



Conducting immunomodulatory therapy in the complex treatment of patients with combined injuries of the Facial Bones

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ABSTRACT: The aim of this work is to study the effectiveness of immunomodulatory therapy with the approved drug polyoxoanion in the complex treatment of patients with combined craniofacial injuries (HSV).

The study involved 22 patients with combined craniofacial injuries who received polyoxoanion at a dose of 6 mg/m once for 5 days as part of complex therapy. Clinical and immunological examinations were performed at admission and on the 10th day after the start of treatment. The examination and treatment of patients was carried out at the clinical base of the Department of Maxillofacial Surgery of the Samarkand State Medical Institute in the specialized department of Maxillofacial Surgery of the Samarkand City Medical Association. The patients were divided into 2 groups:

1-group of 10 patients with combined injuries of the lower face area.

2-group of 12 patients with combined injuries of the middle zone of the face.

The control group consisted of the results of a survey of 11 healthy people of the same age.

It is proved that in patients with combined injuries of the bones of the facial skeleton (STCLS) from the middle zone of the face, the use of polyoxoanion gives a pronounced immunoreacting effect at the level of the cellular link of immunity. In the dynamics of complex treatment, a positive trend was noted in the indicators of the content of CD3, CD4, and CD16-lymphocytes normalized and were statistically significant in patients with a low initial level.

KEYWORDS: combined injuries of the bones of the facial skeleton, immunity, immunosuppression, immunoreaction, polyoxoanion.

INTRODUCTION

Combined trauma to the bones of the facial skeleton (STCLS) is a trigger factor for the violation of the indicators of homeostasis of the body. After the injury, the body develops a traumatic disease, which is accompanied by the development of inflammatory processes, immune imbalance, violation of secretory and humoral factors of the immune response of the body. Today, it is proven that a combined injury is accompanied by brain damage in up to 100% of cases. The severity of immunological disorders depends on the components and severity of the injury, deep violations of the function of vital organs. The severity of the general condition of patients depends on the area of damage to the STCLS. In the last decade, there has been a clear trend of increasing injuries, especially combined craniofacial injuries. Thus, according to various authors, the frequency of combined craniofacial injuries ranges from 2.9% to 42.6% [2,9]. Despite significant progress, the treatment of patients with injuries to the bones of the craniofacial skeleton and the prevention of complications is a difficult and far from solved problem of modern maxillofacial surgery. The seriousness is due, on the one hand, the problem of quality and speed of bone regeneration that suffers as a result of the injuries, and other traumatic complications, among which the highest value in the frequency and severity have complications of inflammatory nature, as much as 30% [6,7,9]. The immune system plays a certain role in the development of bone regeneration and the prevention of purulent-inflammatory complications.

In this regard, it is of great importance to develop new approaches to optimizing the treatment of patients with craniofacial skeletal trauma, one of which is the inclusion of immunomodulatory drugs in the regimens of complex therapy.

Combined trauma to the bones of the facial skeleton is a trigger factor for immune system disorders. From the beginning, the adaptive mechanisms of cellular immunity are triggered. The first manifestation of the body's response is the reaction of natural immune factors, the phagocytic activity of neutrophils, the study of the imbalance of pro and anti-inflammatory factors of immune defense is of important prognostic value.

STCLS midface and stress have a more pronounced immunosuppressive effect on the dynamics of the post-traumatic period than STCLS the lower areas of the face. In the post-traumatic period, there is a system of self-regulation of the balance of pro - and anti-inflammatory cytokines. The content of cytokines can be affected by various complications in the post-traumatic period. For example, an increase in the concentration of IL-6 and a decrease in IL-10 in the blood can serve as a diagnostic sign of pathological changes in the patient's body.

The study of immune parameters with STCLS from the middle zone of the face showed that in the dynamics of treatment there is a deep suppression of both cellular and humoral immunity, this is confirmed by an increase in the number of pro-inflammatory and a decrease in anti-inflammatory cytokines. Therefore, these changes require the use of immunoreaction in these patients in order to prevent post-traumatic inflammatory complications. For this purpose, we used polyoxoanion in this group of patients.

It seems promising to use an immunomodulator-polyoxoanion (azoximer bromide)-an N-oxidized derivative of polyethylene piperazine, which has a wide range of pharmacological effects on the body: immunomodulating, detoxifying, antioxidant and membrane-protective effects. The

immunomodulatory effect is to increase the ability of neutrophils to absorb and kill absorbed *S. aureus*; increase the cytotoxic activity of NK cells; activation of resident macrophages of the reticuloendothelial system, which leads to faster elimination of foreign particles from the body; increased natural resistance of the body to experimental bacterial and viral infections; increased antibody formation to T-dependent and T-independent antigens of both animal and bacterial origin. The detoxifying properties of polyoxoanion are associated with its high molecular weight and the presence of a large number of different active groups on the surface of the molecule, so it actively adsorbs both soluble toxic substances and microparticles circulating in the blood. The antioxidant properties of polyoxoanion are manifested in the interception of reactive oxygen species in the aqueous medium (superoxide anion, hydrogen peroxide, hydroxyl radical) and in a decrease in the concentration of catalytically active divalent iron, which leads to the suppression of lipid peroxidation [1,7,9].

The aim of this study was to study the effectiveness of immunomodulatory therapy with the approved drug po-iodonium in the complex treatment of patients with combined craniofacial injuries (HSV).

Material and methods. In accordance with the intended purpose of the study, we conducted a comprehensive immunological examination of patients with combined craniofacial injuries in the dynamics of treatment with the use of a drug approved for use in healthcare practice-polyoxoanion. 22 patients with combined craniofacial injuries as part of complex therapy received polyoxoanion at a dose of 6 mg / m once for 5 days. Clinical and immunological examinations were performed at admission and on the 10th day after the start of treatment. The examination and treatment of patients was carried out at the clinical base of the Department of Maxillofacial Surgery of the Samarkand State Medical Institute in the specialized department of Maxillofacial Surgery of the Samarkand City Medical Association. The patients were divided into 2 groups:

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Clinical studies were conducted according to the standard scheme and included a survey of patients, collection of anamnesis of the disease, anamnesis of life, physical methods of research (examination, palpation, percussion), laboratory and instrumental additional methods of research (general analysis of blood, urine, if necessary, biochemical blood examination, X-ray examination of the bones of the facial skeleton and skull), as well as consultation of specialists (neurosurgeon, otorhinolaryngologic, ophthalmologist, traumatologist, anesthesiologist). Immunological methods of investigation included: immunophenotyping of cells (CD3+, CD4+, CD8+, CD16+, CD19+ lymphocytes) with monoclonal antibodies, the concentration of immunoglobulins of class A, M and G in blood serum was carried out by enzyme immunoassay.

Statistical processing of the results was carried out according to programs developed in the EXCEL package using a library of statistical functions with the calculation of the arithmetic mean (M), the error of the arithmetic mean (m), the Student's criterion (t), the probability of error (p).

The results of the study. As a result of the treatment, there was no positive change in cellular immunity in patients of group 1, with the exception of CD8, CD16 – lymphocytes. The

revealed changes in the cellular link of immunity in patients with STCLS from the lower zone of the face have a transient character.

The transient nature of changes in cellular immunity is confirmed with the immunosuppression of humoral immunity. The study of humoral immunity factors on the 1st-3rd, 7th, 14th, and 21st days after the injury showed that the concentration of humoral factors (IgA, IgM, IgG) in patients was significantly lower compared to the data of the control group only from the 7th day ($P<0.001$) and remained low both on the 14th and 21st days in the dynamics of treatment ($P<0.001$).

The study of immune parameters with STCLS from the middle zone of the face showed that in the dynamics of treatment there is a deep suppression of both cellular and humoral immunity, this is confirmed by an increase in the number of pro-inflammatory and a decrease in anti-inflammatory cytokines. Therefore, these changes require the use of immunoreaction in these patients in order to prevent post-traumatic inflammatory complications. For this purpose, we used polyoxoanion in this group of patients.

The study of the features of the clinical course of the post-traumatic period in patients with combined craniofacial injuries showed that the immunomodulatory therapy with polyoxoanion in the treatment complex has a high clinical and immunological effectiveness.

Thus, when polyoxoanion is included in the treatment regimen, the general condition of patients is stabilized faster, and there is a faster regression of systemic and local manifestations of the inflammatory post-traumatic reaction. Normalization of temperature occurred 2 ± 3 days after the start of immunomodulatory therapy in patients versus 5 ± 6 after traditional treatment ($p<0.001$). The dynamics of the decrease in the severity of the general intoxication syndrome and the disappearance of its clinical manifestations were clearly observed in the group receiving immunomodulatory therapy with polyoxoanion. Monitoring of general clinical parameters of peripheral blood allowed us to state an earlier normalization when polyoxoanion was included in the treatment regimen. It should be noted that in the group of patients receiving immunomodulatory therapy with polyoxoanion, none of the patients developed a purulent-inflammatory complication.

In the study of the immune status of patients with craniofacial injuries identified patterns of immune response, expressed stories deficit as indicators of T-cell link of CD3+, CD4+, CD8+ cells humoral immunity - CD19+ with depression product IgA and IgG in comparatively close to the normal values of the number of IgM, which was the basis for developing a method of correction of disorders of immunity, with the inclusion of polyoxoanion in the scheme of conventional therapy in patients with SCLC. Thus, the inclusion of polyoxoanion in the scheme of traditional therapy allowed the number of cells of the CD3+, CD4+, CD8+ and CD16+ phenotypes in the peripheral blood in patients of the second group to reach the values of practically healthy individuals. Thus, the patients of the second group showed an increase in the level of T-lymphocytes ($55.1\pm0.21\%$ vs. $47.9\pm0.41\%$ before treatment, $p<0.05$) due to an increase in the content of CD4 + lymphocytes ($37.4\pm0.32\%$ vs. $29.6\pm0.23\%$ before treatment), CD8+lymphocytes ($23.0\pm0.24\%$ vs. $18, 1\pm0.12\%$ before treatment) and CD16+lymphocytes ($17.4\pm0.31\%$ vs. $16.4\pm0.39\%$ before treatment).

Table 1

Indicators of the cellular link of IS in patients with HPLT

Indicators of IS	control group	initial values	traditional treatment	traditional treatment + polyoxoanion
			1-group	2-group
CD3 ⁺ %	56,4±0,57	47,9±0,41 [^]	49,7±1,05	55,1±0,21*
CD4 ⁺ %	35,5±0,37	29,6±0,23 [^]	32,7±0,54*	37,4±0,32*
CD8 ⁺ %	19,1±0,31	18,1±0,12	18,7±0,84	23,0±0,24*
CD16 ⁺ %	18,1±0,74	16,4±0,39 [^]	16,9±0,85	17,4±0,31*

Note: [^] - p<0.05 in comparison with the control; * – p<0.05 in comparison with the indicators before treatment.

The study of the dynamics of humoral immunity against the background of complex therapy with immunomodulator polyoxoanion there is a tendency to normalization of humoral immunity: normalization CD19⁺ to control values, increased levels of IgA, IgM, IgG. In patients of the second group, an increase in the level of B-lymphocytes was noted to 21.9±0.67% versus 18.1±0.37% before treatment (p<0.05).

Table 2

Indicators of the humoral link of IS in patients with HPLT

Indicators of IS	control group	initial values	traditional treatment	traditional treatment + polyoxoanion
			1-group	2-group
CD19 ⁺ %	22,1±0,3	18,1±0,37 [^]	18,7±0,41	21,9±0,67*
IgA _{Mr} %	188,4±11,5	137,7±7,1 [^]	139,7±4,2 [^]	161,7±9,91*
IgM _{Mr} %	111,2±4,47	122,3±6,4	118,1±2,1	132,5±8,1 [^]
IgG _{Mr} %	997,7±24,4	901,2±47,8 [^]	1004,2±31,7	1061,7±17,4*

Note: [^] - p<0.05 in comparison with the control; * – p<0.05 in comparison with the indicators before treatment.

The clinical and immunological data obtained by us showed the advantages of including immunomodulatory therapy in the complex of medical measures in comparison with traditional treatment without the inclusion of an immunomodulator in patients with combined craniofacial injuries and clearly showed that the positive dynamics of changes in immunological parameters in patients directly correlated with the clinical course of the disease.

Thus, in patients with craniofacial injuries noted immunodeficiency with involvement of both cellular immunity, manifested by a reduced level of T-lymphocytes, T-helper cells, NK-cells and v-lymphocytes with depressed production of immunoglobulins. The use of the immunomodulator polyoxoanion in complex therapy in patients with combined craniofacial injuries made it possible to improve the condition of patients in a shorter time and prevent the development of purulent-inflammatory complications due to the positive dynamics of cellular and humoral immunity.

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