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CATECHOLAMINES AND THEIR METABOLITES IN REGULATION OF HEART ENZYMS

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Abstract. Currently in cardiology it is important establish mechanisms of adaptation disorder processes observed during hyperactivity sympathetic nervous system, to develop adequate methods of treating cardiovascular diseases. By nature, sympathetic hyperactivation is accompanied by increased formation of enzymatic and non-enzymatic products enzymatic metabolism of catecholamines, which can change the activity of mitochondrial and cytosolic enzymes, contributing to changes in the level bioenergetic adaptation, antioxidant systemprotection and synthesis of intercellular modulators, such as AMP and adenosine [1]. It is known that catecholamines adrenaline and norepinephrine increases blood glucose levels by stimulating glycogenolysis and gluconeogenesis by activation of β- and α-receptors of hepatocytes, through enhancing glucagon secretion and by inhibiting insulin-mediated glucose uptake into muscle and adipose tissue. Adrenaline activates lipase adipose tissue, increasing the level of free fat acids that undergo β-oxidation in mitochondria. Adrenaline increases the speed of the main metabolism with a subsequent increase in thermogenesis, induces mitochondrial biogenesis and increases aerobic capacity of tissues, changing the content mitochondrial proteins. Causes an increase release of H2O2 and other reactive oxygen species due to stimulation of mitochondrial respiration during simultaneous decrease in the activity of antioxidants enzymes [2]. Active forms in living systems oxygen play a dual role - they can cause oxidative damage and tissue dysfunction and serve as molecular signals that activate stress reactions. Mitochondria, thanks to their ability to produce free forms oxygen, play an important role in oxidative tissue damage, while at the same time providing protection against excessive tissue dysfunction [5].

Key words: Catecholamines, adrenaline, enzymes of mitochondria and cytosol of cardiomyocytes.

According to modern ideas, exchange catecholamines are carried out in different ways, based on which lie the mechanisms influencing the manifestation of their physiological activity. The most important in functionally are the enzyme-catalyzed methylation pathway catecholamine-O-methyltransferase (COMT), monoamine oxidase (MAO) catabolism catecholamines. Moreover, under certain conditions oxidation of adrenaline can occur via the quinoid pathway pathways with the formation of quinones to adrenochrome [4]. Under conditions of spontaneous release catecholamines adrenaline, exposed to COMT, which is O-methylated extraneuronal. Inhibitory effect on COMT has the polyphenol quercetone, flavonoids and even phosphopyridoxal. COMT inhibitor pyrogallol promotes the accumulation of adrenaline in the adrenal glands and increased urinary norepinephrine excretion [6]. Norepinephrine is more affected monoamine oxidase [8]. But, released by the nervous endings or when administering sympathomimetics, norepinephrine may also be affected COMT. In turn, catecholamines through beta-adrenergic receptors without the participation of cAMP can have activating effect on COMT [3]. There are two types of mitochondrial monoamine oxidases - A and B types of MAO [7]. Aldehydes, formed during oxidative deamination catecholamines, can accelerate the apotomic pathway oxidation of glucose due to activation of glucose-6- phosphate dehydrogenase and transketolase, as well as reduce cardiac gamma-amylase activity [5]. In a number cases, aldehydes can react condensation with non-deaminated molecules monoamines, having a hepatotoxic effect [8]. With immobilization stress against the background of high catecholamine levels revealed

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transformation of MAO to adenyl deaminase [6]. Close localization of MAO with enzymes of the mitochondrial respiratory chain showed the presence of a functional relationship between these biocatalytic systems [4]. Studies on quinoid oxidation catecholamines and the biological significance of the resulting products served as the basis for creating the concept of functional significance of exchange of exchange regulators [7]. During quinoid oxidation of catecholamines the corresponding quinones are formed, one of which is adrenochrome. It was found [3] that perfusion isolated rat heart with Krebs-Henseleit solution containing adrenochrome (25 or 50 mg/l) caused contractile failure and necrosis myocardium. Beta receptor blocking drugs propranolol and practolol effectively protect the heart from necrotic damage caused adrenochrome, and partially prevent contractile insufficiency. Quinoid oxidation catecholamines can be catalyzed by many enzymes (cytochrome c oxidase, catechol oxidase, ceruloplasmin). Oxidation of norepinephrine in under oxygen-free conditions, the reductone complex promotes: adenine-Cu++ [9]. In the presence of peroxidase aminosine accelerates the oxidation of catecholamines to corresponding aminochromes [3] and forms with adrenochrome complex is more stable than acetylcholine-adrenochrome complex [8]. Seduxen (diazepam), phenothiazine drugs reduce activity of this enzyme [9]. The first indication of the presence of a specific the enzyme that oxidizes adrenaline into adrenochrome was implemented [3]. Enzyme that oxidizes norepinephrine to noradrenochrome in the presence acetylcholine, hydrogen peroxide and cyanide, was found in the blood serum of patients with schizophrenia [2]. Working in an innovative psychiatric environment, Hoffer A and Humphrey F. formulated in 1952 adrenochrome hypothesis of the biogenesis of schizophrenia [6]. It was found that with thyroid toxicosis, with myocarditis, the level of quinoids increases products in the heart, and when the temperature rises body there is an increase in the excretion of adrenochrome c urine [4].Adrenochrome and adrenoxyl have hemostatic and hemolytic effects . It is known that activation of the sympathoadrenal system aggravates the course of coronary disease hearts. And elevated levels of catecholamines serve risk factor for recurrent infarction myocardium and sudden death. With sympathetic hyperactivation, the most common sinus tachycardia, functional extrasystole, cardialgia, episodic increase blood pressure, hyperhidrosis and others vegetative manifestations. To weaken these symptoms in cardiological practice preference is given to cardioselective beta blockers, not having internal symptomatic activity. These requirements, first of all, Metoprolol answers [6]. Metoprolol, blocking 1- in low doses adrenergic receptors of the heart, reduces stimulated catecholamines form a cyclic adenosine monophosphate (3`5`AMP) from adenosine triphosphate (ATP), reduce intracellular Ca2+ current, and is used in the treatment of ischemic heart disease, heart rhythm disturbances [7]. Researchers found that in the heart administration of adrenaline increases the activity of AD, AMPD, catalase and the AD+AMPD/5'H ratio, increases MDA level. Adrenergic blocker metoprolol at a dose of 25 mg/kg increases the activity of AD, AMPD and increases AD+AMPD/5'H ratio, reduces GR activity, GPO, catalase and MDA and DC levels. There are reports [8] that drugs beta receptor blockers such as propranolol and Practolol effectively protects the heart from necrotic damage caused by metabolites quinoid oxidation of adrenaline. It has been established [7] that the administration of metoprolol in a dose 25 mg/kg reverses the effects of adrenaline in the heart by studied indicators. Leads to activation of AD, AMPD and 5'H, reduces the amount of MDA and DC and is adequate to this enzyme activity decreases antioxidant protection activity of GR, GPO and catalase, which indicates a decrease metoprolol peroxidation processes [3]. Where in decrease in the ratio of enzyme activities AD+AMPD/5'H is directed towards maintenance the required level of adenosine, which has vasodilator and other effects on cardiomyocytes and vascular smooth muscle. Thus, in the heart, β1-blockade metoprolol reduces the peroxidation process, caused by the administration of adrenaline, and adequately to this antioxidant enzyme activity decreases protection. The data obtained reveal

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some features of the metabolic effects of β1- adrenergic blocker metoprolol during administration adrenaline for animals.

Conclusion Non-uniform effects of catecholamines on enzymes of mitochondria and oxidative phosphorylation in cardiomyocytes, associated superimposition on their effects of metabolites of quinoid and monoamine oxidase pathway for the conversion of adrenaline and norepinephrine. This ability of metabolites catecholamines along with whole molecules catecholamines change enzyme activity respiratory chain is the main point in regulation of the process of tissue respiration and oxidative phosphorylation. Metoprolol, as a β1-blocker, weakens severity of the body's stress response animals caused by the administration of adrenaline. For correction of enzyme dysfunctions antioxidant defense and purine metabolism nucleotides observed with hyperadrenalineemia and with oxidative stress of various origins, you can use the β1-blocker metoprolol.

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