Реферати

СТРУКТУРНІ ЗМІНИ ЕНДОКРИННОЇ СИСТЕМИ СЕРЦЯ ПРИ СТРЕПТОЗОТОЦИНОВОМУ ЦУКРОВОМУ ДІАБЕТІ

Жураківська О.Я., Микулець Т.И., Голдак У.М., Клипич Я.И., Миськів В.А, Гречин А.Б., Клипич О.О.

Метою роботи було встановлення особливостей структурної перебудови секреторних передсердних кардіоміоцитів у ранні та віддалені терміни перебігу стрептозотоцинового цукрового діабету (ЦД). ЦД моделювали одноразовим внутрішньоочеревинним введенням стрептозотоцину (6 мг на 100г маси тіла). Матеріал для дослідження забирали на 14 та 56 доби експерименту. Використали електронно-мікроскопічний метод дослідження. Встановлено, що стрептозотоциновий ЦД в секреторних передсердних кардіоміоцитах призводить до перебудови внутрішньоклітинних органел, які відповідають за синтез і секрецію передсердного натрійуретичного пептиду (ПНУП). Слід зазначити, що відбувається перерозподіл різних типів секреторних гранул (СГ) у відповідь на гіперглікемію, при цьому на 14 добу експерименту значно збільшується об'ємна щільність дифундуючих СГ, що вказує на посилення процесів виведення ПНУП із клітини, а на 56 добу об'ємна щільність молодих і зрілих СГ достовірно зменшується, що свідчить про зрив компенсаторних механізмів.

Ключові слова: стрептозотоциновий цукровий діабет, щурі, секреторний передсердний кардіоміоцит.

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СТРУКТУРНЫЕ ИЗМЕНЕНИЯ ЭНДОКРИННОЙ СИСТЕМЫ МИОКАРДА ПРИ СТРЕПТОЗОТОЦИНОВОМ САХАРНОМ ДИАБЕТЕ

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Целью работы было определение особенностей структурной перестройки сердечных предсердных кардиомиоцитов в ранние и отдаленные сроки течения экспериментального стрептозотоцинового сахарного диабета (СД). СД моделировали одновременным внутрибрюшинным введением стрептозотоцина (6 мг на 100г массы тела). Материал для исследования изымали на 14 и 56 день эксперимента. Использовали електронно-микрос копический метод исследования. Определено, что стрептозотоциновый СД в секреторных предсердных кардиомиоцитах ведет к перестройке внутриклеточных органэлл, что отвечают за синтез и секрецию предсердного натрийуретического пептида (ПНУП). Следует отметить, что происходит перераспределение разных типов секреторных гранул (СГ) в ответ на гипергликемию, при этом, на 14 сутки експеримента значительно увеличивается обьемная плотность дифундирующих СГ, что указывает на усиление процессов выведения ПНУП из клеток, а на 56 сутки обьемная плотность молодых и зрелых СГ достоверно уменьшается, что свидетельствует о срыве компенсаторных механизмов.

Ключевые слова: стрептозотоциновый сахарный диабет, крысы, секреторный предсердный кардиомиоцит.

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ULTRASTRUCTURE OF ALVEOLAR MACROPHAGES IN CASE OF EXPERIMENTAL ACUTE RENAL FAILURE

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We have done experiments on Vistar line white male rats using electronic microscope method and studied in dynamics (12, 24, 72 hours) the ultrastructural changes of alveolar macrophages in case of experimental acute renal failure. It has been established that already in 12 hours after beginning of the experiment one can observe increase of quantity and functional activity of macrophage cells. With expansion of experimental timeline (24-72 hours), we have observed both dystrophic-destructive and adaptive changes in the alveolar macrophages.

Key words: lung, alveolar macrophages, experimental acute renal failure

The paper is a fragment of RSW "Pathogenetic Development Mechanisms of Changes in the Respiratory, Endocrine, Nervous Systems in Case of Simulated Pathological Conditions and Correction of Thereof" (number of state registration 0117U001758).

It has been established in the multiple clinical and experimental studies that alveolar macrophages (AM) play an important role in support of resistance of human body in case of exposure to exo- and endogenic factors [1, 2, 4, 6]. Analysis of many works has demonstrated that morphofunctional condition of AMs is closely connected with structural and metabolic changes in lungs in case of different pathological conditions [3, 5, 7, 10].

The purpose of this research was to study in dynamics the ultrastructural changes of alveolar macrophages of the respiratory part of lungs in case of experimental acute renal failure (EARF).

Materials and methods. The experiment was done on 45 Vistar line white male rats weighting 180-220 grams, which were subdivided in two groups: control and experimental. Acute renal failure in rats of the experimental group was induced by intramuscular administration of 50% glycerol aqueous solution in quantity of 10 ml per kg of body mass [14]. Equivalent amount of water for injections has been injected to the control group. Lung tissue sampling for electronic microscope examination was done using ketamine anaesthesia in 12, 24, 72 hours after beginning of the experiment. Pieces of lung tissue were fixed in 2,5% solution of gluteraldehyde with further postfixation in 1% solution of osmium tetroxide. After dehydration, the material

was poured over epon araldite. The cuts obtained on ultramicrotome "Tesla BS-490" were studied using electron microscope "PEM-125K".

Results and their discussion. Electronic microscope examination of the respiratory part of lungs in 12 hours after beginning of the experiment has demonstrated increase of AMs quantity in the air cells to 3,88±0,048 (p<0,001, table 1) as compared with control group. The nuclei of macrophage cells have incorrect form with evenly distributed chromatin. The nuclear membrane has distinct sinuous contours and forms superficial invaginations. In cytoplasm, we observe mitochondria of different size and form with matrix of moderate electronic-optical density. At the same time, we note a significant quantity of small lysosomes and phagosomes different in form, size and content. Golgi apparatus (GA) consists of small blisters and vacuoles.

Table 1

Quantity of alveolar macrophages in lung tissue of white rats in case of experimental acute renal failure

Groups of animals	Statistical index	Periods of monitoring		
		12 hours	24 hours	72 hours
Control	M ± m	2,04±0,06	2,16±0,06	2,24±0,03
Experimental	M ± m	3,88±0,05	5,24±0,08	4,30±0,05
	P	<0,001	<0,001	<0,001

The tubules and cisterns of granular endoplasm grid (GEG) are somewhat dilated with tender fibrous osmiophil content. On the external membrane of the latter are found ribosomes. The plasma membrane of AMs creates a big quantity of cytoplasm bulges. In some cells are defined mitochondria increased in volume with reduced cristae. As per experiment continuance (24 hours), the AMs quantity has significantly increased as compared with control and was 5,24±0,083 (p<0,001, see Table 1). At the present stage of the experiment, we could determine polymorphism of macrophage elements in the alveolar lumen (Fig. 1).

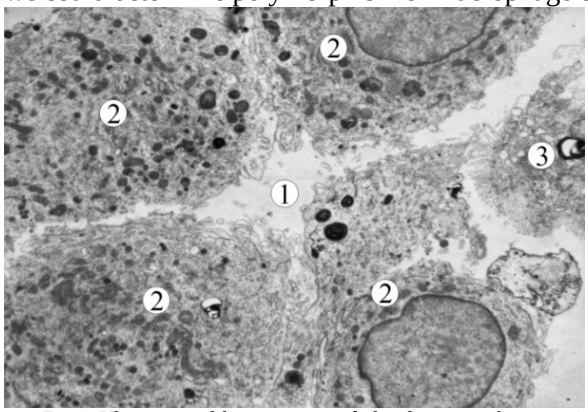

Fig 1. Ultrastructural heterogeneity of alveolar macrophages in 24 hours after beginning of the experiment. 1 – alveolar lumen; 2 – alveolar macrophages; 3 – fragment of type II alveolocytes. Electronic mictophotography x4000.

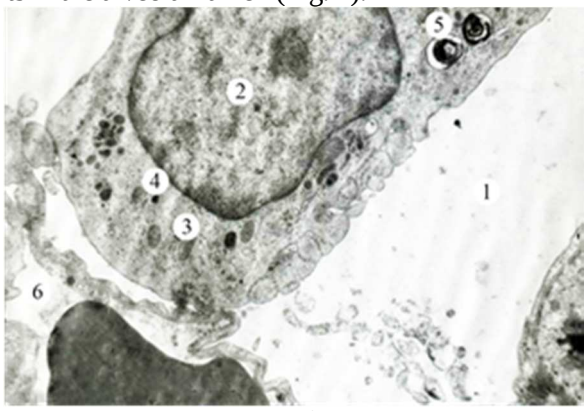

Fig. 2. Ultrastructural organization of the alveolar macrophages in 72 hours after beginning of the experiment. 1 – alveolar lumen; 2 – nucleous; 3 – mitochondria; 4 – lysisome; 5 – phagosome; 6 – hemocapillary lumen. Electronic microphotography. x6400.

Submicroscopically, AMs differ in size, form and ultrastructural organization. Many AMs have nuclei with small-grained nucleoplasm of low electronic optical density. The nuclear membrane forms superficial invaginations. The paranuclear space is locally dilated. Mitochondria have matrix of moderate electronic-optical density and some fragmented cristae. The elements of GA and GEG are dilated. The quantity of ribosomes on the external membrane of the latter is reduced. In some cells, we observe fragmentation of GEG membranes. In cytoplasm, one can note insignificant quantity of lysosomes and some big phagosomes containing polymorphous osmiophil material of different dimensions. On the apical surface of such cells can be identified cytoplasm growing cell membranes small in size. Among AM population, at the level of dystrophic – destructive changes one can observe some cells with characteristic features of increased functional activity (Fig 1.). The nuclei of such cells have matrix of average electronic-optical density. The chromatin granules are evenly placed on the whole area of the nuclei. In the cellular cytoplasm is observed well expressed synthetical apparatus represented by the cisterns of Golgi apparatus and hypertrophic GEG tubules with multiple ribosomes on the membranes of thereof. Mitochondria have matrix of moderate electronic-optical density and are of different size and form. In cytoplasm of AMs can be noted a significant quantity of lysosomes and phagosomes different in form, dimensions and structure. In 72 hours after beginning of the experiment, the quantity of macrophage elements continues increased as compared with control, and is 4,30±0,050 (p<0,001). However, in comparison with the previous stage of the experiment, AMs quantity is reduced (see Table 1.).As on the previous stage of the experiment, heterogeneity of AMs is observed in the alveolar lumens. Among some scanty actively phagocytising AMs are observed the cells with dystrophic and destructive changes (Fig. 2). The nuclei of macrophage elements are deformed. Nucleoplasm

has matrix of low electronic optical density. The granules of chromatin are located along the external surface of nuclear membrane or sometimes appear grouped into separate clusters. Mitochondria are swollen, with shortened and disoriented cristae. The cisterns and tubules of GA and GEG are dilated and vacuolated. In cytoplasm, we observe isolated lysosomes and phagosomes with visible lamellar bodies and fragments of destroyed cells. The study carried out has shown that already after 12 hours of simulation of acute renal failure one can observe increase of quantity and functional activity of AMs in the alveolar lumens. Our data agree with the research results of other scientists that point to the fact that AMs are one of the most reactive elements of lung tissue in case of exposure to different exogenic and endogenic factors [1, 4, 11]. It is evident that such increase of quantity and functional activity of macrophage elements can be considered as primary response of AMs to lung tissue lesion [4, 10, 13]. As per experiment continuance (24 – 72 hours), in the alveolar lumens along with active phagocytising macrophage cells are observed AMs with some lysosomes and increased quantity of big phagosomes that prove the functional deficiency of macrophages. Changes of similar nature in submicroscopic organization of AMs under the influence of exogenic and endogenic factors are reported by other scientists as well [2, 8, 9, 12].

Conclusions

1. Our research has demonstrated that experimental acute renal failure is accompanied by the expressed changes of submicroscopic structure of alveolar macrophages.
2. The nature and degree of expression of ultrastructural changes in alveolar macrophages depends on duration of endogenic factor exposure.

Prospects for further research. *The study of phagocyte activity of alveolar macrophages in case of experimental acute renal failure is in the perspective of future research.*

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Реферати

УЛЬТРАСТРУКТУРА АЛЬВЕОЛЯРНИХ МАКРОФАГІВ ПРИ ЕКСПЕРИМЕНТАЛЬНІЙ ГОСТРІЙ НИРКОВІЙ НЕДОСТАТНОСТІ

Заяць Л.М., Кліщ І.П.

У дослідах на білих щурах-самцях лінії Вістар електронно-мікроскопічним методом вивчено в динаміці (12, 24, 72 год.) ультраструктурні зміни альвеолярних макрофагів при експериментальній гострій нирковій недостатності. Встановлено, що вже через 12 год. після початку дослідження відмічається збільшення кількості і функціональної активності макрофагальних клітин. Зі збільшенням терміну експерименту (24-72 год.) в альвеолярних макрофагах спостерігаються як дистрофічно-

УЛЬТРАСТРУКТУРА АЛЬВЕОЛЯРНЫХ МАКРОФАГОВ ПРИ ЭКСПЕРИМЕНТАЛЬНОЙ ОСТРОЙ ПОЧЕЧНОЙ НЕДОСТАТОЧНОСТИ

Заяць Л.М., Клищ И. П.

В опытах на белых крысах - самцах линии Вистар электронно-микроскопическим методом изучены в динамике (12, 24, 72 часы) ультраструктурные изменения альвеолярных макрофагов при экспериментальной острой почечной недостаточности. Установлено, что уже через 12 часов после начала исследования отмечается увеличение количества и функциональной активности макрофагальных клеток. С увеличением срока эксперимента (24 - 72 часы) в альвеолярных макрофагах наблюдаются как дистрофически-деструктивные

деструктивні так і компенсаторно-пристосувальні зміни.
Ключові слова: легені, альвеолярні макрофаги, експериментальна гостра ниркова недостатність.
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так и компенсаторно-приспособительные изменения.
Ключевые слова: легкие, альвеолярные макрофаги, экспериментальная острая почечная недостаточность.
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HISTOLOGICAL CHANGES IN LIVER AND KIDNEYS IN EXPERIMENTAL TYPE 2 DIABETES MELLITUS AND ITS CORRECTION BY ADMINISTRATION OF PHYTOCOMPOSITIONS COMPRISING *GALEGA OFFICINALIS L.*

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The experimental studies of the morphological state of the white rats' kidney and liver in conditions of the simulated Type 2 diabetes mellitus and the use of pharmaceutical preparation comprising *Galega officinalis L.* and *Vaccinium myrtillus*, as well as administration of "Galevit" liposomal formulation have been carried out. In the group of animals without correction the drastic destructive-degenerative damage to all structural components of the studied organs, as well as significant vascular disorders has been found. Application of the remedial pharmaceutical preparation comprising *Galega officinalis L.* and *Vaccinium myrtillus* has a positive effect on morphofunctional state of the liver and kidneys of laboratory animals, especially the administration of the "Galevit" liposomal formulation. The degree of the reparatory processes in the studied organs in experimental type 2 diabetes mellitus shows that the new "Galevit" composition has more apparent positive effect as compared to the pharmaceutical preparation comprising *Galega officinalis L.* and *Vaccinium myrtillus.*

Keywords: liver, kidneys, Type 2 diabetes mellitus, *Galega officinalis L.*, *Vaccinium myrtillus*, liposomal formulation.

The paperis a fragment of the RSW "Pharmacological and pharmacogenetic aspects of the protective effect of immunobiological drugs, enterosorbents, substances of natural and synthetic origin in different pathological states". State registration number 0116U004148.

Diabetes mellitus (DM) is one of the major medical and social problems, ranking the third place in the world after cardiovascular and oncological diseases. The International Diabetes Federation (IDF) reports about 120 to 180 million patients with diabetes worldwide, accounting for 2-3% of the total population of the planet [1, 3, 4, 6]. This causes the relevance of the study of the novel effective medications to prevent and treat DM sequelae.

The purpose of the paper was to determine the histological changes in the liver and kidneys in streptozotocin-induced type 2 diabetes mellitus and the effect of pharmaceutical preparation comprising *Galega officinalis L., Vaccinium myrtillus* and taurine, as well as its liposomal formulation with conventional name "Galevit".

Materials and Methods. The object of the pharmacological studies was the pharmaceutical combination preparation comprising *Galega officinalis L.* and *Vaccinium myrtillus* and its liposomal formulation «Galevit». The composition is comprised of dry extracts of 50 mg *Galega officinalis L.* and *Vaccinium myrtillus* and 1.4.mg taurine. Liposomal formulation of the composition was obtained by the conventional technique. The study was carried out on 50 outbreed male white rats with body weight of 260-280 g. Type 2 DM was induced by streptozotocin (STZ, "Sigma", United States). STZ was dissolved *extempore* and injected on the citrate buffer (pH 4.5), since in alkaline and neutral medium it quickly degrades to inactive metabolites and loses its diabetogenic activity. To simulate the type 2 DM, rats were injected intraperitoneally with a single dose of (65 mg/kg body weight) STZ solution according to the Islam S., Choi H. (2007) technique [7]. To reduce the diabetogenic activity of STZ prior (15 minutes) to its administration nicotinamide (N) was injected intraperitoneally with a dose of 230 mg/kg. The rats were fed a high-calorie diet for 12 weeks before administration of STZ [8]. The investigated formulations were administered endogastrically once a day for 21 days with treatment-and-prophylactic purpose. The first injection of the drugs started within 24 hours after induction of diabetes. A group of animals of controlled pathology (CP) were administered with distilled water in a similar way. The animals were randomized into 4 groups. Group 1 (the control group; intact animals (IC)); Group 2 (animals of control pathology); Group 3 (STZ + N-induced diabetic animals administered with pharmaceutical preparation comprising *Galega officinalis L.* and *Vaccinium myrtillus* with a dose of 50 mg/kg; *peros* taurine with a dose of 1.4 mg/kg); Group 4 group (STZ + N-induced diabetic animals administered with "Galevit" liposomal formulation. The experiments were performed in compliance with the requirements of international principals of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg,1986) and " General Ethical Principles for Scientific Experiments on Animals", approved by the I National Congress