JOURNAL OF COMPLEMENTARY MEDICINE RESEARCH

RESEARCH ARTICLE

Optimization Of Medical and Environmental Services Using TES Therapy

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ABSTRACT

Experimental studies have shown the presence of antihypoxic, decongestant and immunomodulatory effects of endogenous opioid peptides (OP), as well as their effect on the synthesis of pituitary hormones, these effects are largely due to an increase in the blood content of opioid peptides ((3-endorphin and met-enkephalin), which are released when the structures of the antinociceptive system are activated.

Studying the effect of TES therapy on reparative processes in patients with myocardial infarction and establishing that this accelerates the formation of postinfarction scar and the development of compensatory hypertrophy of extrainfarction parts of the myocardium, increases the number of cases of heart failure and the number of relapses of anginal pain, improves the general state of hemodynamics. However, until now, the question of the possibility of using TES therapy to correct the imbalance of cytokines in the acute period of myocardial infarction, which is an important pathophysiological factor in the development and course of acute cardiac pathology, remains open.

KEYWORDS:
biodiversity, ecosystem, medical ecology, TES-therapy, green economy, monitoring, innovation, cluster, screening, investments, recreation, ecotourism.

ARTICLE HISTORY:
Received April 15, 2021
Accepted April 11, 2021
Published May 16, 2021

DOI:
10.5455/jcmr.2021.12.02.04

VOLUME: 12
ISSUE: 2
ISSN: 2146-8397

INTRODUCTION

In the Russian Federation, morbidity and mortality rates from cardiovascular diseases have an alarming scale – 56,4% of all deaths.

At the working age (from 25 to 64 years) 38% of deaths are caused by diseases of the circulatory system, while the contribution to total mortality of men (36%) and women (41%) is almost the same. These are the highest values in the world. One of the most common diseases of the cardiovascular system in adults is ischemic heart disease (IHD) [1,11].

The prevalence of coronary heart disease in the second half of the 20th century has penetrated the dimensions of an epidemic, although some of its manifestations have been known for a long time. The widespread occurrence of this disease in people of the most working age has turned coronary heart disease into an important medical and social problem.

The most common complication of coronary heart disease is myocardial infarction (MI). Mortality from myocardial infarction is still high and amounts to 39% of the total mortality rate in Russia. During the first year after myocardial infarction, death is recorded in 6,5 - 11% of patients, and about 50% of them die suddenly. More than 300 cases of myocardial infarction for every 100 thousand inhabitants are registered annually in large cities of the Russian Federation, more recently it was considered a disease of the elderly, but in recent years there has been an alarming trend - myocardial infarction is rapidly getting younger, in 2011 alone, 180000 cases were recorded in the Russian Federation acute myocardial infarction [2,16].

Acute myocardial infarction (AMI) is one of the main causes of

death - 39% of the total, and in the first 15 minutes after the onset of the disease, 30-40% of patients die. About the same - in the next two hours.

METHODOLOGY

It seems promising to use a comprehensive assessment of the concentration of a number of cytokines in predicting the course of acute coronary events.

Thus, the preliminary implementation of TES therapy limits the excessive activation of anaerobic processes proceeding with the maximum use of glycogen stores, and thereby protects the cardiomyocyte from the negative effects of under-oxidized lactic and pyruvic acid products.

The aim of this study was to use TES-therapy to improve the state of the myocardium by restoring the cytokine status and the level of P-endorphins in acute myocardial infarction.

RESULTS

The development of acute myocardial infarction entails the emergence of a systemic and local inflammatory reaction, activation of acute phase proteins (APP), in particular - components of the complement system, C-reactive protein (CRP), orosomucoid, al-antitrypsin, kallikrein, transferrin, kinins. The production of C-reactive protein is regulated by cytokines, including interleukin-6 (IL-6), ipterleukin-ip (IL-ip), and tumor necrosis factor-a (TNF-a). Thus, it is of great interest to study specific markers of inflammation - cytokines, which can be more prognostically significant in determining the processes associated with the destabilization of the course of vascular atherosclerosis. Some of them, for example ipterleukin-ip, interleukin-6, tumor necrosis factor - a, have pro-inflammatory properties, the action of others, in particular interleukin-10 (IL-10), is associated with anti-inflammatory reactions, showed a significant role of IL-ip, IL-6, interleukin-8 (IL-8), interleukin-10 IL-10, tumor necrosis factor -a in the progression of atherosclerosis, in the processes of destabilization of atherosclerotic plaques, in assessing the risk of sudden death, the development of acute coronary syndrome in patients with coronary heart disease, especially with unstable forms of the disease [3,17].

When staining with procyon BS on micropreparations of the hearts of animals of groups I and II, staining of the cardiomyocyte was observed mainly of medium intensity, but there were cardiomyocytes with a high intensity of staining.

On micropreparations of the hearts of animals of group III, intensely stained cardiomyocytes predominated, however, there were single cardiomyocytes with an average staining intensity, this indicates an increase in the content of histidine and lysine in comparison with the control.

On micropreparations of the hearts of animals of groups IV and V, staining of cardiomyocytes of mainly medium intensity was detected, but cardiomyocytes with a high intensity of staining were present. With ischemic myocardial damage, even at early stages, there was a decrease in the content of histidine and lysine in cardiomyocytes [4,10].

Preliminary TES therapy was accompanied by a significant decrease in the degree of damage to the cardiomyocyte (cardiomyocytes with a high content of the above-mentioned amino acids are rare), which makes the histological picture almost identical to the control.

With the reaction of deamination with procyon on micropreparations of the hearts of animals of groups I and II, the staining of the cardiomyocyte was predominantly of high intensity.

On micropreparations of the hearts of animals of group III, staining of the cardiomyocyte of medium intensity was revealed. A decrease in the intensity of staining indicates a decrease in the content of histidine in comparison with the control.

On micropreparations of the hearts of animals of groups IV and V, the staining of the cardiomyocyte was predominantly of high intensity and there were cells with very intense staining, which indicates an increase in the content of histidine in comparison with the control group and the group of acute myocardial infarction.

DISCUSSIONS

Thus, TES therapy during the acute period of acute myocardial infarction, as well as before obtaining a model of this pathology, significantly reduced the damage to the cardiomyocyte compared with the control group.

The results of the study of proinflammatory cytokines are presented in table 1 and fig. 1.

Table 1: Indicators of proinflammatory cytokines in the study groups

Group/Indicator	TNF-a pg/ml	IL-ip pg/ml	IL-6 pg/ml
Group I (control)	5,00±0,32	6,8±1,60	1,20±0,37
Group II (false-positive)	12,97±4,07*	29,34±3,16*	3,23±0,46*
Group III (with AMI)	17,67±4,06* +	+68,37±4,56*+	3,00±0,94*
Group IV (AMI+TEStherapy)	5,53±0,88**	56,12±2,12**	1,50±0,69**
Group V (TES-therapy+AMI)	6,92±0,98**++	9,17±3,27**++	1,62±0,49**

Note:
* - p<0,05 compared with group I (control),
** - p<0,05 compared to group III,
+ - p<0,05 compared to group II,

++ - p<0,05 compared to group IV.

We assessed the level of interleukin 10, interleukin 6 and tumor necrosis factor - and during the same period, these cytokines in the acute period of myocardial infarction are actively produced by cardiomyocytes and even by endothelial cells of the vascular wall of coronary arteries. An increase in the level of proinflammatory markers correlates with the severity of left ventricular dysfunction and has a high prognostic value.

The levels of IL-Iß, IL-6 and TNF-a in the dynamics of acute myocardial infarction correlate with the degree of damage to the heart muscle according to ECG data.

The level of TNF-a significantly increased in the group of sham-operated animals 2,6 times compared with the control. Its increase, by 3,5 times, also took place in animals of group III with acute myocardial infarction (p<0,05) [5,12].

At the same time, significant damage to the structure of the myocardium was observed, glycogen stores in the myocardial tissue were depleted, the content of histidine and lysine increased in the myocardium, this was accompanied by an increase in the level of markers of myocardial necrosis and the development of severe oxidative stress.

It is known that tumor necrosis factor -a plays an important role in the initiation of inflammatory processes, including those developing after ischemic injury.

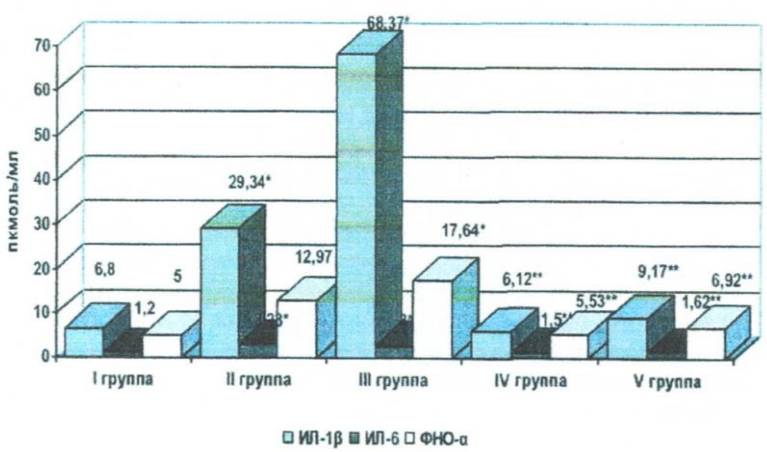

Fig.1: The content of proinflammatory cytokines in the blood serum of different rpjTin animals.

Note:
* - reliable in relation to group I,
** - reliable in relation to group III

Normalization of the level of tumor necrosis factor -a, after treatment of myocardial infarction occurs only on day 21. tumor necrosis factor-a initiates the expression of cell adhesion molecules on the endothelium, activates MF, Nf, enhances the secretion of prostaglandins, has a chemotactic effect on various cells (in particular, a cardiotoxic effect) and causes the synthesis of a number of acute phase proteins.

With the ability to induce apoptosis, tumor necrosis factor -a causes generalization in the cell membrane of ROS, O2, and NO. TNF-a is able to suppress cardiomyocyte contractility, lower blood pressure and promote the development of pulmonary edema. It is impossible not to take into account the ability of TNF-a to enhance the expression of Fas-antigen on target cells, thereby preparing them for programmed cell death - apoptosis. In animals of groups IV and V after TES therapy, the content of TNF-a was significantly (p<0,05) lower than in animals of group III. In animals of group IV, where TES-therapy was used in the acute period of acute myocardial infarction, the level of tumor necrosis factor -a did not exceed the indicator of the control group of animals.

In animals of the V group, where TES-therapy was used before the modeling of acute myocardial infarction, the level of TNF-a did not return to the indicator of the control group of animals and was 1,3 times higher than in the animals of the IV group. Thus, analyzing the dynamics of TNF-a in different groups of animals, it can be concluded that the use of TES-therapy in the acute period of acute myocardial infarction has a pronounced anti-inflammatory effect.

Carrying out TES-therapy with a prophylactic purpose (for animals of group V) reduces the nature of ischemic damage, according to histochemical studies.

Thus, TES therapy has a pronounced cardioprotective effect.

IL-Iß - is the main mediator of the development of a local inflammatory reaction in any type of inflammation, is produced by inflammatory cells, causes the release and expression of other inflammatory mediators of both cellular and plasma origin (cytokines, growth factors, chemokines, bioactive lipids, metalloproteinases and ROS, adhesive receptors), proliferation of resident cells.

In addition, interleukin-f stimulates the release of leukocytes from the red bone marrow, also activates lymphocytes and Nf.

Overproduction of IL-1p at the local level leads to tissue

destruction; at the systemic level - to a catastrophic violation of hemodynamics and often - to death. It was shown that the increased IL-Iß indices in the early stages of myocardial infarction were associated with an increase in the incidence of early complications of myocardial infarction (cardiogenic shock, pulmonary edema). IL-Iß significantly ($p<0,05$) increased in group II of sham-operated animals in relation to the control group. In animals of this group, it increased 4,0 times as compared with animals of group I. This increase is associated with the activation of newly synthesized inflammatory mediators, which include the parameters studied by us, due to tissue damage (surgery).

The content of IL-Iß increased more significantly ($p<0,05$) in rats in group III with simulated acute myocardial infarction. The level of this cytokine increased 10,0 times compared with the control group I animals and 2,3 times compared with the animals of group II. This indicates a parallel initiation of aseptic inflammation (along with ischemia). At the same time, there was a significant damage to the structure of the myocardium. The stores of glycogen in the myocardial tissue were depleted, the content of histidine and lysine increased, which indicates significant damage to the myocardium. This is accompanied by an increase in the level of markers of myocardial necrosis and the development of severe oxidative stress, that a significant drop in the left ventricular ejection fraction was accompanied by a high content of interleukin IL-Iß.

This was explained by the ability of interleukin IL-Iß to weaken the effect of catecholamines on cardiomyocytes, that the content of the studied pro-inflammatory mediators has a similar dynamics in animals of groups IV, V. In animals of these groups, where TES therapy was used, the level of IL-Iß in the blood was significantly ($p<0,05$) lower than in animals of group III (modeling of acute myocardial infarction).

Moreover, in animals of group IV, in which acute myocardial infarction was first modeled, and then TES therapy was carried out, the level of interleukin IL-Iß corresponded to that in animals of control group I. At the same time, there was a decrease in the severity of myocardial damage. The level of glycogen in the cardiomyocyte remained almost at the control level. At the same time, a significant decrease in the intensity of oxidative stress was noted. This indicates the feasibility of TES-therapy in the acute period of myocardial infarction. It appears to have a pronounced anti-inflammatory effect. In animals of group V, the level of IL-Iß was also significantly ($p<0,05$) lower than in animals of group III. However, it slightly exceeded that in the control group (1,3 times) and was 1,5 times higher than in the animals of the IV group.

At the same time, more pronounced (in comparison with group IV) damage to the cardiomyocyte structure remained. The level of markers of myocardial necrosis during this period is increased. Consequently, preliminary stimulation of the opioidergic link of the stress-limiting system, prior to the creation of a model of acute myocardial infarction, also has a cardioprotective effect due to myocardial preconditioning [6,13].

IL-6 is absent in blood serum under normal physiological

conditions, but its amount in serum rises sharply with many microbial invasions, immunological reactions, inflammation or tissue damage. The influence that IL-6 has on the progression of the inflammatory process is quite complex, because it has both pro- and anti-inflammatory effects, as well as the effect of negative feedback in relation to IL-lß and tumor necrosis factor -a. The production of IL-6 begins to increase in myocardial infarction much later than IL-lß and tumor necrosis factor-a. IL-6 contributes to both exacerbations of chronic and chronicity of acute inflammatory processes. Systemic effects are characteristic of IL-6. It can mediate regulatory links between the immune system, bone marrow, neuroendocrine system, liver and other tissues. The role of IL-6 as an anti-inflammatory cytokine is due to its inhibitory effect on the production of IL-1 and tumor necrosis factor-a and activation of the production of RAIL-1 and IL-10.

The maximum concentration of IL-6 and TNF-a, observed in patients with no decrease in plasma concentrations of TNF-a and on day 1 of cardiogenic shock, indicates the progression of myocardial infarction, its complication by cardiogenic shock, an increase in the inflammatory response and an unfavorable prognosis of the disease. IL-6 enhances the production of CRP by the liver during the acute phase of myocardial infarction, which can lead to inhibition of the synthesis of NO, which has a pronounced anti-inflammatory activity, and thus unhindered increase in the factors of aggression in the postinfarction period. A direct correlation was found between the level of IL-6 and the unfavorable outcome of myocardial infarction [7,14].

The content of IL-6 increased in animals of group II of sham-operated animals, it increased 2,8 times and was significant in relation to animals of group I ($p<0,05$). This is due to the surgical trauma. In animals of group III, the level of IL-6 was the same as in animals of group II and remained significant ($p<0,05$) in relation to animals of control group I. An increase in the level of IL-6 by 2,9 times during the modeling of metabolic myocardial infarction occurred only on the 3rd day. An increase in the level of IL-6 in animals of group III was accompanied by significant damage to the structure of the myocardium. The reserves of glycogen in the myocardial tissue were depleted, the content of histidine and lysine increased, which indicates significant damage to the myocardium. In animals of group IV, the level of IL-6 corresponded to the level of this indicator in animals of the I control group. Its content was 2,0 times lower than in the animals of group III. Thus, TES therapy during the acute period of acute myocardial infarction had a pronounced anti-inflammatory effect. In animals of group V, the level of this marker of inflammation was also significantly ($p<0,05$) reduced in relation to animals of group III. This confirms the effectiveness of TES therapy, both in the acute period of AMI,

and preliminarily.

The results of the study of anti-inflammatory cytokines are

presented in table 2, fig. 2

Table 2: Indicators of anti-inflammatory cytokines in the study groups

Group/ Indicator	RAIL-1 pg/ml	RAIL-1 IL-1 conv. units	IL-10 pg/ml.	PVI (IL-1 ß/IL-10) conv.units	TNF-a/IL-10 conv.units
I (control)	45,02±2,61	6,60±1,2	6,03±0,51	0,19±0,06	0,79±0,09
II (falsely operated)	1,10±0,21*	0,04±0,005*	13,22±1,13*	0,24±0,08	0,98±0,08
III AMI	6,02±1,32*	0,09±0,007*	1,78±0,56*	1,68±0,09*	10,39±1,8*
IV AMI +TES	16,19± 5,1**	2,70±0,9**	17,46±2,73**	0,09±0,05**	0,32±0,06**
V TES + AMI	13,04±5,07**	1,40±0,4**	14,70±7,08**	0,11±0,04* *	0,39±0,07**

Note:

* - p < 0,05 compared to the 1st control group,
** - p < 0,05 compared to group III.

IL-10 is an important anti-inflammatory cytokine.

It is produced by T-helpers 2 (Th2) and can be considered as an antagonist of a number of other cytokines. It suppresses the production of all pro-inflammatory cytokines, IGF-y, the proliferative response of T cells to AH and mitogens, and also suppresses the secretion of IL-Iß, TNF-a and IL-6 by activated monocytes. As a result, it promotes the development of a humoral immune response, causing the body's resistance. The main effect of IL-10 is inhibition of the secretion of IL-lß, IL-6, IL-8, IL-12, TNF-a, free radicals O2, reactive nitrogenous mediators and PGE2. With complicated myocardial infarction, the level of IL-10 is 1-14 days higher than with uncomplicated myocardial infarction. By the 21st day, a decrease in its concentration is noted. While the group of patients with uncomplicated course of myocardial infarction continues a rapid increase in the concentration of this anti-inflammatory cytokine [8,11].

When simulating acute myocardial infarction (animals of the III group), the content of IL-10 in the blood serum significantly decreased by 3,4 times compared with the animals of the control group (p<0,05). This indicates the severity of the aseptic inflammatory response in conditions of ischemic myocardial damage. In animals of group IV, in which TES therapy was used during the acute period of acute myocardial infarction, this indicator was significantly increased (9,8 times) compared with animals of group III. This was associated with a decrease in the severity of the morphological consequences of myocardial hypoxia. In animals of group V, where TES therapy was carried out previously, the content of IL-10 was 8,2 times higher than in animals of group III. The production of IL-10 is usually associated with a simultaneous change in the TNF-a content, however, the IL-10 content can also increase independently of the changes in the TNF-a level.

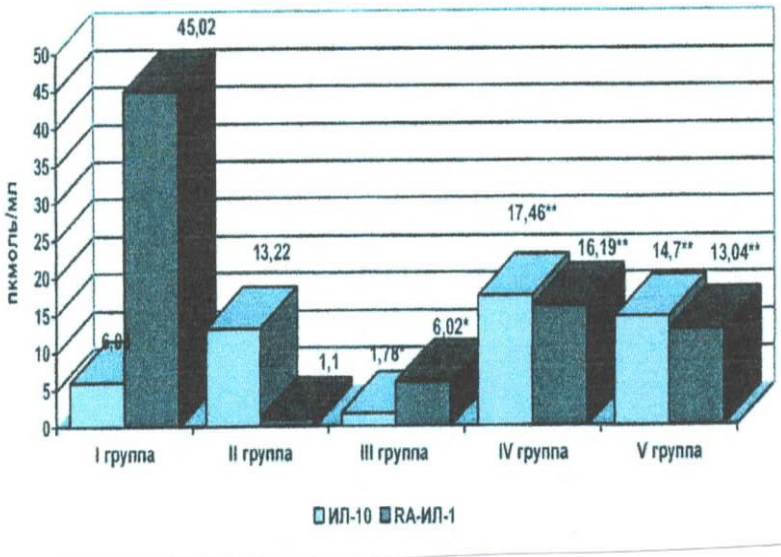

Fig.2: The content of anti-inflammatory cytokines in the blood serum of different groups of animals.

Note:
* - reliable in relation to group I,
** - reliable in relation to group III.

The TNF-a / IL-10 ratio in the simulation of acute myocardial infarction (group III of animals) increased significantly - from 0,79 (in the control group of animals) to 10,39 (13,2 times). This was due to a significant increase in the level of TNF-a with a simultaneous decrease in the content of IL-10. These

shifts indicated severe myocardial damage with a drop in ejection fraction. When using TES therapy, the TNF-a/IL-10 ratio was lower than the control level (0,39 versus 0,79), since the TNF-a content returned to normal, and the level of IL-10 exceeded the control level by 2,9 times. This was associated with less degree of myocardial damage [9,15].

The IL-Iß receptor antagonist (RAIL-1) is an important natural anti-inflammatory protein, the absence or low content of which plays a key role in the pathogenesis of a number of diseases. Quantification of the level of the RAIL-1 receptor antagonist is of great importance in assessing the immune status of an organism. In healthy tissue, RAIL-1 receptor antagonist is synthesized to prevent inflammatory reactions mediated by IL-Iß. The absence of an interleukin-1 receptor antagonist predisposes to increased local production of IL-Iß and its effects. An interleukin-1 receptor antagonist blocks the binding of IL-Iß to cells that have receptors on the surface of group II group, III group, IV group, V group, IL-10 BRA-Mn-I.

Thus, an endogenous interleukin-1 receptor antagonist may play an important role in preventing or limiting local organ damage caused by excess IL-lß. An increase in the level of an interleukin-1 receptor antagonist and an imbalance between IL-lß and an interleukin-1 receptor antagonist may predispose to severe hemodynamic changes in angina pectoris and myocardial infarction. The higher the level of interleukin-1 receptor antagonist, the worse the prognosis. Changes in the concentration of the interleukin-1 receptor antagonist correlate with the dynamics of intracardiac hemodynamics and physical tolerance in patients with myocardial infarction. In order to assess the severity of the inflammatory response, we investigated the level of the interleukin-1 receptor antagonist [1,10].

In the I control group of animals, its level was 45,02±2,61 pmol/ml. After modeling acute myocardial infarction, the content of RAIL-1 sharply decreased and was significant ($p<0,05$). Its level in animals of group III was 6,02 pmol/ml. This coincided with the high activity of IL-1r, the level of which in this group of animals was 68,37±4,56 pmol/ml. In the groups of animals with TES therapy, the level of the antagonist of the receptor for interleukin-1 was significantly ($p<0,05$) higher than in the group of animals with acute myocardial infarction. This was associated with a significantly lower level of IL-1R when using TES therapy.

The dynamics of the coefficient of the interleukin-1/IL-1R receptor antagonist reinforces the ongoing changes, and when modeling acute myocardial infarction (animals of group III), it decreased 73,3 times. This is due, first of all, to a significant increase in the level of IL-1R by 10,0 times compared with the control group of animals. The content of the interleukin-1 receptor antagonist, at this time, decreased by 7,5 times.

After the use of TES therapy, in the acute period of acute myocardial infarction (in animals of group IV), the coefficient of the antagonist of the receptor interleukin-1/IL-1R was 30,0 times higher due to the return of the level of IL-1R to normal and a higher content of the receptor antagonist interleukin - 1–2,7 times. This dynamic reflects positive changes in the state of the structure of the myocardium [4,18].

With the preliminary use of TES therapy (in animals of group V), this coefficient was only 15.6 times higher, which is due to a less pronounced drop in the level of IL-1R (1.3 times higher than the norm).

The proinflammatory coefficient (PVI - IL-1p/IL-10) in the simulation of AMI (group III animals) increased 8,8 times. With the use of TES-therapy, in the acute period of AMI (in animals of group IV), its value was 18,7 times lower, due to the return of the IL-1r level to normal (11,2 times decrease) with a simultaneous higher content IL-10 (9,8 times). This indicated a significant decrease in the pro-inflammatory potential in the myocardium, due to the anti-inflammatory effect of TES therapy. The preliminary use of TES therapy (in animals of group V) led to a less pronounced decrease in the level of pro-inflammatory activity (by 1,2 times). However, it was also lower than in animals of the control group, thus, modeling of AMI caused pronounced negative pro-inflammatory changes in the rat myocardium. This was manifested in a 73,3-fold decrease in the anti-inflammatory coefficient (interleukin-1/IL-1R receptor antagonist), while the pro-inflammatory coefficients (TNF-a/IL-10 and IL-1r/IL-10) increased 13,1 times and 8,8 times, respectively. These changes were accompanied by pronounced morphological disorders in the myocardium [6,17].

Oxidative stress developed and the level of necrosis markers increased. The use of TES therapy had a significant cardioprotective effect, limiting myocardial damage, and

normalized the anti-inflammatory potential of the myocardium.

There was a decrease in the pro-inflammatory coefficients of TNF-a/IL-10; IL-1r/IL-10) 32,5 times and 18,7 times, respectively, while the anti-inflammatory coefficient (interleukin-1/IL-1R receptor antagonist) increased 30,0 times.

Preliminary use (even a single dose) of TES therapy also limited ischemic myocardial damage when modeling AMI, which manifested itself in a lesser degree of fall in the anti-inflammatory coefficient (antagonist of the interleukin -1 - 1/IL-1R receptor), only 4,7 times and the absence of an increase in proinflammatory coefficients (TNF-a/IL-10 and IL-1r/IL-10).

In the study, we evaluated the effect of TES therapy on the content of P-endorphins in the blood serum of rats with AMI (Table 3, Fig. 3).

Table 3: Concentration of P-endorphia in the blood serum of different groups of animals

Group/ indicator	I Control	II Falsely operated	III AMI	IV AMI-TES	V TES - AMI
P-endorphins (pkg/ml)	55,2 ±3,7	18,49± 1,29*	10,3±2,1*+	54,12 ±3,46**	24,71±1,85**++

Note:
* - p<0,05 compared to group I,
** - p<0,05 compared to group III,
+ - p<0,05 compared to group II,
++ - p<0,05 compared to group IV.

Table 3 shows that the content of P-endorphin in the I control group of animals was 55,2±3,75 pkg/ml. Noteworthy is the fact that in the group of sham-operated animals, the content of the latter was significantly (p<0,05) reduced by 2,9 times and amounted to 18,49±1,29 pg/ml.

This is probably indicative of the impact of operational stress. and hyperactivation of stress-realizing systems of the animal's body with the development of the adrenergic-corticoid phase of stress or the shock stage according to G. Selye. In group III animals with modeled AMI, the level of P-endorphin, in relation to group I animals, was significantly reduced (p<0,05) by 5,1 times and amounted to 10,39 ± 2,11 pkg/ml. It was also less in comparison with the content in the II group of animals (1,8 times).

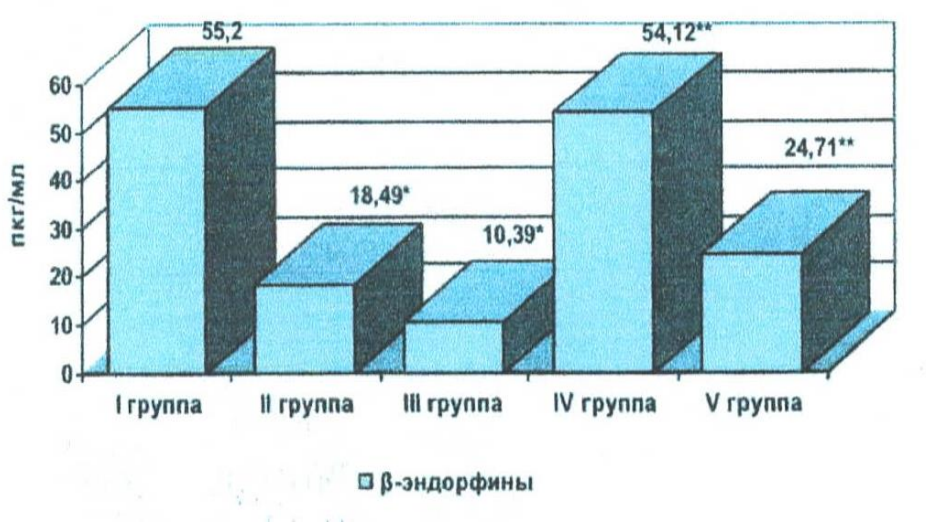

Fig.3: The content of P-endorphin in the blood serum of different groups of animals.

Note:

* reliable in relation to group I,
** reliable in relation to group III

Undoubtedly, the depth of the decrease in the level of P-endorphin is associated not only with surgical stress, but also with the most powerful release of pro-inflammatory cytokines into the bloodstream in the simulation of acute myocardial infarction.

The use of TES-therapy during the acute period of AMI (group IV of animals) returned the content of ß-endorphin to normal values and its level in serum becomes equal to the data of the control group I of animals. Its content in this group of animals was 54,12±3,46 pkg/ml. These data are statistically significant (p <0,05) in relation to the indicators of animals of group III.

A higher level of ß-endorphin (5,2 times) in group IV animals, when using TES therapy, indicates the activation of stress-limiting systems, in particular, the opioidergic system, which have a cardioprotective effect by stimulating the heart's own opioidergic system. In group V animals, where the use of TES-therapy preceded the modeling of acute myocardial infarction, the level of ß-endorphin was 24,71±1,85 pkg/ml. Consequently, the decrease in the content of ß-endorphin is less pronounced – 2,2 times compared to 5,1 times without the use of TES therapy [3,12].

However, the level of ß-endorphin was 2,2 times lower than in animals of the I control group.

Thus, TES therapy has a modulating effect due to the activation of endogenous opioid structures. An increase in ß-endorphin content has a cardioprotective effect due to intracardiac opioidergic structures. Thus, the treatment of patients with acute myocardial infarction is pathogenetically justified. Its use in the most acute period of acute myocardial

infarction increases the effectiveness of the action, preventing the appearance of significant violations of the structure of the myocardium.

CONCLUSION

- The use of TES-therapy in the most acute period of experimental acute myocardial infarction revealed a positive dynamics of the cytokine status, consisting in the normalization of the content of pro-inflammatory cytokines (IL-lß, TNF-a, IL-206), in a sharp decrease in the values of the provocative coefficients (TNF-a/IL -10 and IL-1R/IL-10) by 31,7 times and 96,0 times, respectively, as well as a significant increase in the content of IL-10 (2,9 times) compared with the control group of animals. This led to an increase in the value of the anti-inflammatory coefficient (interleukin-1/IL-1R receptor antagonist) – 29,4 times. Positive changes in the system of pro- and anti-inflammatory cytokines induced by TES therapy were accompanied by an increase in the P-endorphin content in the blood of experimental animals (by 5,2 times) to the control level.

- The use of TES-therapy in experimental acute myocardial infarction led to a lesser degree of damage to the structure of the myocardium, as evidenced by a histochemically proven decrease in edema of the stroma of cardiomyocytes, a decrease in nuclear hyperchromia.

- The results obtained indicate the high efficiency and feasibility of using TES-therapy in the complex treatment of patients with acute myocardial infarction. - In acute myocardial infarction in the acutest stage, TES therapy is recommended to be applied in addition to complex drug treatment as follows: in the bipolar pulse current mode daily, the current strength is selected individually (from 1 to 2 mA, on average 1,7 mA), the position of the electrodes is fronto-mastoid. The duration of the 1st session is 15 minutes, all subsequent ones - 40 minutes. The sessions are held within 7-10 days.

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