რეზიუმე

ქირურგიული ტრავმა და ბეტულინშემცველი მალამოების ჭრილობის შემახორცებელი თვისებები (ექსპერიმენტული კვლევა)

[1]ს.პროშინი, [2]გ.ბადათურია, [3]ი.ჩერივოვი, [3]ო.ხაევი, [3]ა.ოჩირ-გარაევი

[1]უნივერსიტეტი "რეავიზი", სანკტ-პეტერბურგი; [2]სანკტ-პეტერბურგის სახელმწიფო პედიატრიული სამედიცინო უნივერსიტეტი; [3]სანკტ-პეტერბურგის სახელმწიფო უნივერსიტეტი, რუსეთის ფედერაცია

კვლევის მიზანს წარმოადგენდა ბეტულინშემცველი მალამოების ანტიანთებითი თვისებების შესწავლა ნაფლეთი და დამწვრობითი ჭრილობების მოდელებზე.

ბეტულინის აქტივობა შესწავლილია 170 თეთრ უჯიშო ვირთაგვაზე ნაფლეთი ჭრილობით და 15 ბოცვერზე დამწვრობითი ჭრილობით. პრეპარატის ეფექტურობა შეფასდა ჭრილობის (დამწვრობითი) ზედაპირის შემცირების სიჩქარით, ფუფხის მოცილების ვადებით (ჭრილობისათვის), ჰიპერემიის ხასიათით (დამწვრობისათვის), ასევე, ჭრილობის (დამწვრობის) პროცესის ჰისტომორფოლოგიური სურათით მე-7, მე-14 და 21-ე (3, 8 და 13) დღეს და სრული შე-ხორცების ვადების მიხედვით. ჭრილობის ზედაპირის შემცირების სიჩქარე მაქსიმალური იყო ჯგუფში, სადაც ჭრილობა მუშავდებოდა ბეტულინის 0,5%-იანი მალამოთი (შესწავლილი იყო 0,2%-, 0,5%- და 5%-იანი მალამოების კომბინაციები), ჭრილობის სრული ეპითელიზაცია განვითარდა უკვე მე-7 დღეს ($p=0,02$). დამწვრობითი ზედაპირის შემცირების სიჩქარე 0,5%-იანი ბეტულინის გავლენით თავისი მახასიათებლებით არ ჩამორჩებოდა პრეპარატ "პანთენოლს", ხოლო ჰისტოლოგიური მონაცემებით აღემატებოდა კიდეც მას.

ჩატარებული კვლევის შედეგებმა აჩვენა, რომ მაქსიმალური ჭრილობის შემახორცებელი აქტივობა გამოავლინა ბეტულინმა 0,5%-იანი კონცენტრაციით. ბეტულინის 0,5%-იანი მალამოს დამწვრობის საწინააღმდეგო თვისებებიც მეტადაა გამოხატული.

STRUCTURAL CHANGES AND MORPHOMETRIC ANALYSIS OF CARDIOMYOCYTES IN RATS WITH ALLOXAN DIABETES

[1]Osipiani B., [2]Machavariani T.

[1]Tbilisi State Medical University; [2]Iv. Javakhishvili Tbilisi State University, A.N. Natishvili Institute of Morphology, Tbilisi, Georgia

In patients with type 1 diabetes as well as type 2 diabetes, cardiovascular complications are rather more common than in patients without diabetes [24,25,35,41,43]. For example, the development of cardiovascular disease in type 1 diabetes is at least 10 times higher than in the population without diabetes [9,25]. Accordingly, a number of both experimental [18] and clinical [10] studies have focused on the study of cardiovascular complications in conditions of diabetes mellitus. Diabetic cardiomyopathy is a severe complication associated with functional and structural dysfunction of the myocardium and is not related to other conventional factors such as coronary heart disease, hypertension, congenital heart defects, and heart valve defects [4,28,31].

From the viewpoint of a number of authors, [26] but not all of them [29,37] there is a strong link between hyperglycemia and cardiovascular disease, however, the nature and pathogenesis of these changes are not fully understood [44].

Currently, it is believed that the activation of peroxidation processes and the reduction of NADPH-oxidase levels play an important role in the pathogenesis of chronic complications of diabetes mellitus, including the development of cardiovascular complications [3,13,15,16,38]. These changes result in cardiomyopathy, which in turn causes the apoptosis of cardiomyocytes, along with myocardial hypertrophy and an increase in the amount of collagen deposition [13,14,27]. Hypertrophy of cardiomyocytes with subsequent infarction, apoptosis, and fibrosis is a structural change of the diabetic cardiomyopathy. manifested in changes in the size of the heart chambers, as well as a number of functional disorders in the form of systolic and diastolic dysfunction [12].

Interestingly, according to some studies, changes in type 1 diabetes develop only in the left ventricle chambers due to an increase in wall thickness, which is mainly caused by the disruption of microcirculation [18,21,44]. According to other studies, changes in type 1 diabetes also develop in the right chambers of the heart [21,23]. It should be noted that impaired function of the right chambers of the heart in patients with diabetes mellitus, in conditions of heart failure, pulmonary hypertension, and earlier infarction, significantly affects the quality of life and the prognosis of survival [21,30].

Most studies indicate the development of diabetic cardiomyopathy in the later stages of diabetes mellitus, usually in the 8th to 12th week after inducing diabetes [1]. Available studies are mainly aimed at studying the changes in the left chambers of the heart, while the ongoing changes in the right chambers of the heart are studied less.

Based on the above, the aim of our study is to study the ongoing morphological changes in the right chambers of the heart during experimental diabetes.

Materials and methods. The experiment was performed on 20 Wistar rats of both sexes, weighing 200-250 g. Of these, 10 rats were controls, and 10 ones with experimental diabetes. We were inducing experimental diabetes by intravenous administration of 150 mg 10% alloxan solution. The control and target animals were placed in standard Vivarium conditions. We diagnosed diabetes by blood glucose levels. The animals were withdrawn from the experiment by injecting 1% etaminal-sodium into the abdominal cavity (intraperitoneally). We took the material from the left and right chambers of the heart.

In the histological examination, the material was fixed in 10% formalin and Karnua fixation mixture. The 5, 10, and 30 mcg. paraffin slices were stained with hematoxylin-eosin and picrofuxin by Van Gieson method.

In the biochemical examination, the blood glucose levels were determined in both control and target animals. We determined blood glucose levels by means of standard Medi-test indicators.

Computer programs Adobe Photoshop and Image J software were used for morphometric analysis. 5 animals from each group underwent morphometric analysis, and 10 slices were studied from the right and left ventricles and atria of each animal's heart. The size of the bounded area was recorded by a computer program in microns (μm) and automatically transferred to Microsoft Excel spreadsheets.

The Student's T-test was used to test the confidence of the difference between the data indicators

Results of histological examination. Based on a study we conducted earlier [2] at the early stage of diabetes (1 month) after the administration of alloxan, rats showed a decrease in weight. At the early stage of the experiment, namely 1 month after the start of the experiment, the major structures of the myocardium underwent minor changes during the mildly ongoing pathological process. At this stage, most cardiomyocytes maintained their usual structure and did not differ from those of the control animals. Only a few cardiomyocytes showed dystrophic changes and necrosis. During a severe pathological process, at the same stage e.g. 1 month after the start of the experiment, the marked dystrophic changes in cardiomyocytes increased, especially in the left chamber of the heart. No significant changes were observed in the right chambers at the same stage of the experiment (1 month). In histological examination, 3 months after the administration of alloxan, especially in severe experimental diabetes, hypertrophic changes in cardiomyocytes were found along with dystrophic and necrotic changes in the left chambers of the heart. The structure of the myocardium in the right chambers of the heart was disordered as compared to that of the left chambers. Cardiomyocytes experienced the severe dystrophic and necrotic changes, with apoptotic cells found in them In addition, the number of hypertrophic cells was dramatically increased. Interstitial and perivascular fibrosis were found. At the same stage, there were found the changes in the microcirculatory network of the myocardial venous system - manifested venous stasis and quite intense vascular congestion. The blood vessels were dilated, and the aggregation and agglutination of red blood cells were observed in several blood vessels. Dramatic destructive changes in endothelial cells were detected (Fig.).

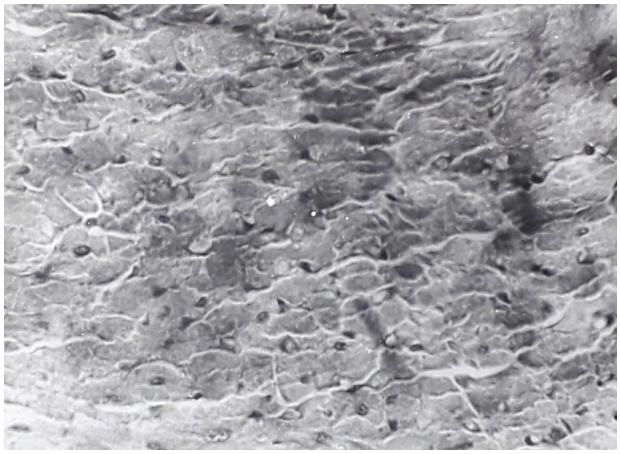

Fig. Micrographs of heart. Myocardium.Right ventricule section. Cardiomyocytes experienced the severe dystrophic and necrotic changes, hypertrophic cells. Interstitial edema. The blood vessels were dilated, and the aggregation and agglutination of red blood cells were observed in several blood vessels. Haematoxylin-Eosin

In alloxan diabetes, changes in the diameter of the cardiomyocytes on myocardial slices were detected in the entire heart. In 1 month after the start of the experiment, the average diameter of the cardiomyocytes in the right and left chambers of the heart was insignificantly increased. In 3 months after the administration of alloxan, the average diameter of cardiomyocytes increased significantly in the right atrium and made 12.992±0.35, i.e. increased by 26.8% ($P<0.05$) as compared to the controls, while in the right ventricle it was 14.935±0.25 and increased by 17.9% as compared to the controls ($P<0.05$). The mean diameter of cardiomyocytes in the left ventricle and atrium was insignificantly increased at 3 months of the experiment and made 13.60±0.3 and 13.900±0.4, respectively, increased by 2% ($P<0.05$) as compared to the control group values. The results of our study match the data of several researchers [5,11,19] (Table).

Therefore, a significant increase in the diameter of the cardiomyocytes in the right chambers of the heart was observed at a later stage and an insignificant increase in the diameter of the cardiomyocytes in the left atrium and ventricle of the animals ($P<0.05$). In the study, hypertrophy of the cardiomyocytes, which was observed in diabetic heart chambers, led to the enlargement of the right chambers, while the changes in the left chambers were insignificantly manifested. These results are consistent with the results of the Charissa E van den Brom., 2010 study, however, there are different data obtained in rats in other studies [18,20]. Ongoing studies on diabetes provide

Table. Changes in body mass, glucose levels, and cardiomyocyte diameter in control and experimental rats

Wistar rat	Control group (n-10)	Alloxan diabetes 4 weeks (n=5)	Alloxan diabetes 12 weeks (n=5)	p
Body weight (g)	250±14,5	225±15,6	210±16,7	<0.05
Glucose mmol/L	6,3±0,2	13,7±0,5	17,9±2,9	<0.001
RV CD (μm)	12.661±0.24	12.722 ±0.24	14.935±0.25	<0.05
LV CD (μm)	13.342±0.37	13.450±0.37	13.620± 0.3	<0.05
RA CD (μm)	10.238±0.27	10.270±0.27	12.992±0.35	<0.05
LA CD (μm)	13.615±0.72	13.790±0.72	13.900±0.4	<0.05

*CD - cardiomyocyte diameter; RV – the right ventricle; LV – the left ventricle; RA – the right atrium; LA – the left atrium. The difference is statistically reliable * P<0.05 compared with the control animals*

different results in terms of changes in cardiomyocyte sizes. The results of our study match with the results of several researchers [7,8,11,17,36]. However, according to other studies, the size of cardiomyocytes in animal experimental diabetes models either did not change at all [22], or there were no changes in the diameter of cardiomyocytes, and only variations in the length of cardiomyocytes were observed [6]. The results of our study directly contradict the findings of a number of researchers [34,40] where a reduction in the diameter of cardiomyocytes in both RV and LV of the diabetic heart was observed.

Conclusion. The obtained results indicate that at a later stage, in particular, 3 months after the start of the experiment, there was a disruption of microcirculation in the myocardium (endothelial lesion, vascular dilatation, stasis, erythrocyte aggregation, and agglutination), interstitial and perivascular fibrosis, dystrophic changes in cardiomyocytes, necrosis, and apoptosis. Cardiomyocyte hypertrophy was observed in several areas. Changes in the diameter of the cardiomyocytes were observed, with a significant increase in the diameter of the cardiomyocytes, especially in the right chambers of the heart, while there were observed insignificant changes in the diameter of the cardiomyocytes in the left chambers. It appears that functional and structural changes in the right chambers of the heart are directly related to systemic sensitivity to insulin [7,32,33]. It is likely that these changes are due to the above metabolic shifts [39,42].

Based on the above, it is possible to assume that the impact (influence) of diabetes mellitus on the structure and function of the right chambers may be more noteworthy than considered earlier.

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SUMMARY

STRUCTURAL CHANGES AND MORPHOMETRIC ANALYSIS OF CARDIOMYOCYTES IN RATS WITH ALLOXAN DIABETES

[1]Osipiani B., [2]Machavariani T.

[1]Tbilisi State Medical University; [2]Iv. Javakhishvili Tbilisi State University, A.N. Natishvili Institute of Morphology, Tbilisi, Georgia

The aim of this research was to study the ongoing structural changes in rat cardiomyocytes during alloxan diabetes and their morphometric analysis in dynamics, in particular 1 and 3 months after the start of the experiment.

The experiment was performed on 20 Wistar rats of both sexes, weighing 200-250 g. Of these, 10 rats were controls, and 10 ones with experimental diabetes. We were inducing experimental diabetes by intravenous administration of 150 mg 10% alloxan solution. Histological, biochemical, morphometric, and statistical methods of research were used in the experiment.

Based on the histological examinations it was stated that dystrophic changes, necrosis, and apoptosis of cardiomyocytes were found in alloxan diabetes.

Microcirculation was disrupted in the myocardium (endothelial lesion, stasis, red blood cell aggregation, and agglutination). At the later stage, all of the above changes were more pronounced in the right chambers of the heart. 3 months after the start of the experiment, along with all the above changes there was found the hypertrophy of cardiomyocytes,

The morphometric study revealed that at the later stage, a significant increase in the diameter of cardiomyocytes, especially in the right chambers of the heart observed, which was most likely caused by the specific functional and structural features of the right chambers of the heart. All this gives us reason to assume that the impact of metabolic changes caused by diabetes mellitus on the right chambers of the heart is quite significant and noteworthy.

Keywords: alloxan, diabetes mellius, cardiomyocytes, rat heart.

РЕЗЮМЕ

СТРУКТУРНЫЕ ИЗМЕНЕНИЯ И МОРФОМЕТРИЧЕСКИЙ АНАЛИЗ КАРДИОМИОЦИТОВ КРЫС ПРИ АЛЛОКСАНОВОМ ДИАБЕТЕ

[1]Осипян Б.С., [2]Мачавариани Т.Г.

[1]Тбилисский государственный медицинский университет; [2]Тбилисский государственный университет им. И. Джавахишвили, Институт морфологии им. А.Н. Натишвили, Грузия

Целью исследования явилось изучение структурных изменений, происходящих в кардиомиоцитах крыс, и их морфометрический анализ при аллоксановом диабете в динамике, в частности спустя 1 и 3 месяца после начала эксперимента.

Эксперимент проведен на 20 крысах линии Вистар обоего пола массой 200-250 г. Из них 10 крыс были контрольными, а 10 - целевыми. Экспериментальный диабет вызывали посредстаовм внутривенного введения 150 мг 10% раствора аллоксана. В эксперименте использовались гистологические, биохимические, морфометрические и статистические методы исследования.

Гистологические исследования показали, что при аллоксановом диабете наблюдаются дистрофические изменения, некроз и апоптоз кардиомиоцитов; нарушение микроциркуляции в миокарде (повреждение эндотелия, стаз, агрегация эритроцитов, агглютинация). На более поздних сроках, в частности спустя 3 месяца от начала эксперимента вышеперечисленные изменения в миокарде были более выраженными, отмечалась гипертрофия кардиомиоцитов.

Морфометрическое исследование показало значительное увеличение диаметра кардиомиоцитов, особенно в правых отделах сердца, что, очевидно, вызвано специфическими функциональными и структурными особенностями правых камер сердца.

Результаты проведенного исследования позволяют заключить, что влияние на правые камеры сердца метаболических изменений, вызванных сахарным диабетом, весьма значительны и заслуживают особого внимания.

რეზიუმე

ვირთაგვების კარდიომიოციტების სტრუქტურული ცვლილებები და მორფომეტრიული ანალიზი ალოქსანური დიაბეტის დროს

[1]ბ.ოსიპიანი, [2]თ.მაჭავარიანი

[1]თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი; [2]ივ. ჯავახიშვილის სახ. თბილისის სახელმწიფო უნივერსიტეტი, ა. ნათიშვილის სახ. მორფოლოგიის ინსტიტუტი, საქართველო

კვლევის მიზანს წარმოადგენდა ალოქსანური დიაბეტის დროს ვირთაგვების კარდიომიოციტებში მიმდინარე სტრუქტურული ცვლილებების შესწავლა და მათი მორფომეტრიული ანალიზი დინამიკაში, კერძოდ ექსპერიმენტის დაწყებიდან 1 და 3 თვის შემდეგ.

ექსპერიმენტში გამოყენებული იყო ორივე სქესის Wistar-ის ჯიშის 20 ვირთაგვა, წონით 200 – 250 გრ. აქედან 10 ვირთაგვა იყო სამიზნე, ხოლო 10 - საკონტროლო. დიაბეტს ვიწვევდით ალოქსანის 150 მგ 10% - იანი ხსნარის ერთჯერადი შეყვანით ინტრავენურად.

ექსპერიმენტში გამოყენებული იყო კვლევის ჰისტოლოგიური, ბიოქიმიური, მორფომეტრიული და სტატისტიკური მეთოდები.

ჰისტოლოგიური კვლევის საფუძველზე გამოვლინდა, რომ ალოქსანური დიაბეტის დროს აღინიშნება კარდიომიოციტების დისტროფიული ცვლილებები, ნეკროზი, აპოპტოზი. ადგილი ჰქონდა მიკროცირკულაციის მოშლას მიოკარდიუმში (ენდოთელის დაზიანება, სტაზი, ერითროციტების აგრეგაცია, აგლუტინაცია). მოგვიანებით ვადაზე ზემოჩამოთლილი ცვლილებები უფრო მეტად გამოხატული იყო გულის მარჯვენა კანებში.

მოგვიანებით ვადაზე, კერძოდ ექსპერიმენტის დაწყებიდან 3 თვის შემდეგ ზემოჩამოთვლილ ცვლილებებთან ერთად აღინიშნა კარდიომიოციტების ჰიპერტროფია. მორფომეტრიული კვლევით დადგინდა კარდიომიოციტების დიამეტრის მნიშვნელოვანი ზრდა, განსაკუთრებით გულის მარჯვენა კანებში, რაც, სავარაუდოთ, გამოწვეული იყო გულის მარჯვენა კანების სპეციფიური ფუნქციური და სტრუქტურული თავისებურებებით.

კვლევის შედეგები იძლევა ვარაუდის საფუძველს, რომ შაქრიანი დიაბეტით გამოწვეული მეტაბოლური ცვლილებების ზემოქმედება გულის მარჯვენა კანებზე საკმაოდ მნიშვნელოვანი და საყურადღებოა.

ФАРМАКОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА ЛЕВОФЛОКСАЦИНА И ЕГО КЛИНИЧЕСКОЕ ПРИМЕНЕНИЕ (ОБЗОР)

Штанюк Е.А., Коваленко Т.И., Красникова Л.В., Мишина М.М., Вовк А.О.

Харьковский национальный медицинский университет, Украина

С открытием антибиотиков такие тяжелые инфекционные процессы, как сепсис, перитонит, гангрена, казалось, стали управляемыми, однако по сей день продолжают уносить жизни миллионов людей. Причина этого явления - растущая устойчивость бактерий к антимикробным препаратам [28,32,35].

На сегодняшний день в мире разрабатывается весьма небольшое количество новых антибактериальных препаратов, причем с каждым годом их производство все меньше и меньше, причиной чего является высокая стоимость создания каждого такого препарата (до 1 млрд. долларов), и фармацевтические концерны, учитывая быстрое развитие резистентности болезнетворных микробов к антибиотикам, все с меньшей охотой берутся за такие разработки.

Развитие резистентности к антимикробным препаратам у многих бактериальных патогенов обусловливает неэффек-