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SCIENTIFIC ASSESSMENT OF THE EFFECTS OF HYPOTHYROIDISM IN EXPERIMENTAL STUDIES

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ABSTRACT

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.

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

INTRODUCTION

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 [3,4]

It is important to take into account that in conditions of thyroid disorders of the mother and fetus, interrelated organs and systems of the offspring are involved in the pathological process, leading to disorganization of metabolic processes. The presence of even a minimal deficiency of thyroid hormones in a child adversely affects the state of his immunity, mental and physical development, puberty, worsens the prognosis of reproductive function [2,6,7].

The importance of the thyroid gland for the normal maintenance of reproductive function is

great: with hypothyroidism, infertility often develops, hypo- and hyperthyroidism of pregnant women adversely affects the offspring, leading to structural and functional disorganization of the whole organism, including the cardiovascular system of the fetus [1,5].

THE MATERIAL AND METHODS

The study process of growth dynamics of the wall thickness of both the left and right ventricles of the heart of rat pups born by mothers in hypothyroidism state, depending on different parts of the heart, showed that the wall thickness of all departments is less than the by control indices. Comparing the thicknesses of wall of the right and left ventricles of the animals of the experimental group with the control group, a significant lag in myocardial indices is revealed. These changes are being most pronounced in pups of 14 days of age. The thickness of the left ventricular myocardium is less than that of the control group by 29 per cent. The thickness of the right ventricle compared with the control group is less by 17 per cent (1- table).

1-table. Indicators of the thickness of the layers of the lateral wall of the ventricles of the rat heart, in microns

Days	Ventricles	Control	1st group of experiment	2nd group of experiment
3	L, n=9	1149±33	960±22,1	958±22,0
	R, n=9	381±12	295±7,4	328,5±8,2
7	L, n=7	1327±33,2**	976±28,3	1045±30*
	R, n=7	442±11,9**	328±6,6**	342±6,84
14	L, n=9	1544±35***	1105±28**	1272±32***
	R, n=9	500±14,0**	360±9,7*	412±11***
21	L, n=8	1738±46,9**	1419±33***	1513±35**
	R, n=8	571±14,3**	470±13***	507±14***
30	L, n=8	1935±21,3***	1565±35,5*	1758±22,3***
	R, n=8	610±18,1**	402±51,1**	540±14,9**

On the 21st day, vascular disorders persist in the myocardium: pronounced plethora of veins, stasis, numerous perivascular hemorrhages of a diapedetic nature and an increase in the intensity of edema is noted. Edematous fluid is located between the muscle fibers, as if pushing them apart. Swelling of not only connective tissue cells, but also their processes was revealed. The swollen processes of neighboring fibroblasts are in contact with each other and, as it were, form syncytium. In the myocardial stroma, numerous small infiltrates from lymphocytes, histiocytes and fibroblasts. In cardiomyocytes, signs of protein hydropic dystrophy with the development of intracellular edema are observed, numerous foci of plasmolysis throughout the myocardium are determined. Plots of plasmolysis (intracellular myocytolysis) look like optically empty spaces. With intracellular myocytolysis, dissolution of myofibrils in certain sections of

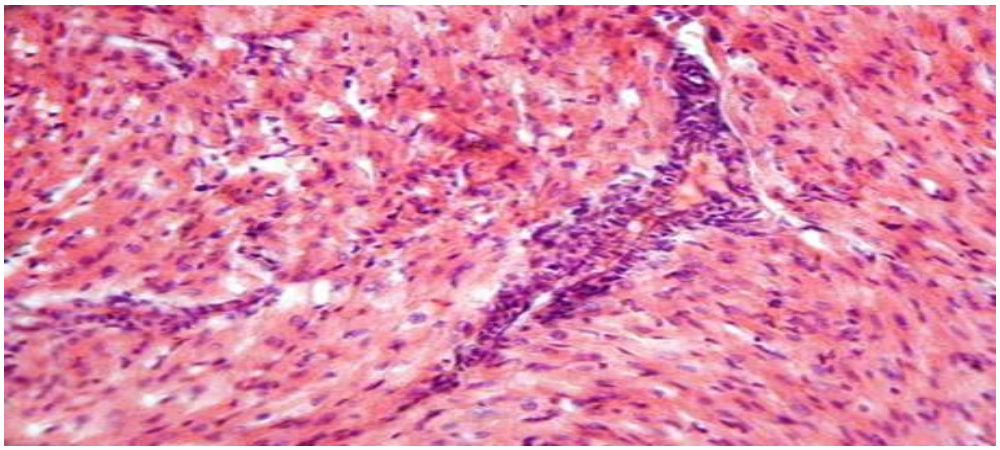
the fiber along its length is noted. In adjacent areas, myofibrils are preserved. With silvering according to Foote, the formation of reticular fibers in the form of coarse clumps and intermittent thick dark brown fibrous structures is determined. A histochemical study using the Van Gieson method reveals loosening and a decrease in the number of collagen structures, especially in the epicardium, and an increase in the content of SHIK-positive substance. Elastic fibers of the endocardium and in the intramuscular stroma in a state of loosening and tearing due to edema and disorganization of the connective tissue.

The study process of the dynamics of growth of wall thickness of both the left and right ventricles of the heart of rat pups born by mothers in a state of hypothyroidism with the use of mexidol depending on different parts of the heart showed that the wall thickness of all departments is less than by the control indices. Comparing the wall thicknesses of the right and left ventricles of the animals of the experimental group with the control, a significant lag in myocardial indices is revealed. These changes are being most pronounced in pups of 21 days of age. The thickness of the left ventricular myocardium is less than that of the control group by 29 per cent. The thickness of the right ventricle compared with the control group is less by 17 per cent (1-table).

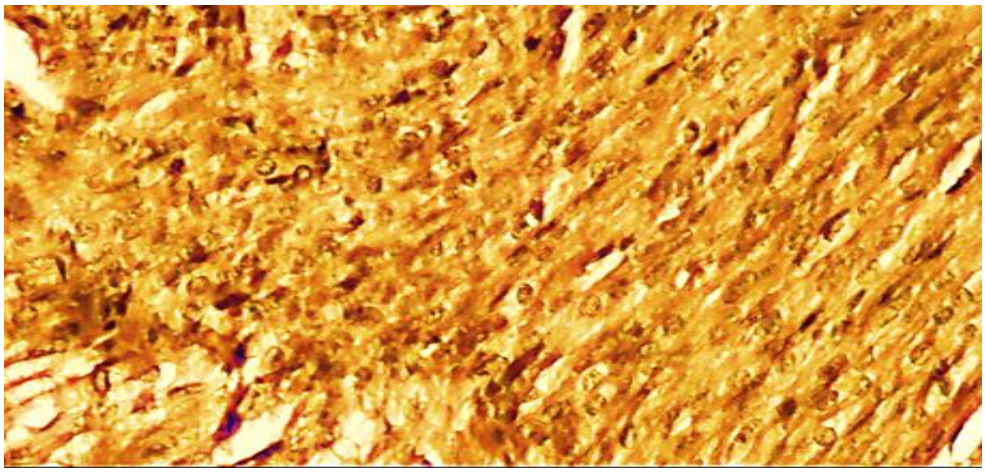
After 30 days, interstitial edema intensifies and spreads to the entire myocardium, reaching the greatest value in the perivenular spaces. Due to edema, swelling of collagen fibers, their delamination and shedding are observed. The main substance swells and collapses, signs of disorganization of the connective tissue appear (See App. H). When stained with toluidine blue, the phenomenon of metachromasia is observed. Dystrophic changes in the myocardium acquire a diffuse character, increased resorption of the cytoplasm, intracellular edema is noted. The foci of plasmolysis are numerous and larger than on the 21st day. Intracellular myocytolysis extends to the entire myocardium; total damage to cardiomyocytes is noted. In the focus of myocytolysis, most myofibrils are absent, single fibrils are visible. At the same time, marked loosening of the subendocardial and intramural layers of the heart wall due to edema and dissociation of cardiomyocytes is noted.

The study process of the growth dynamics of thickness of wall of both left and right ventricles of a heart of baby of intact rats at different stages of postnatal ontogenesis depending on the parts of the heart walls has showed that by the 30th day of the current study, comparing to 3 days of age, thickening occurs on average in all parts of the heart 1.7 times, only in the interventricular septum - 1.5 times. These morphometric data are confirmed by microscopic rearrangements occurring in the dynamics of postnatal ontogenesis (1-table).

The subepicardial layer of the myocardium remains dense, where cardiomyocytes form large muscle bundles. Inflammatory infiltrate and sclerosis are defined around the vessels. When staining according to the Weigert method, it is noted that in the walls of the arteries the inner elastic membrane is thickened, winding, sometimes homogenized. In the muscle layer and in the surrounding connective tissue, elastic fibers are fibrous and lysed.



1- picture. LV wall of a 14-day-old experimental group rat. Lymphohistiocytic infiltration around the vessels. Hematoxylin and eosin stain. Vis.: vol.20, approx. 10



2- picture. Myocardial tissue with slight sclerosis of the capillaries. The staining of the vessel wall is densely red. Coloring according to Van Gieson, Vis.: vol. 40, approx. 10

In cardiomyocytes with small foci of myocytolysis, the nuclei are preserved. In cardiomyocytes with large foci of myocytolysis, the nuclei are destroyed with the development of collicational necrosis. Remains of fibers in the form of tubules surrounded by a sarcolemma are found in foci of collication necrosis; the contents are not stained. Sarcolemma is thickened and well stained with picrofuxin. The described tubules are collapsed, around them there are excessive deposits of glucosaminglycans.

In some areas, counter-abnormalities and small foci of coagulation are determined, fragmentation of muscle fibers is observed in some places. However, collision processes dominate in the myocardium.

Since metabolic imbalance primarily affects the energy supply system of cells, the therapy should be aimed at increasing energy generation and increasing myocardial resistance to hypoxia. The second experimental group included 26 rats, which were daily injected with mercazolyl and antioxidant mexidol.

In rat pups 3 days old born from mothers to hypothyroidism and receiving mexidol, the normal histological picture is determined in the rat myocardium, pathohistological changes in the myocardium are not detected.

After 7 days of birth, vascular disorders in the form of plethora and expansion of veins, stasis, plasmorrhagia are noted (See picture). Vascular disorders persist, there is an increase in plasmorrhagia, plasma impregnation and fibrinoid swelling of the walls of the arteries.

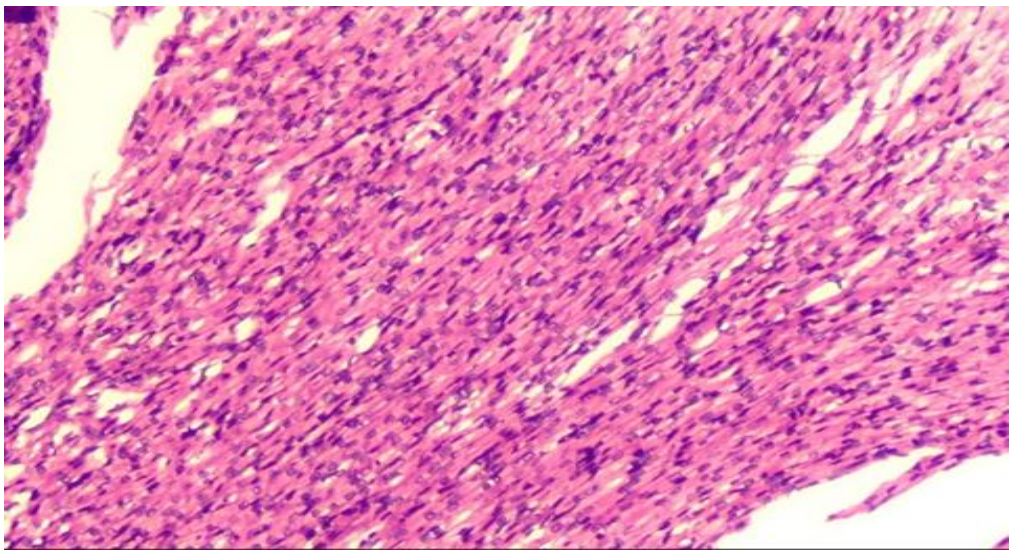
After 14 days from the start of the experiment, against the background of the use of mexidol in the myocardial stroma, a small edema was found mainly around the veins. In individual cardiomyocytes, intracellular edema was detected in the form of accumulations in the cytoplasm of vacuoles filled with tissue fluid.

Intracellular edema is focal in nature. In the myocardial stroma, vascular disorders persist in the form of plethora, stasis and venous stasis. When staining with toluidine blue, metachromasia was not detected; fibrinoid swelling of the walls of the artery is observed.

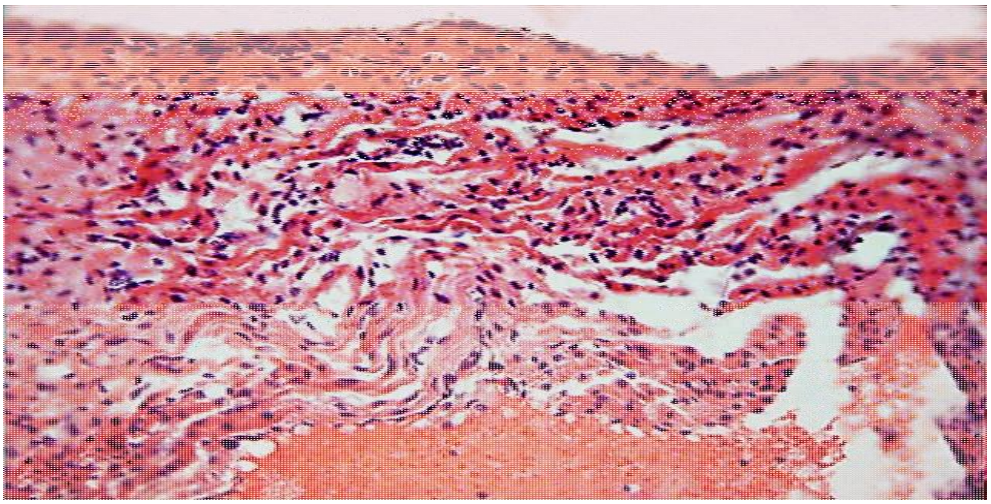
After 21 days, edema was found in some places in the myocardial stroma, which is focal in nature and has a lower intensity than in the first experimental group. In areas of edema, collagen fibers swell and homogenize. There is a superficial disorganization of connective tissue with the accumulation of glycosaminoglycans. On histological preparations, mucoid swelling is observed (See picture).

In places in the cytoplasm of cardiomyocytes, hydropic dystrophy is observed, which is focal in nature. The transverse striation of muscle fibers is preserved, in some areas myofibrils swell. Vascular disorders become less intense.

After 30 days, against the background of daily use of the antioxidant mexidol, partial relief of vascular disorders is noted. In the myocardial stroma, edema develops, which extends to almost the entire myocardium, however, the intensity of the edema is less pronounced compared with the experimental group I. In the connective tissue of the myocardial stroma, swelling and decomposition of the main substance, accumulation of glucosaminglycans, swelling, homogenization and partial decomposition of collagen fibers with the formation of a fibrinoid are observed. At this time, for the first time in the stroma, small focal infiltrates from lymphocytes, histiocytes, and fibroblasts were detected (See picture).



3- picture. The cytoplasm of some cardiomyocytes is unevenly colored, sarcolemma is clearly defined. In the sarcoplasm, transverse bands are visible. Hematoxylin and eosin stain. Vis.: vol. 20, approx. 10



4- picture. Wall of the right heart core of a 30-day-old rat born to mothers with hypothyroidism. Myocardial hypercellularity is preserved. Hematoxylin and eosin stain. Vis.: vol. 20, approx. 10

At the indicated times, a picture of intracellular edema is observed in the myocardium and for the first time against the background of mexidol use, small foci of plasmolysis (myocytolysis) appear. These foci are optically empty portions of the cytoplasm with complete preservation of the plasmolemma. Compared with the experimental group I, the processes of myocytolysis are focal in nature.

Thus, with the daily use of the antioxidant mexidol in rats of the experimental group II, no histological changes in the myocardium were detected in the first 7 days. The first signs of myocardial damage (beginning periventricular edema of single cardiomyocytes) appear on the 14th day, that is, 7 days later than in the first experimental group. An expanded picture of a change in the myocardium such as diffuse intracellular edema, myocytolysis was detected on the 28th day, then the network was later compared by comparison in the first experimental group. Destructive processes with total damage to the myocardial fibers in the experimental group II of rats were not detected. Regenerative processes with the replacement of damaged myocardial cells with connective tissue proceeded more intensively in comparison with the experimental group I. The above suggests that mexidol has a protective effect on the myocardium under conditions of hypothyroidism.

FINDINGS

1. When using an antioxidant in the myocardium of experimental animals, signs of hypothyroidism occur on the 21st day, and a detailed picture on the 30th day.
2. The intensity and prevalence of morphological changes are less pronounced, destructive changes in the myocardium are not detected.

The use of antioxidants in experimental hypothyroidism in laboratory animals has a protective effect and prevents the development of severe destructive changes in the myocardium.

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