The aim of our research was to evaluate the variations of MDA (Malondialdehyde) content in the homogenate in experimental myocardial infarction.

Materials and Methods. Diabetic cardiomyopathy was modeled by intraperitoneal injection of streptozotocin at a dose of 60mg/kg. Four groups were in the experiment. Group 1 (early stage of diabetic cardiomyopathy): animals were removed in three weeks after streptozotocin injection. Group 2 (intermediate stage of diabetic cardiomyopathy): animals were removed in five weeks. Group 3 (late stage of diabetic cardiomyopathy): animals were removed in eight weeks. The control group (4) consisted of 5 intact rats. Immunohistochemical study was performed using monoclonal antibodies Bax (1:300, Abcam) and Bcl-2 (1:300, Thermo Scientific), cytochrome C (RTU, Neomarkers). Using the morphometric program AperioImageScope carried out the calculation of the percentage positivity of expression (PPE) of the studied markers. Statistical analysis was carried out using the standard statistical software package STATISTICA 7.1.

Results. In group 1 (n=15) the PPE of Bax varied from 33.4% to 38.4%, the average value was 34.4%. The PPE of Bcl-2 ranged from 9.4% to 17.3%, the average value was 14.2%. The PPE of cytochrome C varied from 5.9% to 7.4%, the average value was 6.8%. In group 2 (n=15) the PPE of Bax ranged from 16.8% to 40.9%, the average value was 31.9%. The PPE of Bcl-2 varied from 45.3% to 72.4%, the average value was 65.9%. The PPE of cytochrome C ranged from 6.1% to 17%, the average value was 12.8%. In group 3 (n=15) the PPE of Bax varied from 30.1% to 39.9%, the average value was 36.9%. The PPE of Bcl-2 ranged from 58.2% to 74.6%, the average value was 68.5%. The PPE of cytochrome C varied from 24.7% to 30.3%, the average value was 26.1%. In the control group (n=5), the average value of PPE of the analyzed markers was 5.9%, 56.0% and 3.07% (for Bax, Bcl-2 and cytochrome C, respectively). The cell survival index (CSI) was 0.38 (0.36; 0.43) in the first group. CSI was 2.24 (1.61; 2.70) and 1.87 (1.60; 2.04), respectively in 2 and 3 groups. The cell survival index was 9.97 (6.65; 11.25) in the control group. In group 1 the PPE of Bcl-2 was a significant decreased and the PPE of Bax increased. In 2 and 3 groups PPE of Bax was also statistically significant increased, but PPE of Bcl-2 was not statistically significant different to compare to control group. Statistical analysis revealed a significant change of PPE of Bax (H=12.95, p=0.004) and Bcl-2 (H=13.85, p=0.003) in the studied groups. As diabetic cardiomyopathy progressed, there was a significant increase the level of PPE of cytochrome C in the cytoplasm of cardiomyocytes compared to the control group and in the intergroup analysis (H=17.10, p=0.0007). The correlation analysis established a positive relationship between the expression of Bax and cytochrome C (r=0.6, p=0.017).

Conclusion. The study revealed a change in the expression of proteins regulating cell apoptosis. Experimental modeling of diabetic cardiomyopathy showed an increase in the expression of markers of anti-and proapoptotic proteins in cardiomyocytes with a change in the cell survival index, which indicated the activation of the apoptotic system due to glycaemia. The low survival index at the early stage of the experiment indicated increased damage to the heart muscle cells and apoptosis in glycaemia. The increase in the survival index at the intermediate station indicated the formation of adaptive processes to glycemia. Repeated decrease in the survival index of cells in the later stages of the experiment may indicate the depletion of adaptation to the damaging effects of glucose in the dynamics of diabetic cardiomyopathy. The positive correlation between Bax and cytochrome C expression indicates the increasing role of the proapoptotic system in the progression of diabetic cardiomyopathy in the experiment.

Prospects for further research. The obtained data can serve as a basis for correcting the treatment of cardiomyopathy in patients with diabetes mellitus.

Keywords: cytochrome C, Bax, Bcl-2, diabetic cardiomyopathy.

References:


Acute myocardial infarction remains the main clinical model of ischemia/reperfusion injury associated with oxidative stress [1]. The unbalanced production of reactive oxygen species (ROS) accelerates the peroxidation of lipids and generates a large variety of the toxic lipid peroxidation products, including malondialdehyde (MDA) [2]. Reacting with Lys residues, MDA induces the protein modifications (intramolecular and/or intermolecular cross-linking), and alters the cellular responses [3]. The experimental studies performed recently in vitro have suggested the utility to assess MDA as a biomarker of oxidative stress in the myocardium damage caused by ischemia/reperfusion [4]. The aim of our research was to evaluate the variations of MDA content in the homogenate in experimental

MALONDIALDEHYDE VARIATIONS IN EXPERIMENTAL MYOCARDIAL INFARCTION

Timercan T., Timercan V.

Nicolae Testemitsans State University of Medicine and Pharmacy, Republic of Moldova

Acute myocardial infarction remains the main clinical model of ischemia/reperfusion injury associated with oxidative stress [1]. The unbalanced production of reactive oxygen species (ROS) accelerates the peroxidation of lipids and generates a large variety of the toxic lipid peroxidation products, including malondialdehyde (MDA) [2]. Reacting with Lys residues, MDA induces the protein modifications (intramolecular and/or intermolecular cross-linking), and alters the cellular responses [3]. The experimental studies performed recently in vitro have suggested the utility to assess MDA as a biomarker of oxidative stress in the myocardium damage caused by ischemia/reperfusion [4]. The aim of our research was to evaluate the variations of MDA content in the homogenate in experimental

Biological Markers in Fundamental and Clinical Medicine. – Vol.2, №2. – 2018. ISSN 2570-5911 (Print); ISSN 2570-5903 (On-Line) DOI: 10.29256/v.02.02.2018.escbm01-87

Accepted for printing on 24 Sept 2018

DOI: 10.29256/v.02.02.2018.escbm69
Forty adult male rats (Rattus albicans) were randomized into five groups. L1 (n=11) – control, the rats were injected NaCl 0.9%. L3 (n=6), L4 (n=6), and L5 (n=6) – experimental, the rats were injected isoproterenol 100 mg/kg one dose subcutaneously, and sacrificed at 6 hours, 24 hours and 7 days respectively. The MDA content in the homogenate was assessed by Gudumac, et. al. method [5]. The obtained data were analysed by Kruskal-Wallis non-parametric test using SPSS version 23.

Results. The experimental groups have shown the statistically significant difference (p<0.05) compared to intact and control ones. The slight increase of MDA content in the homogenate in L3 was followed by the significant decrease in L4 compared to all groups. We suppose that these changes are due to the increased release of MDA from the damaged myocardium into the blood.

Prospects for further research. High quantities of ROS are produced by oxidative stress in the ischemic heart. Lipid peroxidation generates MDA - a toxic bifunctional electrophile. Our research has shown that MDA content in the homogenate rises at the onset of cardiac ischemia, and has proved the utility of MDA usage as the clinically relevant biomarker of oxidative stress. The obtained results should be treated with caution, as a limited number of samples were assessed. The further research is required.

References:
1. Jeroen Frijhoff, et al Clinical relevance of biomarkers of oxidative stress Antioxidants & Redox Signaling, 2015; 23; 14: 1144-1170
4. Ramon Rodrigo, Matías Libuy, Felipe Feliu, and Daniel Hasson Oxidative stress-related biomarkers in essential hypertension and ischemia-reperfusion myocardial damage Disease Markers, 2013; 35(4):773-790
5. Gudumac Valentin, Tagadiuc Olga, Nastas Ion Procedeu de dozare a dialdehidei malonice în esutul osos. Certificat de inovator nr. 4366 din 15.11.2005 // Gudumac Valentin, Tagadiuc Olga, Nastas Ion Dosage procedure for malondialdehyde in bone tissue // Innovation certificate no. 4366 of 15.11.2005

Key words: cardiac ischemia, oxidative stress, lipid peroxidation, malondialdehyde.

Accepted for printing on 24 Jul 2018

DOI: 10.29256/v.02.02.2018.escbm70

N-ACETYLTRANSFERASE 2 GENE POLYMORPHISM IS A POSSIBLE BIOMARKER OF LUNG CANCER RISK IN YAKUT POPULATION

Tsyandina E.V., Rumyantsev E.K., Nikolaev V.M.
Yakut Scientific Center of Complex Medical Problems, Russia

Lung cancer, like many other oncological diseases, is a multifactorial disease, in the development of which an important role is played by both external (smoking, asbestos, radon, arsenic, etc.) and genetic factors [2, 4, 5, 10]. Some authors have shown that the polymorphic variants of the NAT2 gene contribute to the development of oncological diseases, including lung cancer [3,7]. The NAT2 gene is localized on the short arm of chromosome 8 (8p23.1), has a length of about 9900 bp, contains 2 exons and is predominantly expressed in the liver and intestine [1,8]. The N-acetylttransferase-2 enzyme, encoded by this gene, is a 33 kD protein consisting of 290 amino acid residues. This enzyme, localized in the cytoplasm, participates in the biotransformation process of aromatic amines that are present in the environment. The source of aromatic amines is industrial waste, pollution of water, air, and a number of medicines [1,9].

Material and Methods. We examined 60 patients with lung cancer (43 male and 17 female), Yakut ethnicity, who received treatment in the Republican oncological dispensary of Yakutsk, Republic Sakha (Yakutia), Russia. The mean age of the patients was 58.86 ± 8.72 yrs. As a control, a group of healthy individuals without cancer, corresponding to a group of patients on ethnic origin and sex, consisting of 60 people (mean age 49.5 ± 5.75) was studied. A standard phenol-chloroform extraction method was used to isolate DNA [6]. The isolated DNA was frozen at a temperature of -40°C before genotyping. Analysis of the polymorphic variants 481C> T, 590G> A and 857G> A of the NAT2 gene was carried out using polymerase chain reaction methods on the «Terzik» amplifiers of the company DNA Technology (Russia) and T100 of Bio-Rad (USA) using nucleotide primers (F 5’-GCTGGGTCTGGAAGCTCCTC; R 5’-TTGGGGTGATACATACACAAGGG). To determine the nucleotide substitutions, hydrolysis of the amplified fragment was carried out by the following restriction enzymes: KpnI (481C> T), BamHI (857G> A), Taqi (590G> A).

Results. In order to identify possible associations of polymorphic variants of the NAT2 gene with the development of lung cancer, we performed an analysis of the frequency distribution of alleles and genotypes of the polymorphic variants 481C> T and 590G> A in patients with lung cancer and in people without oncological diseases. We did not find statistically significant differences in the distribution of frequencies of alleles and genotypes between the control and...