cytoplasm of cells, the cells are subdivided with a light and bright pink color or the so-called “dark” and “light” cells. In both cells, the cytoplasm looks gently granular, closer to the basal part contains a rounded nucleus. Most cells contain one or two cell nuclei. Many nuclei are small in size with finely dispersed chromatin and a small nucleolus. In some cells, the apical part of the dome-like acts into the lumen of the tubule or vacuoolate swollen.

The distal section also has a tubular or spherical shape, while the nephrocytes themselves have a highly cubic shape, their cytoplasm is pink, and the basal part contains one or two nuclei. The apical part sometimes forms short outgrowths. The tubular lumen, as a rule, looks empty, whereas vacuolar or foam-like structures appear in the proximal part. In the medulla of the kidney there is a thin division of the nephron and collecting tubules. The descending part of the nephron is represented by tubules with a wide lumen, their wall is lined with a single-layer flat epithelium. The nucleated part of the cytoplasm swells into the lumen of the tubule. In the lumen sometimes exfoliated epithelial cells are detected.

The ascending part of the nephron is lined with low cubic epithelium, its cytoplasm is colored pink, and in the lumen a desquamated epithelium is also detected, the cylinders are sometimes vacuolate or foamy. Collective tubules, in contrast to the ascending part, along with the cubic epithelium contain large cells, the cytoplasm of which is cleared, the apical part is rounded and protrudes into the lumen.

Interstitial tissue is developed moderately and contains blood capillaries and connecting cellular elements (Fig. 1 and 2).

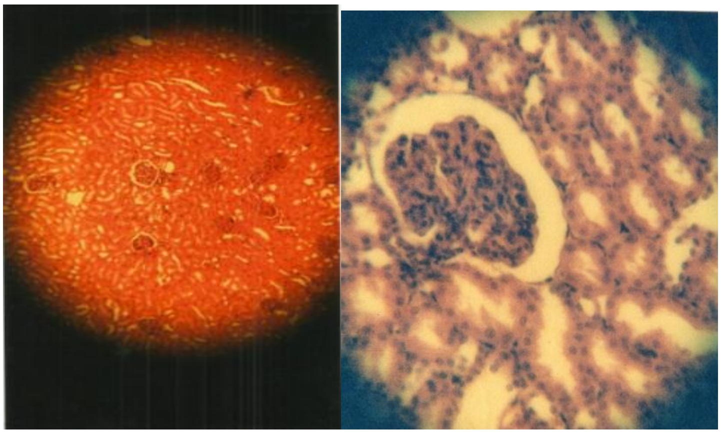

Fig. № 1-2. Histological picture of the kidney.

A heart. It is represented by a powerful layer of the myocardium, consisting of differently oriented bundles of striated muscle tissue, separated by a thin layer of loose fibrous tissue. Muscle bundles are cut in different planes and, accordingly, look differently: obliquely, transversely and longitudinally.

In a strictly cross section, the cardiomyocytes have an elongated shape, the sarcoplasm is filled with densely located myofibrils, and the central part is occupied by a rounded core with filamentary chromatin.

Borders of cardiomyocytes are well distinguishable, blood capillaries are sometimes detected between them. The oblique sections of cardiomyocytes are distinguished by their elongated-oval shape, the sarcoplasm is also occupied by densely located myofibrils, but their contours are not clearly distinguished.

On longitudinal sections, the cardiomyocytes have an elongated rectangular shape; at the junction of the cells, the insertion plates are revealed in the form of a thin transverse line. Myofibrils having a filamentous structure, of equal thickness and painted in pink color are clearly visible on these sections. In addition, they are well distinguished cross-striation. In the center of the cytoplasm, an elongated nucleus is revealed, its contours are sinuous, chromatin is presented in the form of delicate granularity. In places, the intermuscular connective tissue is edematous; there are numerous blood capillaries in it (Fig. 3).

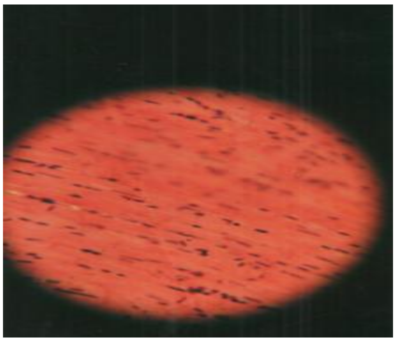

Fig. № 3. Histological picture of the heart.

The above analysis of the histomorphology of the heart of experimental animals allows us to conclude that it is identical with the morphology of the control animals and that no dystrophic abnormalities have been detected under the influence of the drug "vigril".

Spleen. It is outside covered with a thin connective tissue capsule and its parenchyma consists of white and red pulp. White pulp occupies most of the organ and is represented by round or oval lymphoid follicle formations. These follicles consist of accumulations of lymphocytes, the lymphocytes themselves are rounded, their nuclei are hyperchromic, and the cytoplasm is not always clearly distinguished. In most lymphoid follicles, reproduction centers are not expressed. In the white pulp (in the follicles) the central artery is eccentrically located, the wall of which is distinguished by thick layers of smooth muscle cells and with a narrow lumen. In some follicles, a weakly expressed connective tissue capsule is secreted. The red pulp is represented by numerous blood vessels, but mainly by the venous sinuses. The lumen of these vessels is dramatically expanded, and the cavity contains shaped elements, mostly red blood cells, the contours of these erythrocytes are oval or discoid. Red blood cells are also detected perivascular, their contours are uneven, or deformed. Next to these cells, macrophages are detected, the cytoplasm of which is filled with hemosiderin grains. In most macrophages they are detected in the form of large lumps, or small grains, it should be noted that in the white pulp, apparently in the cytoplasm of macrophages, hemosiderin grains are also detected, but they are few and found in the form of small grains.

Thus, with prolonged administration of this drug, no significant changes were found in the structure of the spleen (Fig. 4).

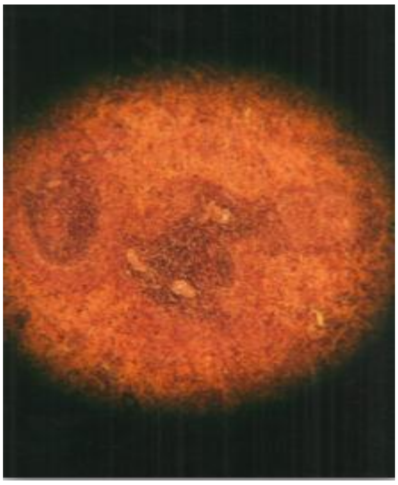

Fig. № 4. Histological picture of the spleen.

Lungs. On the preparation, the lung tissue is represented by numerous alveolar vesicles having a round or oval shape.

Alveoli stretched to varying degrees, most of them are moderately stretched others, on the contrary, slept. The thin wall of the alveoli is lined from the inside with a single-layer squamous epithelium, between the alveoli there are numerous blood capillaries, the lumen of which is small and contain blood cells, in addition, connective elements and cells are detected in the interalveolar spaces.

Mostly in the intermediate tissue there are large round formations of the bronchi, arteries and veins. Bronchioles are characterized by the presence of mucous membranes, submucous membranes are absent in them. In the mucosa, the single-layered multi-row ciliated epithelium stands out well, the structure of these cells is well preserved, the cytoplasm and nucleus stand out, a small layer of mucus is detected over the epithelium, sometimes similar structures are found in small amounts in the lumen of the bronchi together with desquamated epithelial cells.

The muscular plate is thin, it is revealed along the entire circumference of the bronchi, sometimes they are spongy, swollen and separated from their own plate. The submucous membrane of the bronchi consists of loose fibrous connective tissue, which is moderately infiltrated with lymphohistiocytic elements. Occasionally, lymphoid follicles consisting of a collection of lymphocytes are detected in the submucosa. Next to the bronchi, blood vessels, arteries and veins are often found, all the membranes of these vessels have a normal structure, the walls of the veins that have collapsed and contain blood cells in the lumen.

The walls of the small bronchi consist of epithelial layer and adventitia, moderately infiltrated with lymphohistiocytic elements.

In some parts of the vein, blood stagnation differs; in the lumen, they contain adherent red blood cells, as well as small grains of hemosiderin. A small amount of small grains of hemosiderin is found in the perivascular sites, in the cytoplasm of macrophages. In some cells they are in the form of fine grain, in others in the form of clumps, and the walls of the alveoli are deprived of such grains.

Summarizing the results of the study of the histological picture of lungs of experimental animals, it should be noted that the above-described picture corresponds to the picture of the control groups of animals, therefore, under the influence of this preparation, no noticeable structural changes have been identified.

Adrenal system. On the histological preparation of the cross section of the adrenal gland, the cortical and medulla gland is distinguished. Outside the gland is covered with a thin connective tissue capsule, under the capsule are the glomerular, bundle and mesh zones of the gland.

Below the capsule there is an accumulation of loosely arranged small cells, which are grouped into glomeruli, which have an irregular shape, and the cytoplasm is fine-meshed in appearance and is colored in a light pink color. In some cells, the nuclei have a light appearance, while in others they are painted hyperchromic.

Under this zone a small layer of small dark-stained cells with a hyperchromic nucleus is revealed, which corresponds to a layer of low-differentiated cells. Below this layer is a massive beam layer. The cells of this layer are distinguished by a light color, the cytoplasm has a fine-grained appearance, the border of the cells is clearly pronounced, the cells are of large irregular sizes, their nucleus is rounded, and the chromatin is detected as finely dispersed grain. On the border with the mesh zone of the cell of the beam zone without a sharp boundary, they pass into the mesh zone.

Closer to the brain part, the cells of the reticular zone acquire a smaller character, their orientation is disturbed, they acquire a reticular appearance, and the cells themselves are small and the cytoplasm of these cells is small and 8-10 cells are grouped small and more oxyphilous than the cells of the beam zone. Their nuclei occupy most of the cytoplasm.

Cells of the adrenal medulla are very different in color from cortical. They are colored much darker and are represented by clusters of smaller cells, the boundaries of the cells are not clearly expressed, the nuclei are small, painted hyperchromic, they do not differ in the degree of staining of the cytoplasm. The cytoplasm of some cells is fine-grained or in a state of rarefaction (Fig. 5).

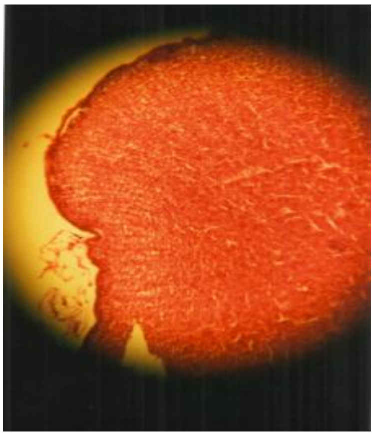

Fig. № 5 Histological picture of the adrenal glands.

Thus, a comparative study of the histomorphology of the adrenal glands of experimental and control animals allowed us to establish that they were built according to the general structure plan and no significant distinctive features were revealed by us.

CONCLUSIONS

A comparative analysis of the morphological picture of the internal organs of all groups of animals treated with various doses of the drug shows that their histological structure is basically comparable with the morphology of the control groups of animals.

Thus, the result of the research shows that long-term administration of the drug Vigitril in the structure of the studied internal organs does not cause changes.

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