Volume 10, Issue 2, 2020, 5237 - 5242 ISSN 2284-6808
Biointerface Research in Applied Chemistry
www.BiointerfaceResearch.com
https://doi.org/10.33263/BRIAC102.237242
Original Research Article Open Access Journal
Received: 05.11.2019 / Revised: 05.02.2020 / Accepted: 06.02.2020 / Published on-line: 12.02.2020

Microscopic and submicroscopic structure of the heart atria and auricles in condition of the experimental thermal trauma

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ABSTRACT

Burns is the damage of the skin or mucous membranes (often with underlying tissues), because of high-temperature influence (thermal burns), chemical, electrical, radiation, combined, thermochemical and electrothermal factors influence. According to the investigations, burns rank third among other injuries, and in some countries, second, second only to transport injuries. Although the level of survival after burns is increasing, the problem of their treatment remains relevant in modern medicine and pharmacy. The aim was to study the peculiarities and the patterns of morphofunctional changes in the structural components of the heart atria and auricles in case of the experimental thermal trauma. The study involves 30 adult guinea pigs with a bodyweight of 630-670 g. The burn was applied under general ether anesthesia with water vapor at a temperature of 96-97 ^{0}C on the surface of the skin of the animal's back for 60 seconds. The size of the lesion area was 18-20% of the body surface. The depth of the lesion corresponded to the degree IIIA -IIIB. The experimental animals were divided into two groups: the first - intact guinea pigs (6 heads); second - animals with thermal trauma (24 heads). Were used a number of methods of investigation, including macrometric and massometric - to establish the structural restructuring of the heart and its parts, microscopic and electron microscopic to detect changes in the structural components of the atrium and auricle of the heart; morphometric - to obtain quantitative parameters of the morphological components of the heart; mathematical and statistical - to ensure the analysis of the reliability of the research results. In intact guinea pigs, the morphological organization of the heart auricles differs from the atria by the direction of the muscle fibers, the ratio of morphometric parameters of their structural components and the content of muscle endocrine cells. Submicroscopically, endocrine myocytes of the auricles of the heart contain more hormonal granules than atria. In the ears of the heart, the relative volume of connective tissue is 1,34 times greater, and the relative volume of muscle fibers is 1,03 times smaller than in the atria. Submicroscopically, endocrine muscle cells of the heart auricle contain more hormonal granules than atria. It has been established that thermal trauma causes significant morphofunctional changes in the atria and auricles of the heart at different levels of their structural organization. The degree of damage depends on the duration of the experiment and develops against the background of increased plasma toxicity. In the stages of burn shock and early toxemia, adaptive-compensatory processes develop in the structures of the heart, and irreversible destructive changes occur in the stages of late toxemia and septicotoxemia.

Keywords: *heart atria and auricles; morphological changes; thermal trauma.*

1. INTRODUCTION

Burns is the damage of the skin or mucous membranes (often with underlying tissues), as a result of high-temperature influence (thermal burns), chemical, electrical, radiation, combined, thermochemical and electrothermal factors influence [1, 2]. According to the investigations, burns rank third among other injuries, and in some countries, second, second only to transport injuries [3].

The actuality of the problem of thermal injuries is determined by the relatively high frequency of their occurrence at home and a job, the severity of burn disease, the complexity, and duration of treatment of such patients, high disability and mortality [4, 5]. After thermal trauma, the development of burn disease is possible, which is accompanied by damage to all body systems capable of self-regulation [6, 7].

It is known that in the area of the thermal injury there is present immediately total or partial destruction of the skin and tissues located under the skin; burns destroy the skin both directly under the influence of the thermal agent and secondary - due to ischemic processes in the tissues [8]. The trigger mechanism of pathological changes is morphological and functional disorders in the area of the burn wound [9, 10].

Today, there is a large number of studies about the morphological status of the cells of the heart atria and auricles in normal and in case of the various pathologies, in particular in diabetes, adrenaline hyperproduction, toxins, under the influence of various exogenous factors, such as physical and electromagnetic physical, etc. [11]. However, studies of the morphofunctional state of the structural components of the heart,

which perform an endocrine function, remain solitary and incomplete in the case of thermal damage of the body.

The aim was to study the peculiarities and the patterns of morphofunctional changes in the structural components of the heart atria and auricles in case of the experimental thermal trauma.

2. MATERIALS AND METHODS

The study involves 30 adult guinea pigs with a bodyweight of 630-670 g. The burn was applied under general ether anesthesia with water vapor at a temperature of 96-97 ^{0}C on the surface of the skin of the animal's back for 60 seconds. The size of the lesion area was 18-20% of the body surface. The depth of the lesion corresponded to the degree IIIA -IIIB. The experimental animals were divided into two groups: the first - intact guinea pigs (6 heads); second - animals with thermal trauma (24 heads).

To study morphofunctional changes in the heart after thermal trauma, animals were decapitated using guillotine under general ether anesthesia for 1, 7, 14, and 21 days, at the times according to the classification which corresponds to the stages of thermal disease: shock, early and late toxemia, septicotoxemia.

For histological examination, the material was taken from pre-weighed animals. After removal of the heart, it was weighed, measured, and cut pieces from the atrium and auricles for microscopic examination. The material was fixed in 10% neutral formalin solution, dehydrated in alcohols of increasing concentration and embedded in paraffin. The sections obtained on the microtome were stained with hematoxylin-eosin [12].

Histological specimens were examined using a SEOSCAN light microscope and photo-documented with a Vision CCD Camera.

Material sampling for electron microscopic examination of heart components was performed according to conventional methods. For the study, small pieces of the atrium and the auricles of the heart were cut, fixed in 2,5% glutaraldehyde solution prepared on Millonig phosphate buffer, postfixation was carried out with 1% osmium tetroxide solution, carried out dehydration in alcohols and acetone and poured into epoxy mixtures. Ultra-thin sections were made on an LKB-3 ultramicrotome (Sweden), later were stained with a 1% aqueous solution of uranyl acetate, counterstained with lead citrate according to the Reynolds method, and examined in a PEM-125K electron microscope.

Morphometric studies were performed using Video Test 5,0 and Microsoft Exel on a personal computer. The ratio of the structural components of the heart atria and auricles were determined.

Experimental material was systematized and processed using the methods of variational statistics using the Student's t test.

3. RESULTS

In the control group of animals, it was found that in the atrial myocardium the relative volume of muscle fibers was (78,32 ± 1,78) %, the relative volume of connective tissue - (9,16 ± 0,32) %, vessels - (12,52 ± 0,47) %. In the heart auricle, the relative volume of muscle fibers was 2,4% less than the same indicator of the atria and was (76,43 ± 1,63) %, the relative volumes of connective tissue and vessels of the myocardium of the auricles were respectively (12,24 ± 0,47) % and (11,33 ± 0,28) %. Submicroscopically, in endocrine cardiac muscle cells, which are the structural components of these parts of the heart, in the sarcoplasm, in addition to organelles of general and special purpose, there were indicated hormonal granules, that have a regulatory effect on the water-electrolyte balance of the body.

On the first day of the experiment, corresponding to the first stage of thermal trauma was established a decrease of the bodyweight of the animal and weight of the heart.

During this period of the experiment, it was found that in the myocardium the relative volume of blood vessels and connective tissue were increased, but the relative volume of muscle fibers was decreased. In the atria, the relative volume of the vessels increased 1,34 times compared to the control group, in the heart auricles – 1,12 times. Relative volumes of muscle fibers and connective tissue were not significantly changed (Tabl. 1).

Submicroscopic changes of the myocardial microcirculation were manifested by changes in the endothelial cells of the blood capillaries in the heart atria and auricles. In particular, an increase in the number of pinocytotic vesicles and caveolae in their cytoplasm, cytoplasmic pseudopodia and microvilli, invaginations of the nuclear envelope, local enlightenment and cytoplasmic edema, and partial damage of the organelles. In the sarcoplasm of contractile cardiomyocytes were observed the local thickening and loosening of myofibrils, partial fragmentation of myofilaments.

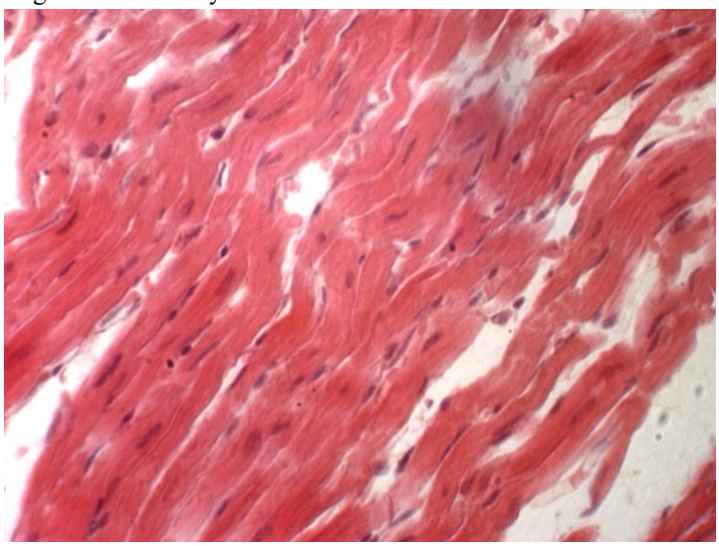

Figure 1. Microscopic changes of the right auricle, 7th day of the experiment. Specimen. Stained with Haematoxylin and eosin x 400.

On the 7th day after the application of thermal trauma, a further decrease of body weight of the animal and heart was established. Their average values decreased by 9,32% and 8,21%, respectively in comparison with the norm. The characteristic feature of this period of experiment was the unequal decrease in the mass of the studied structures of the heart. The average weight of the right auricle decreased by 15,62% and the left one by 14,11% in comparison with the norm. The average value of the left atrium mass decreased by 18,18% and the right one by 7,69% relative to the norm.

Histological studies have shown that the changes, which develop in the myocardium of the atria and the auricles in the stage of toxemia, are manifested by disorders of blood supply and changes in vascular-tissue ratios, partial stratification of muscle fibers.

At this term of the experiment cardiomyocytes in the muscle fibers have heterogeneous eosin stain. Cells, in which the cytoplasm was weakly oxidized, were often found. The basophilic nuclei of the cells had an elongated shape and heterogeneously stained karyoplasm (Fig. 1).

It was visible, that the lumens of most blood vessels, especially veins, were significantly enlarged and over-bloodfilled. Perivascular edema as well as focal leukocyte infiltration of connective tissue were also observed.

Morphometrically, it was found that in the atria the relative volume of muscle fibers decreased by 1,09 times in comparison with the control animals, the relative volumes of loose fibrous connective tissue and vessels increased at 1,36 and 1, respectively, 25 times. Similar changes in the ratio of their structural components were observed in the heart auricles (see Tabl. 1).

Electron microscopic studies of the blood vessels in the microcirculatory bed revealed violations of their structural organization on the 7th day of the experiment. The enlargement of the lumen and blood flow of the blood capillaries was combined with edema and enlightenment of the cytoplasm of the endothelial cells, uneven thickening of the basement membranes and enlargement of the perivascular spaces.

In cardiomyocytes were observed the thinning of the myofibrils and their lysis. Part of the mitochondria was marked by destructive changes, which were manifested by their hypertrophy, matrix enlightenment, and damage to the crysts. However, along with the damaged organelles, mitochondria with moderate structural changes were detected. A combination of adaptive changes with dystrophic ones was also observed in cardiomyocyte nuclei. Their karyolemmma was characterized by deep invaginations and enlargement of the perinuclear space, high content of euchromatin in the karyoplasm, a decrease in the number and density of the nuclei.

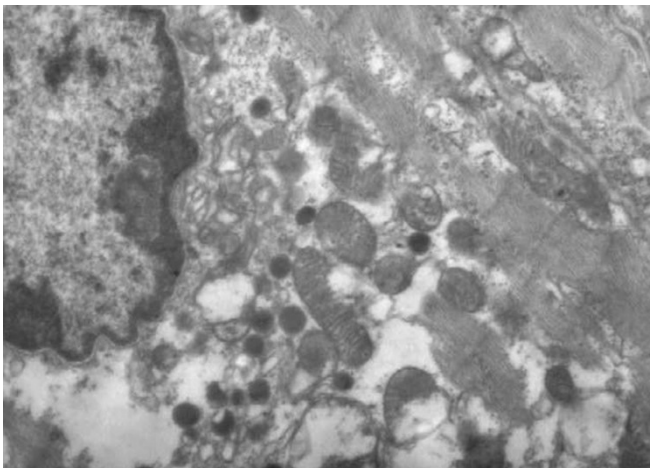

Figure 2. Fragment of the secretory myocyte of the left auricle of the heart, 7th day of the experiment. Electron micrograph. x 21 000.

In the stage of early toxemia, activation of secretory processes was revealed in part of the endocrine myocytes of the atria and auricle of the heart. Morphological features of this were the widening of the tubules of the endoplasmic reticulum, hypertrophy of the Golgi Complex, and an increase in the paranuclear space number of secretory granules in the cells. These granules had different sizes and electron density. However, most cells, especially in the perivascular area of the sarcoplasm, had few hormonal granules (Fig. 2).

There were fewer granules in the right auricle near the nucleus in comparison to the left auricle, but many single secretory granules were found between the myofibrils and in the perivascular zone of the cytoplasm.

Massometric studies at 14 and 21 days after the application of the experimental thermal trauma founded a further decrease in the body weight of animals, weight of the heart and its components. The average weight of animals in these terms decreased by 11.84% and 15.69%, respectively, relative to the norm. The average heart weight decreased by 11,79% and 13,33%, respectively, relative to the intact animal parameters. The average value of the right atrial mass decreased by 15,38% and 23,08%, respectively, and the left one by 27,27% and 31,82%, respectively, in comparison with the norm. The average weight of the right auricle decreased by 25,00% and 34,37% respectively, while the left one by 29,41% and 36,47% respectively.

Morphometrically, it was found that in the later stages the relative volume of muscle fibers in the atria and auricles of the heart was further decreased (see Table 1). The replacement of the muscular structures was due to the increase in the relative volume of the edema loose fibrous connective tissue. On the 14th day of the experiment, the relative volume of muscle fibers in the atria and auricles of the heart decreased by 1,10 and 1,09 times, respectively, and the relative volume of connective tissue increased respectively 1,72 and 1,46 times, compared with relevant indicators of intact animals. For the 21 days of the experiment, the relative volume of muscle fibers in the atria and auricles of the heart decreased by 1,13 and 1,11 times, respectively, and the relative volume of connective tissue increased by 1,99 and 1,67 times respectively. During these experimental periods, a decrease in the relative volume of the vascular component of the myocardium was found at the expense of the vessels whose lumens were sleeping, especially the arteries and arterioles.

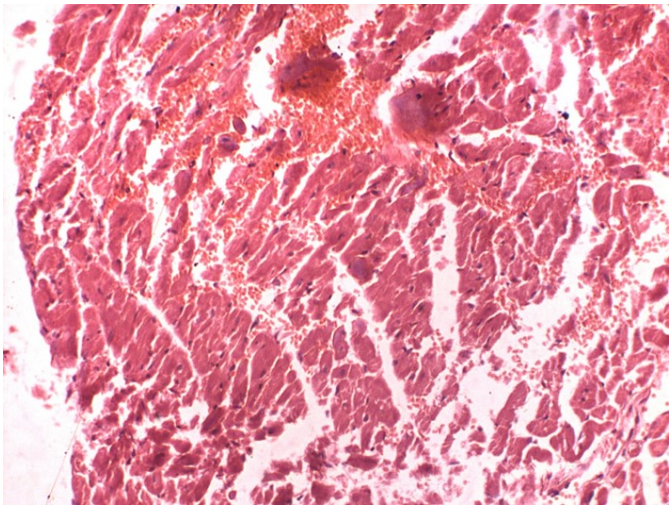

Figure 3. Microscopic changes of the left atrium, 21st day of the experiment. Specimen. Stained with Haematoxylin and eosin x 200.

In the stage of septicotoxemia, irreversible destructive processes developed in the atria and in the auricle of the heart. These processes were manifested by prominent changes in both the connective tissue and the muscular components of the myocardium. Edema of loose connective tissue, stratification and fragmentation of muscle fibers, destruction of the blood vessels' walls were accompanied by hemorrhage (Fig. 3).

Ultrastructure investigations of cardiomyocytes in the atria and the auricles of the heart at 14 and, in particular, at 21 days of the experiment revealed prominent destructive changes in them. Many cells had pycnotically changed nuclei with electron-dense karyoplasm and poorly expressed perinuclear space. The sarcoplasm contained damaged organelles. The contractile apparatus is characterized by fragmentation and lysis of myofibrils, disruption of the ordered arrangement of sarcomeres and intercalated disks. The mitochondria with edema had a light matrix, crysts and outer mitochondrial membrane were destroyed.

During these periods of the experiment, changes in the endocrine myocytes of the heart increased. On the 14th day of the experiment, significantly enlarged tubules of the granular endoplasmic reticulum, cisterns of the Golgi complex and partially their fragmentation were observed in the cells. The number of hormonal granules in the perinuclear zone is small, single granules were found near the sarcolemma, between the myofibrils and in the prevascular part of the cytoplasm. At 21 days of experiment in the endocrine cells of the atria and the auricle, the hormonal granules were single; there was a destruction of the components of the secretory apparatus.

Macroscopic, microscopic, and electron microscopic studies of the atria and auricles of intact guinea pigs have shown that they have general features of structure [13, 14].

Complex studies have shown that the nature and degree of damage of the parts of the heart depended on the duration of the experiment and increased according to the stages of thermal trauma [15].

At the same time, in the first phase of trauma, the average body weight of the burned animals decreased by 2,77% relative to the mass of intact animals, and the average heart mass decreased by 1,54% in comparison with the norm.

Morphological changes in the stage of burn shock were manifested, first of all, by the impaired blood supply to the organ, which, according to some authors, is one of the starting mechanisms for the development of pathological processes in organs of organism systems [16]. Microscopic disturbance of the vascular bed was manifested by enlargement and blood filling of most vessels, stasis of erythrocytes in blood capillaries, enlargement of perivascular spaces, edema of fibrous loose connective tissue.

Disorders of myocardial microcirculation in the atria and the auricles of the heart, which were manifested by changes in blood capillary endothelial cells by the increase in the number of foam cytosis vesicles and caveoli in their cytoplasm, cytoplasmic pseudopodia, and microvilli, indicate an increase in transcapillary metabolism and precapillary exchange and adaptative processes.

The slight local thickening and loosening of myofibrils, and the partial fragmentation of myofilaments revealed in the sarcoplasm of contractile cardiomyocytes by electron microscopy indicate the resistance of myofibrils to the influence of stress factors.

In the stage of burn shock, were visible cells whose cytoplasm contained small hormonal granules that were concentrated mainly around the sarcolemma. In the right auricle, the number of cells with secretory granules was larger than in the left and atria. This content of hormonal granules in the cytoplasm of the endocrine cells of the heart indicates the active excretion of the atrial natriuretic peptide in the bloodstream. Such results are confirmed by the work of scientists, who have biochemically established an increase in the content of atrial natriuretic peptide in peripheral blood during a period of burn shock [17].

On the 7th day after the application of thermal trauma, a further reduction of body weight of the animal and heart was established. A similar tendency of decrease in body weight and weight indicators of internal organs in the stage of early toxemia has been elucidated in the works of many authors [18, 19].

Histological studies have shown that the changes, that develop in the myocardium of the atria and the auricle of the heart in the stage of toxemia are adaptive-compensatory and have signs of the development of destructive processes [20, 21]. Microscopically, this was manifested by a violation of the blood supply to the wall of the heart and changes in vascular-tissue ratios, partial stratification of muscle fibers.

Electron microscopic studies of vessels of the microcirculatory bed on the 7th day of the experiment revealed violations of their structural organization. Disruption of the blood supply to the heart causes myocardial ischemia and adversely affects the morphofunctional status of cardiomyocytes. Submicroscopically, an increase in the intracellular changes was established. Along with the damaged organelles, mitochondria with moderate structural changes were detected. Such a heteromorphic state demonstrates the adaptive-compensatory reaction of the energy supply organelles [22]. A combination of adaptive changes with dystrophic ones was also observed in cardiomyocyte nuclei. A combination of adaptive changes with dystrophic ones was also observed in cardiomyocyte nuclei. High euchromatin content in the karyoplasm can be considered as a consequence of enhanced transcription processes. At the same time, reducing the number and compaction of the nuclei reflects a decrease in their functional activity.

Histological examinations of the atria and the auricles of the heart at 14 and 21 days after the application of the experimental thermal trauma found that in the stage of late toxemia, tare develops destructive changes, which in the stage of septicotoxemia often become irreversible.

Submicroscopically, heterogeneous changes in the blood capillaries were established in these experimental terms. The lumens of some capillaries were expanded, filled with fine material and shaped elements of blood, others - narrowed due to edema of the cytoplasm of endothelial cells and protrusions of the plasmalemma. The decrease in the number of pinocytotic vesicles in the cytoplasm and microvilli on the luminal surface of endothelial cells indicates a significant decrease in metabolic processes in the structures of the heart.

During these periods of the experiment, changes in the endocrine myocytes of the heart increased. On the 14th day of the

experiment in cells, the number of hormonal granules in the perinuclear zone is insignificant, single granules were encountered near the sarcolemma, between the myofibrils and in the prevascular part of the cytoplasm, indicating an impaired secretion of atrial natriuretic peptide.

For 21 days in the endocrine cells in the atria and the auricle of the heart hormonal granules were single, there was a destruction of the components of the secretory apparatus. It means and indicates that secretion of the hormone is stopped and the heart lost its ability to affect regulatory influences on the water-electrolyte balance of the body.

Table 1. The morphological parameters of the structural components of the myocardium of the heart atria and auricles in the dynamics after thermal trauma.

Period	Heart atrium			Heart auricle		
	Relative volume (m ± m) %					
	Musscle fibers	Connective tissue	Blood vessels	Musscle fibers	Connective tissue	Blood vessels
Intact	78,32±1,78	9,16±0,32	12,52±0,47	76,43±1,63	12,24±0,47	**11,33±0,28**
1 day	72,65±2,03*	10,62±0,41	16,73±0,58*	74,15±2,08	13,16±0,38	**12,69±0,42***
7 day	71,87±1,97*	12,44±0,49*	15,69±0,47*	71,82±1,72*	14,67±0,53*	**13,51±0,31***
14 day	71,13±1,68*	15,72±0,62*	13,15±0,42	70,17±1,26*	17,82±0,58*	**12,01±0,32**
21 day	69,46±1,82*	18,24±0,73*	11,60±0,36*	68,73±1,11*	20,37±0,71*	**10,09±0,17***

Note: * - parameters, that are significantly (p <0.05) different from those of intact animals

4. CONCLUSIONS

In intact guinea pigs, the morphological organization of the heart auricles differs from the atria by the direction of the muscle fibers, the ratio of morphometric parameters of their structural components and the content of muscle endocrine cells. Submicroscopically, endocrine myocytes of the auricles of the heart contain more hormonal granules than atria.

The characteristical features and level of morphofunctional lesions in the conditions of thermal trauma are different at different periods of the experiment and develop against the background of increased levels of plasma toxicity and increased endogenous intoxication. In the stage of shock and early toxemia, adaptation-compensatory processes and features of inhibition of regeneration at the cellular and subcellular levels characterize morphofunctional changes. In the long term after deep lesions on the background of increasing levels of endogenous intoxication, prominent destructive changes of all structural components of the atria and auricles of the heart are developed.

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6. ACKNOWLEDGEMENTS

The work is carried out within the framework of the initiative research work of the I. Horbachevsky Ternopil National Medical University (Ternopil, Ukraine)"The using of bio-organic and physical factors for the correction of regenerative processes in thermal trauma".