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The role of prooxidative and antioxidant processes in periodontal tissue in the mechanisms of formation of adrenalin damage of myocardium and experimental periodontitis and their correction with Corvitin

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Abstract

The aim of our study was to determine the antioxidant activity and prooxidative processes in the formation mechanisms in periodontal adrenalin myocardial damage and experimental periodontitis and their correction with corvitin. For this purpose, we conducted a study on 54 nonlinear white male rats, which were divided into six groups. First - control, second, third, fourth and fifth - a group of animals with adrenaline injury of myocarditis during the course of experimental periodontitis before correction of corvitin to according to the 1st, 7th, 10th and 17th days of the experiment and the sixth group - animals with adrenaline injury of myocarditis during the course of experimental periodontitis after adjustment corvitin. The results showed that when combined pathology antioxidant activity of prooxidative processes going towards depression of antioxidant protection against the

growing LPO. After entering corvitin - reduced rates of LPO and increases the activity of enzymes AOC, that indicating the antioxidant and cardioprotective properties of the drug.

Keywords: adrenaline damage of myocarditis; experimental periodontitis; corvitin.

Introduction

Cardiovascular disease remains a pressing problem today, as one of the main causes of disability and death of people of working age. According to WHO, the mortality rate from this disease in Ukraine is over 50%. In terms of incidence majority are men, but the death rate is higher in female, especially in the elderly [1].One of the most common pathologies of cardiovascular disease is myocardial infarction (MI). This is an acute disease caused by the occurrence of one or more foci of ischemic necrosis of heart muscle due to absolute or relative failure of the coronary circulation. According to the definition of MI pathoanatomical - a myocardial cell death due to prolonged ischemia. Myocardial infarction is the leading cause of disability and death in the world today. Every sixth man and every seventh woman in Europe die from MI. [2]In particular, in recent years special attention to one important molecular mechanisms of cell damage, covering the processes of lipid peroxidation (LPO) and antioxidant system (AOS) in adrenaline injury of myocarditis.

Dystrophic-inflammatory periodontal disease is the most common pathology in dentistry. Generalized periodontitis is not only the different manifestations of clinical disease in some patients, but in the dynamics of pathological process in periodontal each patient. The development of generalized periodontitis should be seen as the result of interaction of microbial factors and the patient. Currently comprehensively studied the effect of microbial, trauma, immune, vascular and other local factors in the development of generalized periodontitis. On the one hand, the progress of local inflammatory reaction depends on the immunological properties of the organism of the patient, the other - inflammation in periodontal tissues affects the whole body. There is a vicious circle that worsens tissue damage reparation and restoration of homeostasis. One of the causes of persistent effect after the therapy on periodontitis can be as dysbiotic phenomenon in the mouth of instability normal microflora and change reactivity in general. This contributes to the growth of aggressive environmental impact of stress factors, the increase in the population of people with various immune deficiencies, improper use of antibiotics. It is possible that complex therapy of generalized periodontitis, which involves the use of antimicrobial agents with a broad spectrum of activity can contribute to total inhibition of endogenous oral microflora and

all levels of protection [3], therefore, the study of combined periodontitis is one of the priority areas of medicine in general and cardiology and dentistry in particular, and the establishment of pathogenetic therapy to correct these disorders.

In recent years in the treatment of cardiovascular diseases, great attention is given to drugs of multimodal properties. These include such drug as Corvitin - soluble form bioflavanoyid quercetin. Corvitin has antioxidant, immunomodulating, membrane stabilizing, cardioprotective, anti-hypoxic and anti-inflammatory effect, enhances the reparative processes. For corvitin typical cerebroprotective and neuroprotective effect caused by the decrease in glutamate excitotoxicity, intracellular hypercalcemia and regulation of nitric oxide synthesis. Corvitin antiatherogenic effect at the expense of reduced activity of lipid peroxidation and inhibition of lipoperoxidation. Quercetin has an intense reduction of catabolic enzymes that breaks the structure of the phospholipids of cell membranes during ischemia and reperfusion, kinases (protein kinase C, protein tyrosine kinases, phospholipase, lipoxygenase, cyclooxygenase), RNA and DNA polymerase, lactate dehydrogenase and many others that determines its membrane-stabilizing action. Membrane effect of quercetin manifested in the ability to inactivate free radicals to inhibit formation of superoxide radicals, increase the effectiveness of antioxidant protection.

Corvitin has vasodilating effect by reducing the concentration of arachidonic acid and leukotriene C4, which is a strong vasoconstricting effect, degrade coronary blood flow [4].

Quercetin is also inhibits platelet aggregation, the formation of thromboxane B4 which exerts its antithrombotic effect [5]. Results of clinical and experimental studies demonstrate the therapeutic efficacy of quercetin in myocardial infarction and in acute ischemic stroke [6, 7].

Therefore, corvitin has a multimodal spectrum of pharmacological effects: antioxidant, antihypoxant, anti-inflammatory, membrane-stabilizing, activates energy-saving function of mitochondrial. Effects of quercetin on the main factors of ischemic cascade of biochemical determines prospects of its application in the treatment of vascular diseases of the heart and brain. Efficacy and safety of quercetin was evaluated in the works of Parkhomenko A. N. et all, Vynychuka S. M., Prokopova M. M. [6, 7].

Purpose (Purpose)

The aim of our study was to determine the activity of prooxidant and antioxidant processes in the periodontal tissue in the formation mechanisms of adrenalin damage of myocardial and experimental periodontitis and their correction with corvitin.

Material and methods (Materials and Methods)

The experiments were performed on 54 nonlinear white male rats weighing 0,17-0,21 kg, which were divided into six groups (9 animals in each). The First - control, second, third, fourth and fifth - a group of animals with adrenalin damage of myocardial (ADM) during the course of experimental periodontitis (EP) before Corvitin correction according to the 1st, 7th, 10th and 17th days of the experiment and the sixth group - animals with adrenalin myocardial damage during the course of experimental periodontitis after adjustment Corvitin, which was administered intraperitoneally at a dose of 40 mg / kg body weight of animals from the 10th to 17th day of the experiment. Acute myocardial injury by adrenaline was modeled by a single intraperitoneal administration of epinephrine hydrotartrate 0.18% ("Darnitsa", Ukraine) at the rate of 1 mg / kg, by the method of O. Markova [8]. Reproduce the model of experimental generalized paradontitis by the method of Sukmanskoho O. I., Makarenko O. A. through a modified diet for rats that contains soft consistency with high in carbohydrates. [9] The animals were taken out of the experiment on the 1st, 7th, 10th and 17th days according to the groups under nalbuphin anesthesia in dose of 182 mg / kg of body weight of rat [10] and periodontal tissue were taken for biochemical research. This experiment was conducted according to the principles of bioethics in accordance with the provisions of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 1986), Council Directive 2010/63/EU, the Law of Ukraine № 3447-IV «About the protection of animals from cruelty» general ethical animal experimentation adopted the first National Congress on bioethics of Ukraine of Danylo Halytsky Lviv National Medical University (protocol number 4 on January 18, 2017 g.). The content in periodontal tissues diene conjugates (DC) determined by the method of Gavrilov V. H. [11], malonic dialdehyde (MDA) - the method of Korobeynikova E. N. [12], superoxide dismutase (SOD) - method Fried R. [13], catalase (CT) – by the method of Holmes R. [14], ceruloplasmin (CP) - method Kolb V. H., Kamyshnikova V. C. [15]. The obtained digital results were statistically analyzed by Student’s method.

Results and Discussion

Results of biochemical studies have established that on the 1st, 7th, 10th and 17th days of the formation of adrenalin myocardial injury (AMI) during the course of experimental periodontitis (EP) without correction of corvitin, in periodontal tissues observed increase content of diene conjugates (DC) respectively by 54,5% ($p < 0,05$), 72,7% ($p < 0,05$), 90,9% ($p < 0,001$), 109,1% ($p < 0,001$) against group of intact animals. Determination of another

indicator of lipid peroxidation - malondialdehyde (MDA) in periodontal tissues showed a similar direction of violations. This indicator increased by 41,6% (p <0,05), 50,0% (p <0,05), 66,7% (p <0,05), 83,3% (p <0,05) respectively on the 1st, 7th, 10th and 17th days of AMI and EP relative control, wich indicating activation of free radical oxidation (FRO). Thus, the study of FRO markers in the dynamics of the cardiomyopathy formation and experimental periodontitis showed a gradual stimulation of lipoperoxidation processes. It is known that excessive formation of LPO products gradually depletes the antioxidant system. Along with the study of prooxidant system disorders studied particularities of changes in antioxidant protection for activity of superoxide dismutase (SOD), catalase (CT), ceruloplasmin content (CP) in periodontitis in the dynamics AMI and EP without correction. It is found that on the 1st, 7th, 10th and 17th days of AMI and EP the SOD activity decreases by 14,6% (p <0,05), 24,4% (p <0, 05), 46,3% (p <0,05), 54,9% (p <0,001) accordingly to the control. Changes also occur with the activity of CT and CP content that is reduced as well as SOD, gradually, on the 1st, 7th, 10th and 17th days of the combined pathology experiment by 23,9% (p <0,05), 41,2% (p <0,05), 45,1% (p <0,05), 56 9% (p <0,001) and 40,0% (p <0,05), 50,0% (p <0,05), 58,3% (p <0,05), 66,7% (p <0,001) relative to the first group of animals. (Diagram 1). Also the results of biochemical studies on the 17th day of formation of adrenalin myocardial injury (AMI) and experimental periodontitis (EP) with correction of corvitin showed decrease in the content of periodontal diene conjugates (DC) by 26,1% (p <0,05).

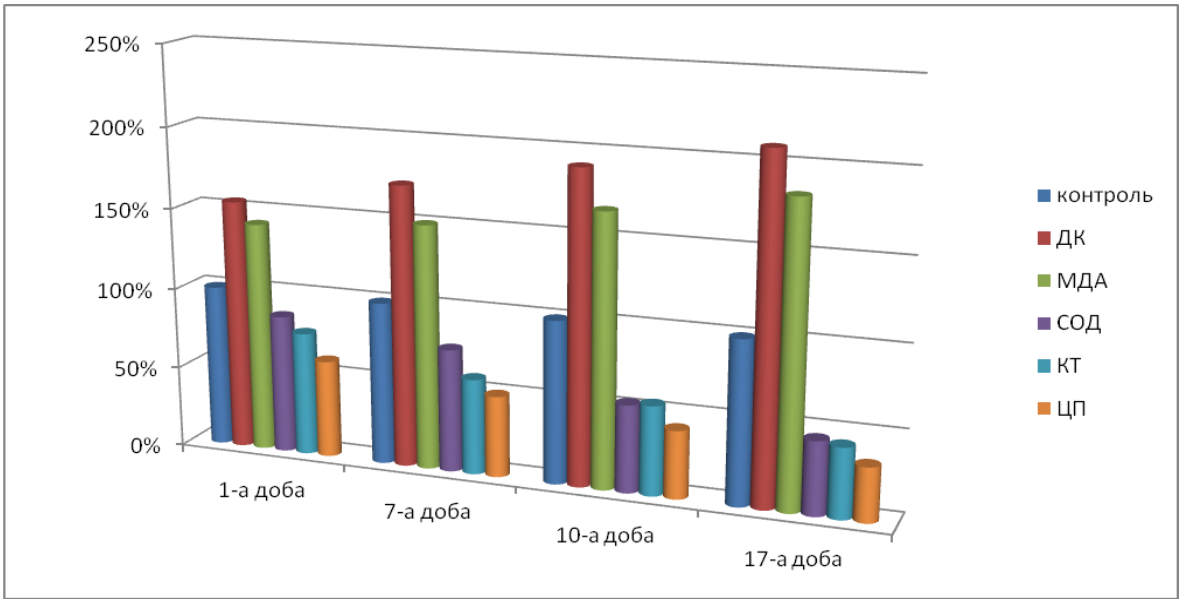

Fig. 1 Level of activity of prooxidant and antioxidant processes in the periodontium at AMI and EP without correction with corvitin. (% compared to control)

(Diagram 2). Malone dialdehyde (MDA) - by 31,9% (p <0,05), respectively on the 17th day of AMI and EP with the introduction of corvitin relatively group of animals without correction on the 17th day. At the same time, the activity of superoxide dismutase (SOD), catalase (CT) and ceruloplasmin content (CP) in the periodontium of AMI and EP with correction of corvitin by 17th day increased to 70,3% (p <0,05), 63,6% (p <0,05), 87,5% (p <0,05) respectively, relative to a group of animals with combined pathology, on the 17th day of the experiment without correction of quercetin. (Diagram 2).

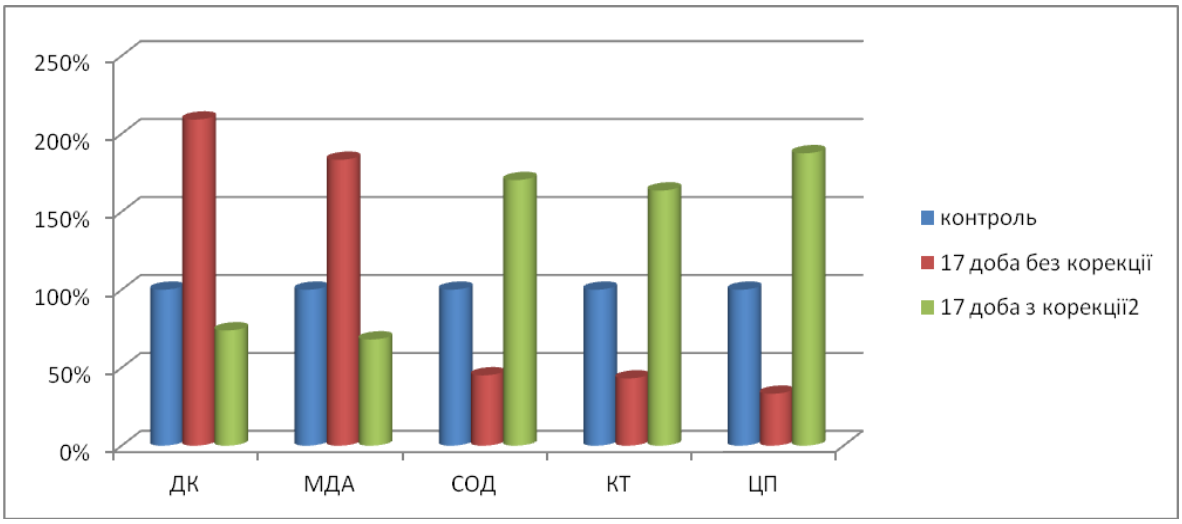

Diagram 2. Level of activity of prooxidant and antioxidant processes in the periodontium at AMI and EP compared with groups of animals on the 17th day of the experiment as a percentage without correction and after correction of corvitin

Conclusions

Given the above data, we can conclude that with combined pathology of experimental periodontitis and adrenalin myocardial injury, the activity of prooxidant and antioxidant processes occurs in the direction of gradual depression of antioxidant protection against the growing LPO, especially from the 10th to the 17th day of formation of pathology, that Indicating the development of oxidative stress. After entering corvitin at the condition of combined pathology, the indicators are different - markers FRO (DC and MDA) and AOS (SOD, CT, CP) in periodontitis showed a decrease in LPO and increased enzyme activity of AOS, that indicating of the antioxidant and cardioprotective properties.

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