

PRACA ORYGINALNA
ORIGINAL ARTICLE**MORPHOFUNCTIONAL STATUS OF CARDIO-VASCULAR SYSTEM OF RATS WITH CONGENITAL HYPOTHYREOSIS****STATUS MORFOLOGICZNO-CZYNNOŚCIOWY UKŁADU SERCOWO-NACZYNIOWEGO SZCZURÓW Z WRODZONĄ NIEDOCZYNNOŚCIĄ TARCZYCY****Svitlana M. Chuhray¹, Viktoria E. Lavrynenko³, Rostyslav F. Kaminsky², Iryna V. Dzevulska², Olexandr V. Malikov², Olexandr I. Kovalchuk^{2,3}, Liudmyla M. Sokurenko^{1,3}**¹DEPARTMENT OF HISTOLOGY AND EMBRYOLOGY, BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE²DEPARTMENT OF HUMAN ANATOMY, BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE³DEPARTMENT OF FUNDAMENTAL MEDICINE, TARAS SHEVCHENKO NATIONAL UNIVERSITY OF KYIV, KYIV, UKRAINE**ABSTRACT****Introduction:** There is an increasing number of cases of congenital hypothyroidism. One of the most common complications of hypothyroidism is damage to the cardiovascular system, which in 30-50% of patients leads to the development of arterial hypertension.**The aim:** studying the features of the ultrastructure of myocardial capillaries in mature rats with hypothyroidism.**Materials and methods:** Experiments were conducted on 40Wistar line rats with congenital hypothyroidism: juvenile young (45-day) and sexually mature (100-day) rats, as well as intact animals of the corresponding age. While extracted from the experiment rats of all experimental groups had their arterial pressure measured using a plethysmograph while the development of hypothyroidism was controlled by the immune-enzymatic method. Electron microscopic examination of the left ventricular myocardium and morphometric study of volumetric and quantitative densities, cross-section area, and form factor of micropinocytotic vesicles were conducted.**Results:** In the sexually mature rats with congenital hypothyroidism the quantitative density of the capillaries in the myocardium decreases. Activation of transcytosis is accompanied by significant violations of vesiculation. Some of the endothelial cells of experimental animals contain a moderate amount of transport vesicles, while others are overfilled with these structures and desquamate into the lumen. In older rats with congenital hypothyroidism there is a further dilution of capillaries, the development of hypoxic state in them, mucinous edema of interstitial space, decrease of biosynthetic and transport processes activity.**Conclusions:** In young (45-day) rats with congenital hypothyroidism the direction and expressiveness of compensatory processes is to enhance the transcytosis processes. Dystrophic-destructive changes are manifested by apoptosis in some endothelial cells, decrease in the number of biosynthetic organelles, lysis and edema of their cytoplasm. In sexually mature (100-day) rats with congenital hypothyroidism destructively-dystrophic processes in the blood capillaries of the myocardium are approximately balanced with compensatory-adaptive.**KEY WORDS:** myocardium, blood capillaries, rat, congenital hypothyroidism, electron microscopy

Wiad Lek 2019, 72, 2, 229-233

INTRODUCTION

In recent decades more and more attention of researchers is being attracted by prevalence of hypothyroidism – a disease caused by decrease in the biological effect of thyroid hormones on the tissue level or their deficiency in the body. The number of cases of congenital hypothyroidism (CHT) is increasing. One of the most common complications of hypothyroidism is a violation of the cardiovascular system, which in 30-50% of patients leads to the development of arterial hypertension [1-3]. However, although in people of different ages clinical manifestations and the course of hypothyroidism differ significantly [4, 5], data on morphofunctional changes in organs and tissues in the age aspect has not been identified in the literature.

THE AIM

In this regard, the purpose of the research was to study the features of the ultrastructure of myocardial blood capillaries in mature rats with hypothyroidism, that is, structures where metabolism occurs and which are largely responsible for tissue damage in the heart.

MATERIALS AND METHODS

Experiments were performed on 40 white rats of the Wistar line, which were under standard vivarium conditions of the Bogomolets National Medical University. The juvenile (45-day) and sexually-grown (100-day) Wistar rats with CHT were studied. Control was provided by intact rats of the Wistar line of the same age. Congenital hypothyroidism was modeled by inhibition of thyroid gland by threo-

static – Mercazolil. Starting from the 14th day of perinatal development pregnant females were administered with the drug. After birth, the animal received it with the mother's milk, and in the future – while self-feeding. The drug was administered throughout the experiment daily at a dose of 20 mg / kg of body weight. The solvent was water. The development of hypothyroidism was controlled by the immune-enzymatic method on the Sunrise RC device, TEKAN in both control and hypothyroidic rats when they were removed from the experiment. Experiments with animals were carried out in accordance with the Law of Ukraine “On protection of animals from cruelty” (2006), “General ethical principles of animal experiments”, adopted by the First National Congress on Bioethics (Kiev, 2001).

While extracted from the experiment rats of all experimental groups had their AP (arterial pressure) measured using a plethysmograph, while the development of hypothyroidism was controlled by the immune-enzymatic method on the Sunrise RC device, TEKAN.

Electron microscopic examination of the left ventricular myocardium of experimental rats was conducted. The material was processed in accordance with the generally accepted techniques of electron microscopic examination [6]. Ultra-thin sections were made with ultratome Reihart (Austria) and examined using an electron microscope PEM-125K.

Morphometric studies were carried out on a semi-automatic device for graphic research processing using the program “Organelle”. Volumetric and quantitative densities, cross-section area, form factor of micropinocytotic vesicles (MPV) were studied. Statistical processing was carried out using the Student parametric criterion and the nonparametric Kolmogorov-Smirnov criterion according to the principle of variation statistics.

RESULTS

CHANGES IN FUNCTIONAL PARAMETERS IN EXPERIMENTAL RATS

At 45-day rats with CHT AP does not reach meaningful quantities yet. At 100 days after birth AP increases compared with control animals. In this case, about half of animals with CHT showed increase of this parameter (Table I).

The existence of persistent hypothyroidism is confirmed by a significant decrease in the concentration of free thyroxine in blood plasma during the whole experiment, starting with the early stages of the disease and becoming the most pronounced in the final stages (Table I), compared with control.

Ultrastructure of blood capillaries of myocardium in rats

In the myocardium of 45-day rats with congenital hypothyroidism, capillaries with both narrowed and enlarged lumen (Fig.1A, B) as well as flattened microvessels can be observed. This may indicate, on one hand, the decrease in the intensity of the capillaries formation, and, on the other, the involvement of a greater number of capillaries in the microcirculation, which leads to the decrease in the

number of reserve, non-functioning microvessels. Most capillaries have a flattened lumen surface, which contains single microvilli and invaginations (Fig. 1B).

However, there are capillaries with different magnitude of cervical protrusions at different stages of separation from the cell. Such microclazmatosis outgrowths can further lose connection with endothelial cells and get into the bloodstream.

Endothelial cells of moderate electron density with well-preserved cytoplasm are prevalent. They contain large nuclei of oval or somewhat irregular shape. Mitochondria in a small number are located mainly in the near-nuclear zone. They are usually oval, with an unevenly enlightened matrix and irregularly located crystae (Fig.1.A). The channels of the endoplasmic reticulum are mainly short, contain ribosomes on their membranes. The latter, in the form of discrete units and polyribosomal complexes unevenly fill the nuclear-containing and peripheral regions of the endothelial cells. Lysosomes, multivesicular corpuscles, secretory vesicles of the Golgi complex, secretory granules are not expressed. There are also rare elements of the cytoskeleton – microfilaments and microtubules.

In 100-day rats with congenital hypothyroidism ultrastructural changes become more expressed and more prevalent in the blood capillaries of the myocardium. Part of the capillaries have dilated lumen and thinned nuclear-containing and peripheral areas. Endothelial cells that form these capillaries have a preserved ultrastructure, but they also show damage to organelles. Some cells have only isolated tubules and ribosomes even within the nuclear-containing regions. Channels of the granular endoplasmic reticulum are often fragmented, degranulated, dilated. Dictiosomes of the Golgi complex are flattened and have blurred membranes that give them a look of a homogeneous mass of moderate electron density.

The number of mitochondria is negligible. They show electron-dense matrix, destruction of external mitochondrial membranes, fragmented crystae. In some mitochondria, the outer membrane is spirally twisted, thus resembling myelin sheaths. That is, the formation of myelin-like structures, which is a sign of a violation of lipid peroxide oxidation.

Attention is drawn to increasing electron density of inter-endothelial junctions, enlargement of the obliteration spots and storage of finely dispersed material, which may worsen the paracellular route of substances transport. Basal lamina is sometimes thinned, destructured, sometimes thickened, and loose.

Another feature that further increases in 100-day rats with congenital hypothyroidism is the prevalence of blood capillaries at different stages of destruction. Endothelial cells with increased electron density of the cytoplasm, picnotically altered nuclei, a large number of microclazmatosis outgrowths on the luminal and in some cases on basal surfaces are observed. In the myocardium, areas of perivascular edema are common.