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DYNAMICS OF ENDOTHELIAL CHANGES IN MULTIPLE INJURIES AND THEIR CORRECTION WITH POLYOXIDONIUM PREPARATION

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Abstract

Objective: to study the role of endothelial dysfunction in combined and multiple injuries of long bones and ways of its correction.

Material and methods. The objects of clinical study were 48 patients with polytrauma admitted to the department of emergency traumatology of the Multidisciplinary Clinic of the Tashkent Medical Academy.

Results: In patients with polytrauma in the acute period, there is an increase in the serum content of endothelin-1 and a decrease in the level of nitric oxide metabolites. Their severity corresponds to the severity of the injury and the patient's condition. The favorable course of polytrauma is characterized by a moderate decrease in the level of endothelin-1 and an increase in nitric oxide metabolites in the dynamics of traumatic disease, especially when the immunocorrector polyoxidonium is prescribed.

Conclusion: in polytrauma, endothelial dysfunction reflects the adaptive reactions of the body, allows you to determine the severity of the injury and predict the outcome.

Keywords: multiple injuries, traumatic illness, treatment, polyoxidonium, endothelin-1, nitric oxide.

Recently, there has been a clear trend of an increase in the number of emergencies around the world [2, 4, 6, 8]. The most common are road traffic accidents, which more often than other peacetime disasters, about 70%, lead to mechanical and other kinds of damage [2, 4, 6]. The study of the activity of functional systems in traumatic illness and the regularities of the formation of adaptive reactions, as well as the restoration of the body's life support functions to extreme conditions and the limits of their stability under the influence of damaging factors will help specialists to choose the necessary

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therapy, which ultimately will allow success in the treatment of such patients [3, 7, 8].

Various regulatory and executive systems of the human body take part in the formation and outcome of shock as a typical reaction of the body to aggression, among which the endothelial system undoubtedly occupies one of the main places [8]. The versatility of the vascular wall response to any traumatic injuries is currently beyond doubt [3,7, 10]. Morphological rearrangement, repair of the artery wall, both in the vascular suture zone and in the injury zone is inextricably linked with biochemical changes in the artery wall, with changes in endothelial function, inflammatory response to injury. Currently, enough information has been accumulated about the essence of morphological changes. In a simplified form, these changes are reduced either to physiological repair of the artery wall, or to the development of arterial intima hyperplasia in the intervention zone [3, 7].

According to modern concepts, the functional state of the endothelium largely depends on the activity of endothelin-1 (E-1) and nitric oxide (NO) [5, 7, 9, 11]. Endothelin-1 functions as a local hormone that has an autocrine/paracrine effect on vascular smooth muscle cells (MMC), fibroblasts, pericytes, and has a pronounced long-lasting vasoconstrictor effect. Its natural antagonist is NO – vasodilator, which has a wide range of biological effects.

The purpose of this study was to study the role of endothelial dysfunction in combined and multiple injuries of long bones and the ways of its correction.

Material and methods of research. The objects of clinical study were 48 patients with polytrauma who were admitted to the department of emergency traumatology of the Multidisciplinary TMA Clinic. The age of the victims ranged from 18 to 47 years, there were 34 men (70.8%) and 14 women (29.2%).

According to the mechanism of injury , patients were distributed as follows: domestic – 11 (22.9%); industrial -8 (16.7%); street - 3 (6.25%); as a result of a traffic accident - 19 (39.6%); catatrauma - 4 (8.3%) and during sports -3 (6.25%).Open fractures – 11 (22.9%), closed fractures – 37 (77.1%).At the same time, femoral fractures were observed in 17 patients; 31 patients had a fracture of the shin bones. According to the type of damage, the distribution was carried out according to the AO-ASIF classification as follows: A1-16; A2-8; A3-1; B1-3; B2-1; C1-7; C2-9; C3-3.

In open fractures, primary surgical treatment of wounds with osteosynthesis with a rod apparatus was performed in 5 (10.4%) cases, compression-

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distraction osteosynthesis with Ilizarov apparatus in 3 (6.25%) patients, with spokes – in 3 (6.25%).

Osteosynthesis was performed in a delayed-planned manner: with a bone plate in 11 (22.9%) cases, intramedullary osteosynthesis in 6 (12.5%), blocking intramedullary osteosynthesis in 12 (25%) patients. With a combination of fractures of the pelvic bones, the imposition of a spoke-rod apparatus was performed in 7 patients. In 8 (16.7%) patients, conservative treatment was continued because on the control radiography, the standing of bone fragments of long bones was satisfactory.

All patients included in the study underwent complex treatment: infusion-transfusion therapy; inotropic, vascular and respiratory support; enteral nutrition; antibacterial therapy, of which 27 patients continued to receive basic therapy (control group), and 21 patients additionally underwent immunological therapy with the inclusion of polyoxidonium for 10 days at a dose of 6 mg, intramuscularly, every other day, No. 5 (main group).

To assess the general condition of the patient's body and its homeostatic functions, in addition to traditional clinical and radiological studies (X–ray, computed tomography, magnetic resonance imaging, general blood and urine analysis, blood biochemistry, etc.), an analysis of the spectrum of endothelial changes was carried out. To obtain objective data on the spectrum of endothelial changes in patients with multiple and combined injuries, we determined the level of ET-1 by the enzyme immunoassay using the Endotelin kit (1-21), Biomedica (Austria) and the concentration of NO by the sum of the metabolites of nitrates and nitrites (NO2 and NO3) [1].

The analysis of quantitative indicators was carried out on a personal Computerpentium IV under the control of the MicrosoftWindows 2000 Server operating system, using the statistical programs MicrosoftExcel and MicrosoftAccess, with the determination of average values (M), average error (m). The reliability of the difference in indicators was determined using the Student's t-test with confidence $p \leq 0.001$ and $p \leq 0.005$.

Results and their discussion. In the implementation of the inflammatory response, the development of organ dysfunction, vascular endothelin plays an important role, exercising its influence through receptors in the tissues of various organs and systems [7].Analysis of the level of ET-1 in the blood serum of victims with polytrauma on the third day of admission to the clinic showed a significant increase of 2.57 ($P<0.001$) and 2.47 ($P<0.001$) times in both

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examined groups (Table). Its values ranged widely (from 23.77 to 32.04 pg/ml) and were associated with the severity of the injury, the state of shock and the presence of severe damage to internal organs. So, if in patients with multiple injuries, the values of this indicator ranged from 23.77 pg/ml to 28.48 pg/ml, then in patients with combined injuries – from 27.21 pg/ml to 32.04 pg/ml. In fractures of large bones, especially with displacement of bone fragments and the presence of significant compression of soft tissues, the level of endothelin-1 increased more pronounced.

Carrying out osteosynthesis in various ways in the victims led to a slight decrease in the level of ET-1 on the 7th day of surgery. If in the control group this decrease was 1.55 times (P<0.05), then in the main group it was 1.84 times (P<0.01) relative to the initial values, i.e. it was more pronounced in patients who additionally received polyoxidonium, but still significantly exceeded the values of practically healthy individuals. At the same time, it should be noted that in patients with combined injuries and who underwent severe surgical interventions, the ET-1 level remained at initially high values. As the homeostatic constants of the body stabilized, the level of ET-1 in the blood serum gradually approached the values of practically healthy individuals, also more pronounced when using polyoxidonium.

Table

Dynamics of changes in the level of endothelin-1 and nitric oxide metabolites in blood serum in patients with polytrauma, M ±m

Groups	Practically healthy	Terms of the study, day		
		3	7	14
NO, мкмоль/л	19,43±1,22	8,97±0,63[a] 9,12±0,76[a]	12,98±0,83[a] 15, 71±0,54	15,78±1,12[a] 17,62±1,34
Эндотелин-1, пг/мл	7,67±0,47	19,71±1,32[a] 18,98±1,44[a]	12,70±0,98[a] 10,33±0,76[a]	9,11±0,68[a] 8,04±0,48

Note: 1) the numerator represents the values of the control group of patients, the denominator represents the main group; 2) a – the differences between the indicators of practically healthy individuals and patients are significant (P<0.05), b – the differences between the indicators of the main and control groups of patients are significant (P<0.05).

In the physiological state, biologically active substances synthesized by the endothelium create conditions for adequate local blood flow by synthesizing powerful anticoagulants, which are also vasodilators, thereby providing organ trophism and performing a protective function due to the presence of highly

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organized self-regulation mechanisms in the endothelium[5, 9, 11]. Among the vasodilators synthesized by the endothelium is nitric oxide.Analysis of the level of final metabolites of nitric oxide in the blood serum of the victims showed a significant decrease of 2.17 ($P<0.001$) and 2.13 ($P<0.001$) times, respectively, in the control and main groups. Its values also varied widely and depended on the severity of injury, shock, combined damage to other organs and systems. Dynamic monitoring of the victims after surgical interventions showed a gradual increase in its content in patients with uncomplicated course of the postoperative period, in other cases its values only tended to increase. On the 7th day after surgical interventions, the values of the final metabolites of nitric oxide increased statistically significantly by 1.45($P<0.05$) and 1.72($P<0.05$) times, respectively, in the control and main groups of patients relative to the initial values. However, these values were still significantly lower than the values of practically healthy individuals. By the 14th day of observation, the values of these compounds increased by 1.76($P<0.01$) and 1.93($P<0.01$) times, and somewhat approached the standard values, especially in patients who additionally received polyoxidonium.

It should be said that NO has a direct inhibitory effect on hyperplasia, which is important due to the fact that even with cell death by necrosis, variants of activation of hyperplastic processes in the endothelium are possible [5, 9]. This is explained by the fact that when a cell is killed and destroyed necrotically, cell components enter the intercellular space, which induces a local inflammatory reaction. In addition to the described positive properties, nitric oxide is a functional antagonist of E-1. The expression of E-1 detected by us in polytrauma causes vessel spasm, and, therefore, can act as a promoter of hyperplasia, whereas a high concentration of NO contributes to vasodilation and indirectly reduces the likelihood of intimal hyperplasia. On the other hand, the high concentration of ET-1 can have an inhibitory effect on the expression of nitric oxide synthase and the formation of nitroxide in the vascular wall [5], which is manifested in our studies by the minimum values of the nitrite/ET-1 ratio.

Patients in a state of traumatic shock, starting from the first day of injury, develop both adaptive and pathological reactions of the immune system [7, 10]. Apparently, the use of polyoxidonium in these conditions leads to stabilization of the immune system and, as a consequence, a more pronounced restoration of the functional parameters of the endothelium.

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Thus, these data indicate adaptive changes in the vascular wall during trauma and after surgical treatment, their comprehensive analysis will allow determining the severity of the injury and the patient's condition, predicting the risk of complications, as well as identifying ways to correct pathological changes.

Conclusions:

1. In patients with polytrauma in the acute period, endothelial dysfunction is noted, manifested by an increase in the serum content of endothelin-1 and a decrease in the level of nitric oxide metabolites.
2. The severity of endothelial dysfunction corresponds to the severity of the injury and the patient's condition.
3. The favorable course of polytrauma is characterized by a moderate decrease in the level of endothelin-1 and an increase in nitric oxide metabolites in the dynamics of traumatic disease, especially when prescribing immunocorrectorapolyoxidonium.

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