Proceedings of the II International Scientific and Practical Conference

"Topical Problems of Modern Science"

November 18, 2017
Warsaw, Poland

Vol.5

Publisher –
RS Global Sp. z O.O.,

Scientific Educational Center
Warsaw, Poland

Numer KRS: 0000672864
REGON: 367026200
NIP: 5213776394

Publisher Office's address:
Dolna 17,
Warsaw, Poland,
00-773

Website:
https://ws-conference.com/

E-mail:
rsglobal.poland@gmail.com

Tel: +4(857) 898 55 10

CONTENTS

CHEMISTRY

BIOLOGY

MEDICINE

ANALYSIS INFLUENCE OF AN EXPERIMENTAL HEMODYNAMIC OVERLOAD ON THE SECRETORY COMPONENTS STATE OF A HEART

[1]PhD of Medicine Zharikov M. Y.,
[2]Zharikova V. M.,
[1]PhD of Medicine Lukianenko D. M.,
[1]PhD of Medicine, assistant professor Hryhorenko L. V.,
[3]MD of Medicine, professor Baibakov V. M.

Ukraine, Dnipro
[1]SE "Dnepropetrovsk Medical Academy of Ministry of Health of Ukraine";
[2]SE "Specialized multidisciplinary hospital №1 of Ministry of Health of Ukraine";
[3]Dnipro Medical Institute of Traditional and Non-Traditional Medicine

Abstract. *In this research were described mast cells and secretory myocardiocytus of a heart at the people with different age groups – youth, mature, elderly and senile, in a norm, and numerous changes of the heat parts in the conditions of experimental aortic narrowing and at the action of epinephrin and dexamethazon. It was found out the distinctions in morphology of secretory components in the different departments of heart. With age there is multiplying the amount of connecting tissue and amount of secretory myocardiocytus, which was also correlated with different types of mast cells changes.*

Hemodynamic overload and adrenalin activates the secretory components of heart, and dexamethazon activates the secretory myocardiocytus, but reduces activity of mast cells.

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

Introduction. Research of heart as an endocrine organ has attracted attention of researchers for many years, but several questions are still remain disputable [2,7,8]. Presence secretory function of a heart allows us to speak about participation of this organ in the humoral regulation of the organism's homeostasis. This is important issue in the research of pathogenesis for several cardiac diseases. Of particular interest is the study morphology of the heart components, that are responsible for the synthesis, accumulation and secretion of biologically active substances – secretory component (SC) of a heart, their age peculiarities, and influence of various factors and diseases on the morphology and functioning of these components [1,5,6,9]. Among them are myo-endocrine cells (MEC), which contain specific secretory granules (SSG) and cardiac tissue basophils (TB). Research of morphology these components at the normal state and in conditions, close to the pathogenesis of certain cardiovascular diseases, as well as influence of the certain pharmaceuticals, applicated in a clinical practice, - is relevant today. It would help to establish a role of endocrine component of the heart on the mechanisms of development and compensation of cardiac pathology.

Purpose of research is to establish morpho-functional state of the secretory components of a heart at the normal and in experimental hemodynamic overload on the heart, as well as impact on the SC of adrenaline and dexamethasone.

Material and Methods of Research. Material of study SC in the normal state was hearts of 67 people with different genders, which had been divided on a youth, mature, elderly and senile age. Given persons were died from diseases, not pathogenetically associated with pathology of a cardiovascular system.

Fence of pieces for histological research were performed with a right and left chambers of the heart wall: auricles, atrial, ventricular and from interatrial and interventricular septa. We produced given samples by a standard method of preparation of the semi-thin slices with thickness 1-2 microns, colored with 2 % solution of toluidine blue. For study MEC secretory granules were used methods of immunohistochemistry research with the specific monoclonal antibodies, produced by a firm DAKO to chromogranin A (N1535 clone), NSE (neuron specific enolase - clone N1516) and synaptophysin (clone N1566) – substances, which are located in the MEC granules.

Material for experimental research of SC was sexually mature white rats, male, Wistar line, weighing 160-180 grams, which were distributed into the following groups: 1) 17 rats – to study effect of adrenaline and dexamethasone: the first (5 rats) and second (8 rats) experimental groups, which were

intraperitoneally administered solution of epinephrine (0.3 mg/kg) and dexamethasone (0.2 mg/kg), the third control group (4 rats); 2) 30 rats – to study hemodynamic overload of a heart, which were divided into 5 experimental groups, i.e. 5 rats in each group, depending on the duration of experiment, 5 rats – were in the control group. Rats were performed a silk ligature under narcotization ether above region of the renal arteries departure, and fixed on a probe with diameter, which was equal to ½ of the aorta diameter in its abdominal part. Rats were withdrawn from experiment by a decapitation under ether anesthesia, in accordance with "Methodological recommendations under removal animals from the experiment" (1985), for 5 rats on the 1, 3, 5, 10 and 30 days after surgery [4].

For histological research were carried out fence pieces from the right and left chambers of a heart (auricles, auricles, ventricles), an interatrial and interventricular septa. Hereafter, there were produced samples from this material by a conventional method of preparing histological, semi-thin slices, which were stained by toluidine blue and hematoxylin-eosin and samples for electronomicroscopic research. Visualization of histological preparations was performed under Leica microscope (increased on 10 X 100), followed by photographing with a digital camera Canon. Statistical processing of the obtained results was performed, according to the standard technique.

Results of Research and their Discussion. In the research of histological preparations of the hearts in all these age groups of people and in all divisions had been shown tissue basophils, which were corresponded to the three major topographical types [3]. I type – TB, which are located closely to the vessels of all sizes; II type – TB, located in a thick layer of connective tissue; III type – TB, that were closely to the cardiomyocytes, and specific secretory granules, that are located in the myocardial cells by the several groups 7-22 granules mainly in a perinuclear area.

Table 1. Percentage ratio of muscle and connective tissue in the different parts of a human myocardium (muscle/ connective)

Division of the cardiac wall Age	Left ventricle	Right ventricle	Left atrium	Right atrium	Left atrial auricle	Right atrial auricle
Youth	80/20	81/19	72/28	68/32	67/33	67/33
Mature	78/22	77/23	70/30	68/32	66/34	65/35
Elderly	74/26	73/27	62/38	66/34	60/40	59/41
Senile	72/28	71/29	61/39	62/38	56/44	58/42

We focused on the research of correlation link between a connective tissue and muscle tissue (table 1), distribution of TB different types (table 2), and relative number of cardiomyocytes, containing SSG to the total number of cardiomyocytes (table 3) in the research sections of a cardiac wall.

Table 2. Percentage ratio different types of TB in the different parts of a human myocardium (type I / type II / type III)

Division of the cardiac wall Age	Left ventricle	Right ventricle	Left atrium	Right atrium	Left atrial auricle	Right atrial auricle
Youth	15/3/82	12/4/84	14/47/39	11/51/38	12/55/33	14/56/30
Mature	10/4/86	9/6/85	8/52/40	10/55/35	12/52/36	10/58/32
Elderly	12/7/81	9/10/81	11/61/28	14/49/37	10/50/40	17/54/29
Senile	15/13/72	12/14/74	15/60/25	8/63/29	14/58/28	11/65/24

Table 3. Percentage ratio of the cardiomyocytes quantity, which containing SSG to the total number in the different parts of a human myocardium (%)

Division of the cardiac wall Age	Left ventricle	Right ventricle	Left atrium	Right atrium	Left atrial auricle	Right atrial auricle
Youth	46-50	51-60	92-94	94-96	95-97	99-100
Mature	42-48	48-62	90-93	94-96	93-95	95-98
Elderly	46-54	51-67	93-95	94-98	96-99	97-99
Senile	50-55	52-66	95-96	95-96	96-100	98-100

Hemodynamic overload of a myocardium is one of the main manifestations of numerous cardiovascular diseases. In order to study its effects on SC, we conducted an experimental research on the rats with a creation of artificial coarctation of aorta. The histological and electron microscopic

intraperitoneally administered solution of epinephrine (0.3 mg/kg) and dexamethasone (0.2 mg/kg), the third control group (4 rats); 2) 30 rats – to study hemodynamic overload of a heart, which were divided into 5 experimental groups, i.e. 5 rats in each group, depending on the duration of experiment, 5 rats – were in the control group. Rats were performed a silk ligature under narcotization ether above region of the renal arteries departure, and fixed on a probe with diameter, which was equal to ½ of the aorta diameter in its abdominal part. Rats were withdrawn from experiment by a decapitation under ether anesthesia, in accordance with "Methodological recommendations under removal animals from the experiment" (1985), for 5 rats on the 1, 3, 5, 10 and 30 days after surgery [4].

For histological research were carried out fence pieces from the right and left chambers of a heart (auricles, auricles, ventricles), an interatrial and interventricular septa. Hereafter, there were produced samples from this material by a conventional method of preparing histological, semi-thin slices, which were stained by toluidine blue and hematoxylin-eosin and samples for electronomicroscopic research. Visualization of histological preparations was performed under Leica microscope (increased on 10 X 100), followed by photographing with a digital camera Canon. Statistical processing of the obtained results was performed, according to the standard technique.

Results of Research and their Discussion. In the research of histological preparations of the hearts in all these age groups of people and in all divisions had been shown tissue basophils, which were corresponded to the three major topographical types [3]. I type – TB, which are located closely to the vessels of all sizes; II type – TB, located in a thick layer of connective tissue; III type – TB, that were closely to the cardiomyocytes, and specific secretory granules, that are located in the myocardial cells by the several groups 7-22 granules mainly in a perinuclear area.

Table 1. Percentage ratio of muscle and connective tissue in the different parts of a human myocardium (muscle/ connective)

Division of the cardiac wall Age	Left ventricle	Right ventricle	Left atrium	Right atrium	Left atrial auricle	Right atrial auricle
Youth	80/20	81/19	72/28	68/32	67/33	67/33
Mature	78/22	77/23	70/30	68/32	66/34	65/35
Elderly	74/26	73/27	62/38	66/34	60/40	59/41
Senile	72/28	71/29	61/39	62/38	56/44	58/42

We focused on the research of correlation link between a connective tissue and muscle tissue (table 1), distribution of TB different types (table 2), and relative number of cardiomyocytes, containing SSG to the total number of cardiomyocytes (table 3) in the research sections of a cardiac wall.

Table 2. Percentage ratio different types of TB in the different parts of a human myocardium (type I / type II / type III)

Division of the cardiac wall Age	Left ventricle	Right ventricle	Left atrium	Right atrium	Left atrial auricle	Right atrial auricle
Youth	15/3/82	12/4/84	14/47/39	11/51/38	12/55/33	14/56/30
Mature	10/4/86	9/6/85	8/52/40	10/55/35	12/52/36	10/58/32
Elderly	12/7/81	9/10/81	11/61/28	14/49/37	10/50/40	17/54/29
Senile	15/13/72	12/14/74	15/60/25	8/63/29	14/58/28	11/65/24

Table 3. Percentage ratio of the cardiomyocytes quantity, which containing SSG to the total number in the different parts of a human myocardium (%)

Division of the cardiac wall Age	Left ventricle	Right ventricle	Left atrium	Right atrium	Left atrial auricle	Right atrial auricle
Youth	46-50	51-60	92-94	94-96	95-97	99-100
Mature	42-48	48-62	90-93	94-96	93-95	95-98
Elderly	46-54	51-67	93-95	94-98	96-99	97-99
Senile	50-55	52-66	95-96	95-96	96-100	98-100

Hemodynamic overload of a myocardium is one of the main manifestations of numerous cardiovascular diseases. In order to study its effects on SC, we conducted an experimental research on the rats with a creation of artificial coarctation of aorta. The histological and electron microscopic

examination of the experimental animals hearts was shown visualization of all three described topographic types of TB. In the rats from control group, was shown domination of II and III types of TB in all parts of myocardium. It was also demonstrated MEC, which contained three types of secretory granules. The I type – was determined with a massive electron-content content; II type – with a less electronic content; III type – were membrane-free granules, having the electron-transparent content. Granules were predominantly in the perinuclear space, for 8-26 in the groups. Number of cardiomyocytes (CMCs), having SSG in the heart auricles were 94-98 %, in the atrium - 90-95 %, in the ventricles - 48-60 %. CMCs was higher in the corresponding right departments.

On the first day after coarctation of aorta in the myocardium was increased a relative number I type of TB, which caused due to their movement into a vascular space, as well as an increased number of degrading forms of TB. These changes were more deformed in a left ventricle, but were poor observed in other departments. In addition, in the secretory CMCs was observed transfer of SSG from the perinuclear to subarachnoid space, with increasing SSG of III type.

On the third day of experiment was more pronounced changes. There was continued migration of TB into a vascular space, and movement of SSG into the subscale terminal space, as well as an increased III type of SSG. These changes of varying severity were observed in all heart parts, which occurred on the fifth day, however, it were signs of activation the synthetic processes in the secretory CMCs – increasing of the I and II types of SSG. Percentage of CMCs from SSG in the ventricles was also increased on 55 -68 %.

On the tenth day of experiment there was increasing number of TB per unit area, appearance signs of the fibroblasts proliferation. Primary, it was observed a more pronounced activation of secretory reserve of the myocardium due to the increased number of SSG, I and II types, in the ventricles CMCs. Secondly, was shown increasing of a relative number of CMCs in the ventricles, which containing SSG to 75-80 %. On the 30 day of experiment was shown a significant increase of TB per unit area (on 1.8-2.4 times, compared to the control). It was covered about 50-65 % of the degranulated TB. Signs of depletion of the secretory CMCs were observed: reduction I and II types of SSG, on a background of increasing III type of SSG. Quantity of CMCs with SSG and an amount of SSG in the CMCs was increased significantly in all sections of the myocardium.

Views on the effects of adrenaline and dexamethasone on a state of the heart SC were not always unambiguous, because these preperates are widely used in a reanimation practice, including cardiology. We have investigated effects of adrenaline and dexamethasone on the state of SC heart at the rats, because these animals have SC a most similar to the human. In the histological and electron microscopic study, the following changes were visualized. After a single-dose administration of adrenalin in the myocardium, number of TB I types increased relatively to the other topographic types, probably, due to the activation of TB migration in a vascular space. Amount of the degranulatory forms increases. After a single-dose administration of dexamethasone solution in the another experimental group, there were no reliable changes in a quantitative ratio of the topographic types of cardiac TB, compared with the normal, but number of degrading forms of TB was reduced. In addition, it should be noted that after the systematic introduction of the drug (4 times a day for 5 days) was reduces number of TB per unit area in 1.3-1.5 times. In the myoendocrine cells, both pharmaceuticals initiated changes similar to those, which occurring in the early stages of hemodynamic overload of myocardium: migration of secretory granules from the perinuclear to the subarticle terminal space, with increasing III type of SSG.

Conclusions.

1. In the tissues of all sections of myocardium from the given research age groups of human was found tissue basophils, which, according to the topographical principle, should be divided into three types. Normally, in the studied age groups of people, SSG could contain in the cardiomyocytes cytoplasm in all parts of the heart, mainly in the perinuclear zone.
2. Amount of SSG is the greatest in cardiomyocytes of the heart's auricles, the smallest – in cardiomyocytes of the ventricles. There are differences in the morphofunctional state of tissue basophils in the ventricles, atriums, heart auricles, due to the differences in a structure different part of the heart. Number of CMCs, containing SSG in the auricles and atria was in 1.5-2 times greater than in the ventricles, with right-handed sections, larger than the left ones.
3. Comparing morphological picture of the myocardium in all departments at the different age groups, it was shown that with the age of myocardium there are numerous changes, which focused on the increasing number of the connective tissue and CMCs, containing SSG. There is also observed redistribution of the different types of TB. However, it should be noted that in adolescence, the

number of CMCs, containing SSG, is slightly higher than in the adulthood, which, obviously, could be explained by a greater activity of secretory processes.

4. Hemodynamic overload of the myocardium is a powerful factor in activation of the secretory components of a heart and stimulates redistribution of topographic types of TB, activation of their degranulation. In the conditions of a factor prolonged effect, it leads to the increasing of fibroblast proliferation and growth of a connective tissue, which occurs during myocardial remodeling. Activation of secretory CMCs occurs in a form of increased secretory processes in the early stages of factor's action. It was demonstrated in a case of increasing III type of SSG and its migration to the subscale terminal space. In the future, there is increasing synthetic processes in the secretory CMCs: increased I and II types of SSG, as well as increasing number of cardiomyocytes, containing SSG in the heart ventricles, which can be considered as an additional overload compensation reserve.

5. Adrenaline and dexamethasone have an opposite effect not only on the activity of tissue basophils of a heart, but also on their migration and quantity. The first one activates migration of TB in a vascular space, the second one – inhibits the process of degranulation, due to the effect on a state of cell membranes, "closing" biologically active TB substance in the granules. But these drugs have a similar effect on the myoendocrine cells.

Prospects for the further developments. In view of the fact that secretory components of a heart play an important role, both in the pathogenesis and mechanism of compensating of cardiological pathology, further researches should be continued in the direction of searching mechanisms of influence on the secretory apparatus of a heart, in order to optimize correction of hemodynamic disorders in some of the cardiovascular diseases.

REFERENCES

1. Gavrysheva N. A., Tkachenko S. B. Mast cells of the heart in the normal state and in pathology // Cardiology. - 2003.-№6.- P. 59-65.

2. Zharikov M. Yu. Tissues human heart basophils in the norm (review of literature) / Zharikov M.Yu. // Ukrainian Morphological Almanac. - 2013, Vol.11, № 3. - P. 96-99.

3. Zharikov M.Yu. Secretory components of a heart in the normal state and under influence of external factors (review of literature) / Zharikov M.Yu. // Ukrainian Medical Almanac. - 2013.- Vol.16, № 4. - P. 65-69.

4. Kozlov V. O., Zharikov M. Yu. Morphofunctional state of tissue basophils of a heart at the people of mature age // Bulletin of morphology.-2005.-Vol.11, № 2.- P.162-164.

5. Kozlov V. A., Kosharny V. V., Zharikov M. Yu., Kozlov S.V. Method of modeling aortic coarctation // Declarative patent of invention (11) Patent 6234, MKI A61B 17/00.

6. Hablak G. V., Stupina A. S., Quitnitskaya-Ryzhova T. Yu. Age changes of the secretory cardiomyocytes ultrastructure // Clinical anatomy and operative surgery .- 2006.-Vol.5, № 2.- P. 64-65.

7. Li M, Liu K, Michalicek J, Angus JA, Hunt JE, Dell'Italia LJ, Feneley MP, Graham RM, Husain A. Involvement of chymase-mediated angiotensin II generation in blood pressure regulation // J. Clin. Invest.- 2004.-Vol.114, № 1.- P. 112-120.