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PECULIARITIES OF THE MORPHOLOGY OF THE SECRETORY COMPONENTS OF THE HEART UNDER INFLUENCE OF HEMODYNAMIC OVERLOAD

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The study of the heart as an endocrine organ has attracted the attention of researchers for many years, but a number of issues remain debatable today. Of particular interest is the study of the morphology of the components of the heart, which are responsible for the synthesis, accumulation and secretion of biologically active substances.

Aim: to establish the morphofunctional state of the secretory components of the heart in normal conditions and in the conditions of experimental hemodynamic overload of the heart. The material for the study was white rats, which were created with artificial coarctation of the aorta, the other two groups were exposed to adrenaline and dexamethasone.

There are differences in the morphofunctional state of mast cells in the ventricles, atria, and auricles, which is related to the differences in the structure of different parts of the heart. Hemodynamic overload of the myocardium is a powerful factor in the activation of the secretory components of the heart and stimulates the redistribution of topographic types of mast cells, the activation of their degranulation, which, under the conditions of prolonged action of the factor, leads to increased proliferation of fibroblasts and growth of connective tissue, which occurs during remodeling of the myocardium. Activation of secretory cardiomyocytes occurs in the form of an increase in secretory processes in the early stages of the effect of the factor, which can be considered as an additional reserve for compensation of overload.

Adrenaline and dexamethasone have the opposite effect not only on the activity of tissue basophils of the heart, but also on their migration and number.

Key words: *heart, myoendocrine cells, mast cells, specific secretory granules, experiment.*

Connection of the publication with planned research works. The research was carried out within the framework of the scientific topic "Morphogenesis of organs and systems of the human body and experimental animals in ontogenesis in the norm and under the influence of external factors", state registration number 0117U006976.

Introduction. The study of the heart as an endocrine organ has attracted the attention of researchers for many years, but a number of issues remain debatable even today [1, 2, 3]. The presence of a secretory function in the heart allows us to talk about the participation of this organ in the humoral regulation of the body's homeostasis. This is important in the study of the pathogenesis of a number of cardiac diseases. Of particular interest is the study of the morphology of the components of the heart, which are responsible for the synthesis, accumulation and secretion of biologically active substances – the secretory components (SC) of the heart, as well as their age characteristics, and the influence of various factors and diseases on the morphology and functioning of these components [3, 4, 5, 6]. These include myoendocrine cells (MEC) of the heart, which contain specific secretory granules (SSG) and cardiac mast cells. The study of the morphology of these components in the norm and in conditions close to the pathogenesis of some cardiovascular diseases, as well as the study of the effect of some pharmaceuticals that are used in clinical practice, is relevant today and will allow us to further establish the role of the endocrine component of the heart in the mechanisms of development and compensation of cardiac pathology [7].

The aim of the study was to establish the morphofunctional state of the secretory components of the heart in normal conditions and in conditions of experimental hemodynamic overload of the heart, as well as the effect of adrenaline and dexamethasone on SC.

Object and methods of research. The material for the experimental study of SC was white mature male Wistar rats weighing 160-180 grams, which were divided into groups as follows: 1) to study the effect of adrenaline and dexamethasone 17 rats: the first (5 rats) and the second (8 rats) experimental, which accordingly, a solution of adrenaline (0.3 mg/kg) and dexamethasone (0.2 mg/kg) was administered intraperitoneally, the third was a control solution (4 rats); 2) to study hemodynamic overload of the heart [8] – 30 rats, which were divided into 5 experimental groups of 5 each depending on the duration of the experiment, 5 rats made up the control group. Rats anesthetized with ether were subjected to a silk ligature above the exit point of the renal arteries, and fixed on a probe with a diameter equal to ½ the diameter of the aorta in its abdominal part. Rats were removed from the experiment by the method of decapitation under ether anesthesia at 1, 3, 5, 10 and 30 days after the operation. Pieces for histological examination were taken from the right and left parts of the heart wall: auricles, atria, ventricles, as well as from the atrial and interventricular septum, from which preparations were made according to the standard method of making semi-thin sections 1-2 microns thick, stained with a 2% solution of toluidine blue [9]. To study the secretory granules of MEK, we used the method of immunohistochemical research with the use of specific DAKO monoclonal antibodies to chromogranin A (clone N1535), NSE (neuron specific enalase – clone N1516) and synaptophysin (clone N1566) – substances found in MEK granules.

For histological examination, pieces were taken from the right and left parts of the heart (atria, atria,

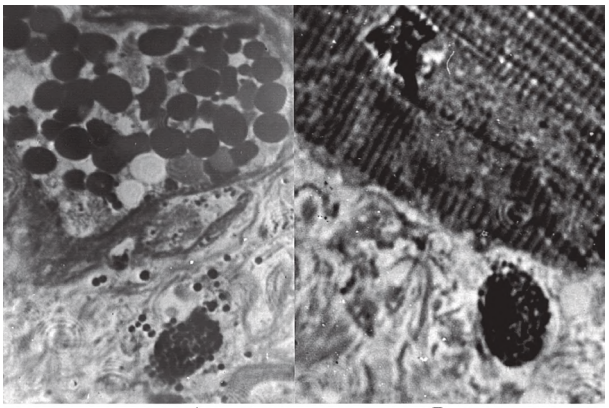

Figure 1 – Types of mast cells. A – type I; B – type III. Electron microscopic study. Inc.: x 10000.

ventricles), atrial and interventricular septum. Further, preparations were made from them according to the generally accepted method of preparing histological, semi-thin sections, which were stained with toluidine blue and hematoxylin-eosin, and preparations for electron microscopic examination.

Statistical processing of the obtained results was carried out according to generally accepted methods (using the MS Excel computer program).

Research results and their discussion. During the study of histological preparations of human hearts in all the specified age groups of people in all the studied departments, tissue basophils of three main topographic types were visualized [2]: Type I – mast cells, which are located near vessels of different caliber; II type – mast cells located in thick layers of connective tissue; Type III – mast cells located near cardiomyocytes, as well as specific secretory granules located in cardiomyocytes in several groups of 7-22 granules, mainly in the perinuclear area **(fig. 1).**

Since hemodynamic overload of the myocardium is one of the main manifestations of many cardiovascular diseases, in order to study its effect on SC, we conducted an experimental study on rats with the creation of artificial coarctation of the aorta. During histological and electron microscopic examination of the heart of experimental animals, mast cells of all three described topographic types were visualized. In rats of the control group, types II and III mast cells prevailed in all sections of the myocardium. MEC containing three types of secretory granules were also determined: type 1 – with the most electron-dense content; Type 2 – with less electron-dense content; Type 3 – membraneless granules that had an electron-transparent content. The granules were contained mainly in the perinuclear space in groups of 8-26. The number of cardiomyocytes (CMCs) that had SSG in the auricles of the heart was 94-98%, in the atria – 90-95%, in the ventricles – 48-60% and was slightly higher in the corresponding right sections.

On the first day after the creation of coarctation of the aorta, an increase in the relative number of mast cells type 1 in the myocardium was noted due to their movement into the perivascular space, as well as an increase in the number of degranulating forms of mast cells. These changes were more pronounced in the left ventricle, but were also observed in other departments to a somewhat lesser extent. In addition,

Figure 2 – SSG of the right ventricle of the heart of rats on the 10th day of coarctation of the aorta. Electron microscopic study. Inc.: x 10000. Designation: 1- nucleus, 2- mitochondria, SSGs are marked with arrows.

in the secretory CMCs, there was a movement of SSG from the perinuclear to the subsarcolemmal space, with an increase in type 3 SSG.

On the third day of the experiment, they were of a more pronounced nature. The migration of mast cells into the perivascular space, and the movement of CSF into the subsarcolemmal space continued, and there was also an increase in CSF type 3. These changes of varying degrees of severity were observed in all parts of the heart, which also occurred on the fifth day, however, there were signs of activation of synthetic processes in secretory CMCs – an increase of 1 and 2 types of SSG, and the percentage of CMCs with SSH in the ventricles increased to 55 -68%.

On the tenth day of the experiment, there was an increase in the number of mast cells per unit area, the appearance of signs of fibroblast proliferation. A more pronounced activation of the secretory reserves of the myocardium was noted due to an increase in the number of SSG types 1 and 2 in the cardiomyocytes of the ventricles, as well as an increase in the relative number of CMCs in the ventricles, which contained SSH up to 75-80% **(fig. 2)**.

On the 30th day, there was a significant increase in mast cells per unit area (1.8-2.4 times compared to the control), degranulated mast cells was 50-65%. There were signs of depletion of secretory CMCs: a decrease of 1 and 2 types of SSH against the background of an increase of type 3 SSH, the number of cardiomyocytes with SSH and the number of SSH in CMCs increased significantly in all sections of the myocardium.

Opinions on the effect of adrenaline and dexamethasone on the state of the SC of the heart are not always clear-cut, and since these drugs are widely used in resuscitation practice, including cardiology, we investigated the effect of adrenaline and dexamethasone on the state of the SC of the rat heart, since these animals have the most similar SC to human During histological and electron microscopic examination, the following changes were visualized: after a single injection of adrenaline in the myocardium, the number of type I mast cells increased relative to other topographic types, presumably due to the activation of mast cells migration into the perivascular space, the number of degranulating forms increased. After a one-time administration of dexamethasone solution in another experimental group, we did not

detect significant changes in the quantitative ratio of topographic types of cardiac mast cells compared to the norm, but the number of degranulating forms of mast cells decreased. In addition, it should be noted that after systematic administration of the drug (four times a day for 5 days), the number of mast cells per unit area decreases by 1.3-1.5 times. In myoendocrine cells, both drugs initiate changes similar to those processes that occur in the early stages of hemodynamic overload of the myocardium, namely: the migration of secretory granules from the perinuclear to the subsarcolemmal space, with an increase in SSH type 3.

Conclusions. Tissue basophils, which can be divided into three types according to the topographical principle, were found in the tissues of all sections of the myocardium. Normally SSH are contained in the cytoplasm of cardiomyocytes of all parts of the heart, mainly in the perinuclear zone.

The amount of SSH is the largest in the cardiomyocytes of the auricles of the heart, the smallest in the cardiomyocytes of the ventricles. There are differences in the morphofunctional state of tissue basophils in the ventricles, atria, and auricles, which is related to the differences in the structure of different parts of the heart. The number of CMCs containing SSG in the auricles and atria is 1.5-2 times more than in the ventricles, and more in the right chambers than in the left.

Hemodynamic overload of the myocardium is a powerful factor in the activation of the secretory components of the heart and stimulates the redistribution of topographic types of mast cells, the activation of their degranulation, which in the conditions of long-term action of the factor leads to increased proliferation of fibroblasts and growth of connective tissue, which occurs during remodeling of the myocardium. Activation of secretory CMC occurs in the form of an increase in secretory processes in the early stages of the effect of the factor, which can be seen in the increase of SG type 3 and migration of SG into the subsarcolemmal space. Subsequently, there is an increase in synthetic processes in the secretory CMCs: an increase in SG 1 and 2 types, as well as an increase in the number of cardiomyocytes containing SG in the ventricles, which can be considered as an additional reserve for compensation of overload.

Adrenaline and dexamethasone have the opposite effect not only on the activity of tissue basophils of the heart, but also on their migration and number: the first activates the migration of mast cells into the perivascular space, the second inhibits the degranulation process due to its influence on the conditions of cell membranes, «closing» biologically active substances of mast cells in granules. But these substances have a similar effect on myoendocrine cells.

Prospects for further research. Considering the fact that the secretory components of the heart play an important role in both the pathogenesis and compensation mechanisms of cardiac pathology, it is advisable to continue further research in the direction of finding mechanisms of influence on the secretory apparatus of the heart, with the aim of optimizing the correction of hemodynamic disorders in some cardiovascular diseases.

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ОСОБЛИВОСТІ МОРФОЛОГІЇ СЕКРЕТОРНИХ КОМПОНЕНТІВ СЕРЦЯ ЗА УМОВ ВПЛИВУ ГЕМОДИНАМІЧНОГО ПЕРЕВАНТАЖЕННЯ

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Резюме. У цьому дослідженні описано огрядні клітини та секреторні міокардіоцити серця в нормі, а також зміни їх складу серця щурів в умовах експериментального звуження аорти та при дії епінефрину та дехаметазону. Встановлено відмінності в морфології секреторних компонентів різних відділів серця. Вивчення серця як ендокринного органа привертало увагу дослідників на протязі багатьох років, але ряд питань і сьогодні залишаються дискутабельними. Особливий інтерес становить вивчення морфології компонентів серця, які відповідають за синтез, накопичення та секрецію біологічно активних речовин.

Мета: встановити морфофункціональний стан секреторних компонентів серця в нормі та в умовах експериментального гемодинамічного перевантаження серця.Матеріалом для дослідження послужили білі щури, яким була створена штучна коарктація аорти, інші дві групи були піддані впливу препаратів адреналіну та дексаметазону

Кількість ССГ найбільша в кардіоміоцитах вушок серця, найменша – в кардіоміоцитах шлуночків. Існують відмінності морфофункціонального стану тканинних базофілів у шлуночках, передсердях, серцевих вушках, що пов'язано з відмінностями будови різних відділів серця. Гемодинамічне перевантаження міокарда є потужним фактором активації секреторних компонентів серця і стимулює перерозподіл топографічних типів ТБ, активацію їх дегрануляції, що в умовах тривалої дії чинника призводить до посилення проліферації фібробластів і росту сполучної тканини, що має місце при ремоделюванні міокарда. Активація секреторних КМЦ відбувається у вигляді збільшення секреторних процесів на ранніх стадіях дії чинника, що можна вважати як додатковий резерв компенсації перевантаження.

Адреналін та дексаметазон мають протилежний вплив не тільки на активність тканинних базофілів серця, але й на їх міграцію та кількість: перший активує міграцію ТБ у навколосудинний простір, другий – за рахунок впливу на стан клітинних мембран гальмує процес дегрануляції.

Ключові слова: серце, міоендокринні клітини, тучні клітини, специфічні секреторні гранули, експеримент.

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Abstract. In this research were described mast cells and secretory myocardiocytus of heart in a norm, and also changes of their consisting of heart of rats in the conditions of experimental aortic narrowing and at the action of epinephrin and dexamethazon. It is set that distinctions are in morphology of secretory components of different departments of heart.

The study of the heart as an endocrine organ has attracted the attention of researchers for many years, but a number of issues remain debatable today. Of particular interest is the study of the morphology of the components of the heart, which are responsible for the synthesis, accumulation and secretion of biologically active substances.

Aim: to establish the morphofunctional state of the secretory components of the heart in normal conditions and in the conditions of experimental hemodynamic overload of the heart. The material for the study was white rats, which were created with artificial coarctation of the aorta, the other two groups were exposed to adrenaline and dexamethasone.

The number of SSG is the largest in the cardiomyocytes of the auricles of the heart, the smallest in the cardiomyocytes of the ventricles. There are differences in the morphofunctional state of tissue basophils in the ventricles, atria, and auricles, which is related to the differences in the structure of different parts of the heart. Hemodynamic overload of the myocardium is a powerful factor in the activation of the secretory components of the heart and stimulates the redistribution of topographic types of mast cells, the activation of their degranulation, which, under the conditions of prolonged action of the factor, leads to increased proliferation of fibroblasts and growth of connective tissue, which occurs during remodeling of the myocardium. Activation of secretory CMCs occurs in the form of an increase in secretory processes in the early stages of the effect of the factor, which can be considered as an additional reserve for compensation of overload.

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Key words: heart, myoendocrine cells, mast cells, specific secretory granules, experiment.

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Conflict of interest:
The Authors declare no conflict of interest.

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