BIOLOGICAL SCIENCES

ATF-LONG AS AN ALTERNATIVE FOR PROHIBITED PREPARATORS: EFFICIENCY AND SAFETY OF ITS APPLICATION IN SPORT

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Nowadays, due to the high frequency of sudden coronary death in athletes, the problem of preventing cardiovascular overstrain and its main manifestations – hypertrophic cardiomyopathy – is acquiring special significance. For representatives of cyclic sports, in which most often there is an overstrain of the heart, eccentric myocardial hypertrophy can be considered as typical. On the contrary, concentric myocardial hypertrophy is typical of sports with a predominant expansion of forces and provide a share of static loads [1]. With an electrocardiographic study, it is easy enough to diagnose the main signs of cardiac overstrain and prescribe pharmacological products for its correction. More reasonable and logical is the use of such products that help not only to maintain the functional capabilities of athletes, but also to ensure proper health and quality of life.

Thus, in sports, especially top sports, today we are talking about the systematic use of myocardial protection products – cardioprotectors. However, many of these pharmacological agents that are widely used in general cardiological practice for moderate manifestations of myocardial dysfunction – in particular, all preparations of trimetazidine and meldonium – cannot be used in top sports due to the prohibitions of WADA that entered into force during 2015-2016. We believe that these prohibitions are not entirely justified, first of all, according to the «harm / benefit» criterion [2], which should be guided in such situations, but this topic is the subject of another discussion.

From a metabolic point of view, overstrain and the subsequent formation of a pathological sports heart can be accompanied by numerous and multidirectional biochemical shifts [4]. According to the views of leading modern sports cardiologists [6], metabolic shifts that entail the development of overwork, overtraining and overstrain may include biochemical changes in the body that are different in severity and direction. This implies the urgent

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need for the use of pharmacological means of myocardial protection in the dynamics of training athletes.

According to modern views, agents with a cardioprotective effect should affect at least, firstly, cellular metabolism; secondly, on the structure and function of cell membranes, preventing their irreversible damage during reperfusion; and thirdly, ionic homeostasis [5; 6]. Cardioprotectors are pharmacological agents for preventing disorders and optimizing heart function under normal physiological and pathological conditions. Unfortunately, in sport today, in our opinion, and in agreement with the views of other researchers, the use of cardioprotectors occurs haphazardly, without taking into account the main points of application of action, and the list of drugs used is quite narrow [7] and mainly comes down to metabolic agents [8; 9]. Therefore, it is understandable that the WADA ban on the use of the most widespread cardioprotective substances such as trimetazidine and meldonium, etc., which are metabolitotropic drugs, provoked a strong reaction among sports doctors.

Therefore, in sports medicine and sports pharmacology, the search for alternative ways to replace the aforementioned cardioprotectors with drugs approved for use in the practice of sports training does not stop today. The most widely used for the prevention and correction of overstrain in athletes are direct cardioprotectors, among which a special place is occupied by metabolic regulators in the myocardium. In turn, among them, interesting and promising from these positions are, first of all, pharmacological agents with an effect mainly on energy processes. This group includes those already banned during 2015-2016 preparations based on trimetazidine (trimetazidine, preductal MR, angio retard, trimexal, etc.) and meldonium (metamax, midolate, mildroxin, mildronate, vazoproMR, etc.), as well as panangin (seu asparkam), ATP-long, cratal, and another preparations of a similar type of action.

ATP-long occupies a special place in the effectiveness and almost complete absence of toxic effects among these drugs. This is the first original domestic drug in the group of direct cardioprotectors of a new class of drugs – multi-ligand coordination compounds with macroergic phosphates, which has a pronounced cardioprotective, energy-saving, membrane-stabilizing, metabolic effect in acute and chronic diseases of the cardiovascular system, as well as its overstrain and dysfunction in athletes. The drug was obtained by targeted synthesis, taking into account the results of numerous studies regarding the protective effect of ATP, amino acids, macrocells on organs and tissues during ischemia. ATP-long is synthesized in such a way that the macroergic phosphate ATP, magnesium ion, histidine amino acid and potassium ions that are part of it are coordinated so that the molecule is easily

integrated into various parts of metabolic processes, has an affinity for cell membrane receptors, which determines its multilateral pharmacological effect [10; 13]. Due to the original structure of the molecule, it has a pharmacological effect that is characteristic only for it and is not inherent in each of its chemical components (ATP, histidine, K +, Mg2 +), which allows the drug to have a corrective effect on various structures and functions on the systemic, cellular, subcellular and molecular levels. So, magnesium ions, which is a natural antagonist of calcium ions, provide a negative inotropic effect on the heart muscle, thereby reducing its oxygen consumption, reduce peripheral resistance by reducing the tone of smooth muscle structures of blood vessels; magnesium also inhibits deamination and dephosphorylation. Potassium ions support the osmotic and acid-base homeostasis of the cell, participate in providing a transmembrane potential difference, activate the synthesis of ATP, creatine phosphate. The amino acid histidine is a natural trap of free radicals, it inhibits lipid peroxidation, thereby protecting the structural components of membranes from oxidation and hydrolysis, preventing their degradation. Inorganic phosphorus formed after ATP hydrolysis, together with the imidazole ring of histidine, increase the capacity of the cell buffer, thereby ensuring a more stable preservation of the structural elements of the cell membrane under ischemic conditions [10]. The preservation of the cell's membrane structures occurs due to the fact that with an increase in cellular pH, the imidazole and phosphate groups that enter the microenvironment of the membranes will release protons, and with a decrease in pH, on the contrary, they will bind, and thus, the local pH around the membrane structures will be maintained within physiological values, despite changes in intracellular pH, thereby increasing the degree of preservation of cellular structures under conditions of hypoxia, including hypoxia load [11]. Due to the above factors, the ATP-long drug is more effective in a number of indicators than the well-known ATP disodium salt, which is currently used to treat a number of pathologies of the cardiovascular system [12-14].

ATP-long is the first tablet preparation in the world containing macroergic phosphate (ATP) in its structure and is available in the form of sublingual tablets in two doses – 10 mg and 20 mg of the active substance, which is very convenient for athletes in real training conditions. The use of ATP-long sublingually (under the tongue) allows you to get the primary effect in 20-30 seconds, which is almost equal in speed of the onset of action of intravenous administration of drugs. A great advantage, in comparison with other similar drugs, is the absence of toxicity and side effects, which is inherent in metabolitotropic substances [15]. The results of in-depth experimental studies substantiated [16], and data on the practical use of ATP-long showed a very high activity of this drug in athletes [17].

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