THE EFFECT OF HYPOTHYROIDISM ON OFFSPRING IN AN EXPERIMENT ON LABORATORY ANIMALS

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ABSTRACT

The morphological changes in the myocardium of the offspring were studied when the mother had hypothyroidism in the rat to the female mother during the feeding of the rats.

The aim of our work was to identify structural and morphological changes in the walls of the heart of baby rats born to mothers in a state of hypothyroidism.

The material for the experiment, served microscopic myocardial preparations of 65 rats of different periods of early postnatal ontogenesis.

Results. The morphological structure of the myocardium of the heart of baby rats born to mothers, dystrophic changes were observed in a state of hypothyroidism. The observed changes reached a maximum by the 14th day of studies, manifested by perivascular and interstitial lymphohistiocytic infiltrate. Changes should also occur in the ultrastructure of the heart, which leads to changes in myofibrils, damage to the mitochondria, which affect the microvessels with a violation of the components of the vascular walls, which are developing intercellular edema.

Keywords: heart, myocardium, hypothyroidism, myocytolysis, mexidol.

INTRODUCTION

The relevance of the problem of hypothyroidism in the practice of doctors of various specialties is undeniable, since with a deficiency of thyroid hormones, which are necessary for the normal functioning of almost every cell of the human body, severe changes develop in all organs and systems without exception.

The thyroid gland has a hormonal effect on all types of metabolism, determining the individual level of homeostasis, playing the role of an integrative link in neuro-immune-endocrine regulation in the physiological and pathological processes of the body, among which pregnancy occupies a special position.

The structural foundations of the influence of the thyroid systems of mother and offspring in the presence of thyroid dysfunction in a pregnant woman are devoted to a few works [2,4].

Pathology of the thyroid gland is one of the factors of increased risk during pregnancy in women and the development of homeostatic mechanisms of the fetus [5,7].

Analysis of the latest data shows that even subclinical hypothyroidism is a risk factor for fetal loss and fetal abnormalities. This is especially true of the hypothyroid state during pregnancy and lactation [3,6].

According to the WHO, worldwide, diseases of the cardiovascular system occupy the first place in the list of causes of death. The likelihood of developing heart disease depends on many reasons. All factors that cause the development of heart disease are divided into two categories: internal and external [1,2]. The danger of cardiac pathologies is that many of them do not manifest themselves clinically until a certain point, proceeding in a latent form. Since the heart is a very important organ of the human body, the violation of its functions has a dramatic negative effect on the entire body. That is why cardiovascular diseases (to the same extent as malignant neoplasms) are the main cause of premature death. Heart disease begins with vascular damage and proliferation of the connective tissue stroma. Structural changes are necessarily accompanied by clinical symptoms in the form of impaired cardiac activity.

The aim of our work was to identify structural and morphological changes in the walls of various parts of the heart of baby rats born to mothers in a state of hypothyroidism and the use of the antioxidant mexidol.

THE MATERIAL AND METHODS

The object of the study was the hearts of 65 white outbred rats of the following age groups: 3, 7, 14, 21, 30 days. Animals were divided into 3 groups. The first group of animals consisted of female rats receiving mercazolil at a dose of 5 mg per 100 g of body weight for 30 days, then for the month before pregnancy, a maintenance dose of mercazolil was used at a rate of 2.5 mg per 100 g. After pregnancy and during feeding, rats were injected with mercazolil in a maintenance dose of 2.5 mg per 100 g through a probe. As a solvent for mercazolyl used 1% starch paste. The second group of the experiment consisted of female rats who were injected with mercazolilum on the same days of the experiment as in the first group, and after pregnancy they received mexidol at a dose of 0.5 mg per 100 g of weight together with mercazolilum. The third group included female rats of the mother of the control group, which, after birth, rat pups were daily fed on an empty stomach, depending on the term, in the amount of 1 ml distilled water. After each experimental week, the hormone level from the rat caudate vein was determined.

RESULTS AND DISCUSSION

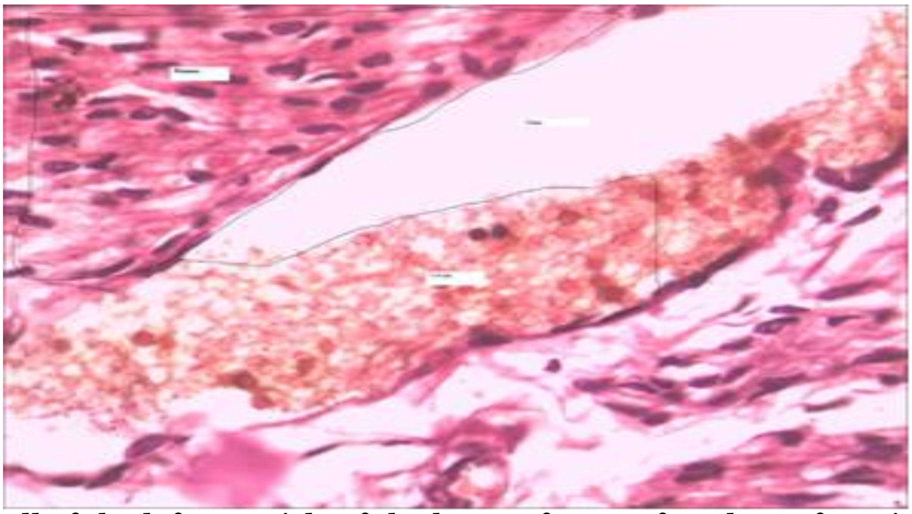
The control and experimental groups of animals were kept in the same vivarium conditions. At the end of the experiment, the rat pups of the experimental and control groups were killed under ether anesthesia. After that, the heart was isolated from animals, fixed in 10 per cent neutral formalin, followed by piping in alcohols, pouring in paraffin and preparing histological sections. Sections of 8-10 microns thick were prepared from paraffin blocks. Microsections were stained with hematoxylin and eosin, van Gieson.

The ventricular endocardium of the control group of animals consisted of longitudinally directed bundles of collagen fibers. A histological section reveals places where longitudinally lying bundles of collagen fibers interwoven with each other. Bundles of collagen fibers located closer to the ventricular myocardium are intertwined with bundles of collagen fibers from connective tissue layers located between bundles of cardiomyocytes of the myocardial inner layer (See App. A). The bundles of elastic fibers of the ventricular endocardium lie loosely compared to bundles of collagen fibers. In bundles of fibers adjacent to the myocardium of the ventricles, the density of arrangement increases, the direction of which changes from longitudinal to oblique, and are interwoven with bundles of connective tissue located between bundles of cardiomyocytes of the inner layer of the myocardium. Reticular fibers in the endocardium of the ventricles are located close to each other.

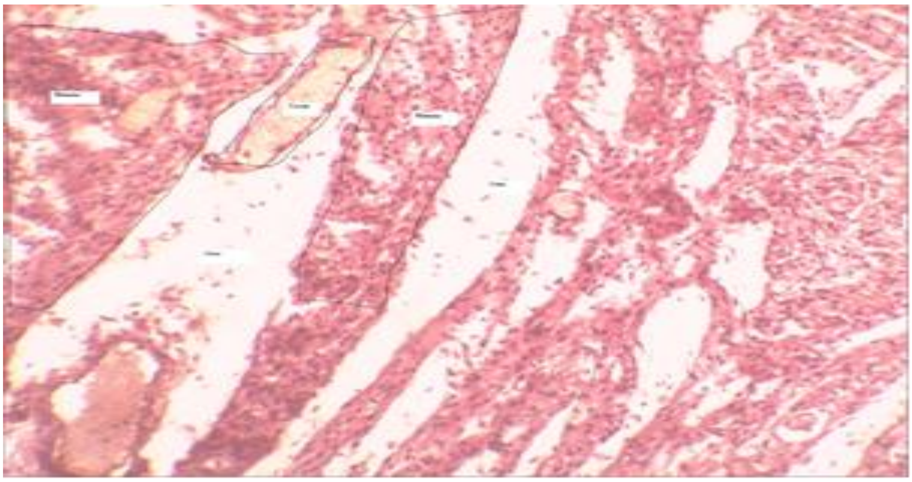
Upon further study of the slice, the cardiomyocytes of the outer layer of the myocardium are directed longitudinally, in the middle layer circular directed beams are detected; the inner layer contains weakly obliquely oriented bundles of cardiomyocytes. The inner bundles of fibers as they approach the endocardium acquire a more oblique direction and pass into the papillary muscles. A study of the direction of the bundles of ventricular myocardial fibers showed that the circularly directed layer does not always have a clear orientation. The bundles of fibers of the middle layer on the lower wall of the ventricles are directed obliquely and deviate towards the endocardium. Between the layers of ventricular myocardial cardiomyocytes, the border is weakly expressed. They fit snugly together. The inner layer of the myocardium consists of parallel located bundles of cardiomyocytes running in parallel with the endocardium. The outer layer of the myocardium has a loose structure in which cardiomyocytes are located in different directions (See App. B).

In the middle layer of the myocardium of the left ventricle of the heart, bundles of cardiomyocytes are located perpendicular to the inner layer. In the center of cardiomyocytes, 1-2 oval-shaped nuclei are determined. The nucleus of cardiomyocytes is located in the center of the cell, while myofibrils are located on the periphery. In the right ventricle, bundles of cardiomyocytes in the layers of the myocardium are similar to the left ventricular myocardium. However, unlike the left ventricle in the myocardium of the right ventricle, the thickness of the circular layer of cardiomyocytes is 2-3 times thinner than the thickness of the longitudinal layers of cardiomyocytes.

In the myocardium of the ventricles of the heart, depending on the site, bundles of collagen fibers have different directions. At the top of the heart, the bundles of collagen fibers are directed obliquely, while part of the bundles of collagen fibers changes direction from oblique to longitudinal. In the inner layer of the myocardium, bundles of collagen fibers lie in the longitudinal direction, separating bundles of cardiomyocytes from each other. In the middle layer of the myocardium, collagen fibers form bundles having a circular direction. When studying the outer layer of the myocardium, bundles of collagen fibers lie obliquely between bundles of cardiomyocytes. In the inner layer, the reticular fibers lie longitudinally and in the region of the apex of the heart they are intertwined with the reticular fibers from the outer layer of the myocardium of the heart. In the middle layer of the myocardium, the reticular fibers are located in a circular direction between the bundles of cardiomyocytes. Reticular fibers around bundles of cardiomyocytes form a network of various sizes and shapes (See App. C). The direction of the bundles of connective fibers depends on the direction of the cardiomyocytes.



1 – picture. The wall of the left ventricle of the heart of a rat of 14 days of age in the control group. Collagenic fibers of the endocardium. Coloring: according to van Gieson. Vis.: approx. 10, vol. 40.

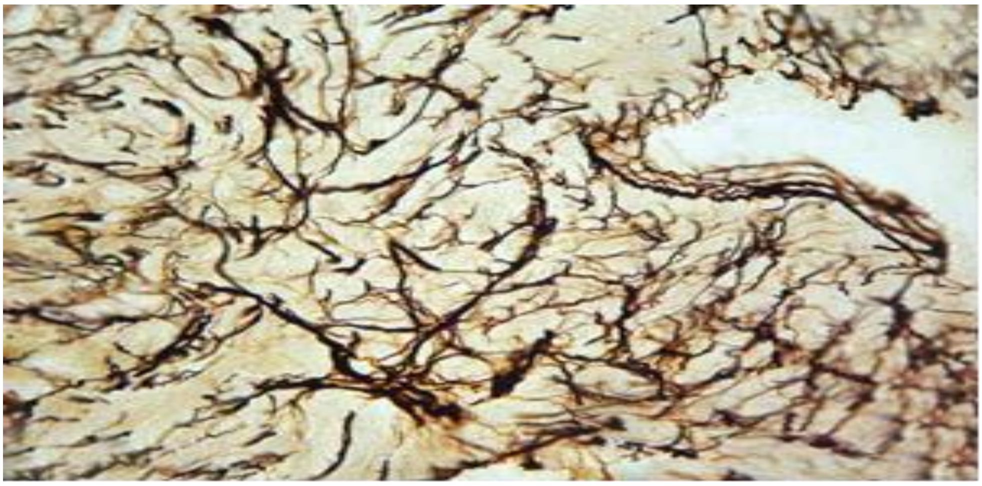


2 – picture. The side wall of the right ventricle of 21 days of age of the control group. Coloring: hematoxylin and eosin. Vis.: approx. 10, vol. 20.

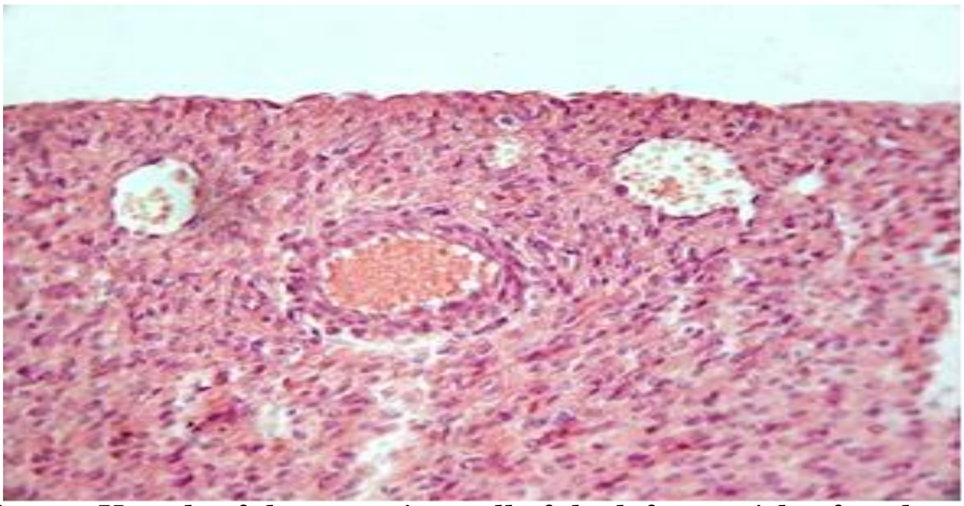
The interventricular septum consists of two longitudinal and one circular layer. The longitudinal layers on the left and on the right are from the corresponding longitudinal layers of both ventricles, and the middle circular layer is formed due to the circular layer of the left ventricle of the heart. The internal diameter of the arteriole ranges from 9.5 to 15.2 microns and an average of 11.7 ± 0.6 microns. The inner diameter of the venules ranges from 15.7 to

20.5 microns. Myocardial sinusoids are elongated, oval or irregular in shape. The thickness of the inner diameter of the capillaries is from 5.7 to 11.4 microns, an average of 9.3 ± 0.6. Myocardial blood vessels are direct along the bundles of cardiomyocytes (See App. D). Around the cardiomyocytes and blood vessels are bundles of collagen and elastic fibers. The fibrous structure of the connective tissue of cardiomyocytes connecting with the blood vessels captures the capillaries around the muscle fibers.

In the epicardium of the ventricles of the heart, bundles of collagen and elastic fibers lie longitudinally, and have a higher density than bundles of collagen and elastic fibers of the endocardium. In the epicardium of the ventricles, the reticular fibers are located longitudinally.



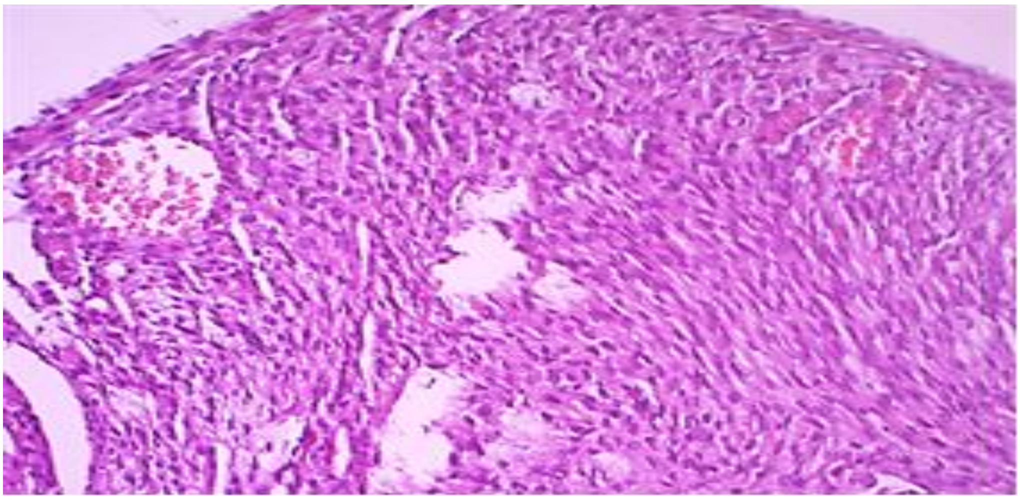
3 – picture. The front wall of the left ventricle of the heart of rats of 14 days of age in the control group. 1. Increased content of endocardial reticular fibers. 2. Reticular myocardial fibers. Coloring: imputation according to Foot in the modification of Yurina. Vis.: approx. 10, vol. 40.



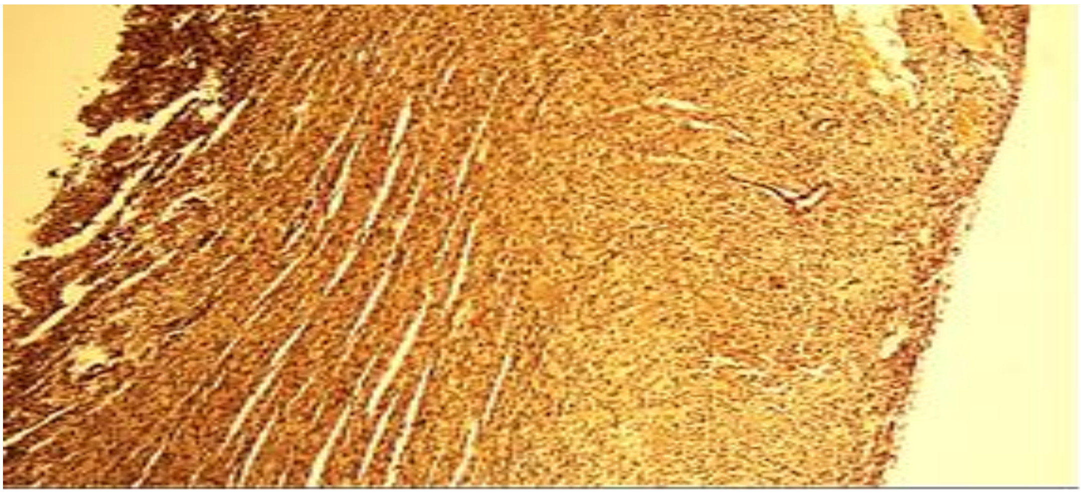
4– picture. Vessels of the posterior wall of the left ventricle of 21 days of age in the control group of animals of the subepicardial layer. Coloring: hematoxylinandeosin. Vis.: approx. 10, vol. 40.

The histological picture of 3-day-old rats undergoing hypothyroidism did not reveal significant differences compared with the control group. Cardiomyocytes had an oblong shape, formed muscle fibers, in the center of the fiber an oval-shaped nucleus was determined and myofibrils were clearly differentiated. In the subepicardial zone of the myocardium, dilated and full-blooded veins were detected with signs of redistribution of blood by the presence of clotted red blood cells, and in the myocardial stroma, beginning edema was observed. The endocardium is also somewhat thickened and uneven, in some places foci of depression and deepening in the form of cracks and vessels of Tebesia are visible. Endothelial cells are somewhat hypertrophied and hyperchromic, sometimes with foci of enlightenment in the basement membrane.

A morphological study of the heart of 7-day-old pups born to mothers in a state of hypothyroidism, with minor changes in the form of expansion of visible vessels (See App. E). An increase in the permeability of microvessels and vessels of the venous link was accompanied by the release of the liquid part of the blood through the vessel wall to the surrounding connective tissue (See App. F). Due to inflammatory infiltrate, the vascular wall thickens and the lumen narrows. These discirculatory disorders lead to perivascular edema, loosening of the intramuscular space. At the same time, cardiomyocytes are loosened with the development of dystrophy and vacuolization in their cytoplasm. Myofibrils have a granular appearance, of different thickness and density. During this period, the epicardium of the heart is significantly thickened due to the proliferation of young connective tissue cells and swelling of fibrous structures. The endocardium is also swollen, in places forms uneven thickenings from proliferative endothelial cells.



5– picture. Anemia of the pancreatic vessels of the heart and blood supply. Hematoxylinandeosinstain. Vis.: vol. 20, approx. 10.



6– picture. Pancreatic tissue of a 7 day old rat with blood and vasodilatation. Painting according to Van Gieson, Vis.: vol. 10, approx. 10.

At the age of 14 days, destructive and inflammatory phenomena join the above-described discirculatory and dystrophic changes. In the myocardial stroma, increased swelling was noted mainly in the perivenular and pericapillary spaces. Collagen fibers are swollen, loosened, in some places there is a separation of collagen bundles, swelling of the main substance of the connective tissue with the initial signs of surface disorganization. Connective tissue cells are also swollen, their nuclei slightly increase in size. Vascular disorders are common, endothelial cells in the vessels, acquire a rounded shape. In the cytoplasm of cardiomyocytes, small vacuoles were found filled with a clear cytoplasmic fluid, i.e. hydropic dystrophy develops. Intracellular edema is focal in nature, along with dystrophically altered cardiomyocytes, unaffected cells are found. In the myocardium of the left ventricle of the heart, around the vessels and in places in the stroma, inflammatory foci consisting of lymphohistiocytic cells appear (See App. G). In this case, cardiomyocytes are loosened with the development of dystrophy and vacuolization in their cytoplasm. Myofibrils have a granular appearance, different thickness and density. The endocardium is also swollen, in places forms an uneven thickening of proliferative endothelial cells. At this time, the epicardium of the heart is significantly thickened due to the proliferation of young connective tissue cells and swelling of fibrous structures. A histochemical study reveals a significant decrease in the number of collagen structures in the composition of the epicardium, instead of them, the content of SHIK-positive substance increases, especially in the walls of blood vessels. Endothelial cells are somewhat hypertrophied, hyperchromic, sometimes with foci of enlightenment in the basement membrane.

FINDINGS

In transient experimental hypothyroidism, the use of mercazolil in animals in the ventricular myocardium results in dystrophic, destructive and atrophic changes in cardiomyocytes, diffuse edema and stromal fibrosis. The first signs of hypothyroidism were detected on days 7-14, a detailed picture develops on the 21st day.

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