EFFECTIVENESS OF LOCAL APPLICATION OF FIBRINOLYTIC DRUGS TO REDUCE THE NUMBER OF COMPLICATIONS IN PATIENTS WITH MAXILLARY AND ZYGOMATIC BONE FRACTURES

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Abstract

Introduction. The main purpose of this research was to study the effectiveness of local fibrinolytic therapy in the rehabilitation of patients with traumatic injuries of the zygomatic-orbital complex. **Materials and methods**. Patients in the control group (15 persons) received in the postoperative period standard antibiotic therapy, and analgesic, anti-inflammatory and anti-edematous therapy. Patients in the main group (17) received into the parabulbar tissues an additional injection of „Hemase" 5000 ME once a day, for 4-5 days. The effectiveness of the treatment was compared by determining the state of microcirculation, sensory sensitivity and level of enolase in the venous blood. **Results and discussion**. The general conjunctival index in the control group was 18.9 ± 1.2 points on the 7th day and 16.1 ± 1.8 points on the 14th day, and 15.7 ± 1.0 ($p < 0.05$) and 11.7 ± 1.1 points ($p < 0.05$), respectively, in the experimental one. The threshold of electrical excitability of the infraorbital nerve in patients of the control group on the 7th day was 68.4 ± 5.2 μA, while in the main one - 48.1 ± 5.3 μA ($p < 0,05$). On day 14, the difference in the excitability threshold was even more pronounced: in the control - 52.9 ± 4.8 μA, in the main group - 33.2 ± 3.4 μA ($p < 0.05$), with the index on the healthy side at 27.1 ± 1.9 μA. It was also found out that, in the control group, the level of enolase on both the 7th and 14th day exceeded the values obtained during the examination of patients in the main group: 24.5 ± 1.5 ng/ml to 19 , 4 ± 1.3 ng/ml and 15.6 ± 1.4 ng/ml to 15.1 ± 1.5 ng/ml. **Conclusions**. The obtained data allowed stating that application of the proposed course of postoperative rehabilitation helps restore the conduction of nerve trunks, has an anti-edematous effect on the soft tissues of the infraorbital area and improves the hemodynamics of the suborbital artery and vein.

Keywords: fibrinolitic drugs, zygomatic-orbital fractures.

1.INTRODUCTION

Over the last decade, there has been an upward trend in injuries among the population, caused by natural, man-made disasters, and social cataclysms. In terms of frequency, mid-facial bone injuries take the 2nd place among fractures of the maxillofacial area (MFA) and reach 20 - 35% [1]. After analyzing the data of the studied literature sources, we can state that all mid-facial injuries have a number of common features [2-5]. In all cases, such injuries are accompanied by multiple, often multi-fragment fractures of the zygomatic-orbital complex, upper jaw, bone base of the nose. One of the problems that scientists pay attention to [6,7] is local changes in the area of damage, namely, microcirculatory disfunction of the bulbar conjunctiva, which is manifested by vascular tone disorders, slow blood flow, hemorrhages, while the development of edema and hematomas damages the peripheral nerves that run in the middle area of the face. According to many authors, partial or complete restoration of their function is observed only in 56% of cases [8,9]. Literature indicates the effectiveness of topical injection of drugs with fibrinolytic activity (including „Hemase", which contains proenzyme prourokinase) in the treatment of traumatic orbital hemorrhage, hemophthalmos in diabetic retinopathy, and retinal vein thrombosis.

Given the above data and the significant practical interest in the treatment of patients with combined trauma of the maxillofacial area, the present work is aimed at studying the effectiveness of local fibrinolytic therapy in the rehabilitation of patients with traumatic injuries of the zygomatic-orbital complex.

2. MATERIALS AND METHODS

To comply with the rules of evidence, we divided the patients so as to minimize the difference in the features of postoperative treatment. All selected patients had an important pecularity – the fractures of the zygomatic-orbital complex were characterized by significant displacements (belonging to the group of severe fractures, according to the classification of Bernadsky [11]) and ran along the bottom of the orbit.

These patients belonged to calsses 1, 3, 4, 7, according to the above classification; all of them showed a sharp displacement of fragments with disorders of both tactile and pain sensitivity in the front part of the temporal and infraorbital area, together with the lower eyelid, half of the nasal wing and upper lip, which indicated the simultaneous injury of both the infraorbital and zygomatic nerves. The total number of patients under supervision was 32.

The control group consisted of 15 patients who, after fragment repositioning, underwent a traditional conservative treatment, prescribed after consultation with a neurosurgeon, including standard antibiotic therapy (clandimycin - 600 mg 2 times a day for 7-8 days), and also analgesic and anti-inflammatory therapy (ketoprofen - 100 mg 2 times a day for 5-6 days), anti-edema therapy (L-lysine escinate - intravenously 5-10 ml of the drug).

The main group included 17 patients who received an additional injection in parabulbar tissues with the fibrolytic drug «Hemase» manufactured by Technogen (Russia) at 5000 ME in 0.5 ml of 0.9% sodium chloride solution, 1 time per day, for 4-5 days.

Studies of angioarchitectonics and microcirculation of the bulbar conjunctiva were performed using an ophthalmic microscope ShchL-56, according to the Kniselyet-Harting method modified by Shulpina and Daktarravichene. The condition of microcirculation in vessels of bulbar conjunctiva was described by the quantitative and qualitative technique of Smirnov [12]. According to this method, the condition of the microcirculatory tract was assessed by the value of the «Common conjunctival index», comprising four other indices: «Perivascular change index», which determines the presence of perivascular conjunctival edema, hemorrhage, hemosiderosis and lipoid (from 1 to 2 points), «Vascular change index», which revealed the presence of uneven vascular caliber, aneurysms, tortuosity and changes in vascular caliber, «Arteriolo-venular ratio», normally 1: 2, «Capillary change index», which assesses the condition of capillaries: their caliber and number on a two-point scale, «Intravascular change index», which assessed blood flow velocity, its blockage and retrograde on a two-point system, the severity of the «sludge phenomenon» on a four-point system, aggregation of erythrocytes in arterioles, capillaries and venules on a two-point system.

The degree of damage to the suborbital and zygomatic nerves was assessed according to the classification of Seddon, which allows to determine the degree of damage to the nerve trunk by changes in the conductivity in each of its segments. The degree of damage to the branches of the maxillary nerve was determined according to electrophysiological tests, by the method of Nechaeva and co-authors [13]. The obtained values of electrosensometry are interpreted as follows: indicators of electrical sensitivity of facial skin are normally 25-35 microns, and tooth pulp - 6-10 microns. With the values of the electropotential (EP) of facial skin 36-55 mkA and electroodontometry (EOD) of teeth of 12-25 mkA, temporary disturbance of nerve conduction is diagnosed, which indicates a mild nerve damage (neuropraxia); moderate degree of nerve damage (axonotmesis) - EP of facial skin 55-80 μA and EOD of teeth 26-50 μA; severe nerve damage (neuromesis) - EOD of teeth 51-100 μA, EP of facial skin 80-150 μA.

Electrodiagnostics of the sensitivity of superficial branches of a maxillary nerve was carried out by imposing sensors on skin in a projection of their exit on the face surface. To do this, we used the «Radius-01 FT» device (Belarus) in the electrical stimulation mode of operation. The following guidelines were chosen for this purpose: the sensitivity of the zygomatic-temporal nerve was tested at 15.0 + 0.5 mm laterally frontal-zygomatic suture and

at 23.0 + 0.5 mm above the upper edge of the zygomatic arch [14], the zygomatic-facial nerve was tested at the point located 8.5 + 0.5 mm laterally to the lower outer corner of the orbit and lower by 24.0 + 0.5 mm from the frontal-zygomatic suture [15], while the suborbital nerve was examined at the point located 6, 7 ± 1.62 mm below the lower edge of the orbit (at the level of the maxillary-maxillary suture) and 17.5 ± 0.5 mm medially from the pear-shaped foramen [16].

Measurement of the electrical sensitivity of dental pulp on the corresponding side of the upper jaw was performed by electroodontodiagnostics (EOD), which was performed using a portable digital electroodontometer «Pulptester» (Taiwan).

In addition, the concentration of neuron-specific enolase (NSE), which is a neuronspecific isoform of enolase present in neurons, was determined in the peripheral venous blood of patients. The level of NSE increases in diseases of the nervous system, being accompanied by a fairly rapid destruction of neurons, so it is used in the diagnosis and assessment of the prognosis of recovery from nervous system lesions of various origins (traumatic, ischemic). It was studied by the immunochemical method with electrochemiluminescent detection, using an analyzer and test system Cobas 6000, RocheDiagnostics (Switzerland). The reference value of NSE is up to 16.3 ng/ml.

Mathematical and statistical processing of all obtained digital research results was performed on a PC, with the appropriate software package «StatSoftStatistica8» and «MicrosoftExcel», recommended for this type of processing methods. Given that all studied data belonged to the variation series with a statistical set of normal (symmetrical) distribution, in the analysis of statistical characteristics of individual groups, indicators of descriptive statistics with the definition of values as: mean (M) ± standard error (m) were used.

The average values of the different groups were compared using Student's method, while the relative values - using the parametric criterion χ2Pearson. The differences were considered significant at $p < 0.05$.

3. RESULTS AND DISCUSSION

Determination of microcirculation in the vessels of the bulbar conjunctiva by quantitative and qualitative methods established (Table 1) that, on the 14th day, the total conjunctival index in patients with fractures of the zygomatic-orbital complex was significantly lower in the main group (11.7 ± 1.1 points) than that in the control group (16.1 ± 1.8 points).

Examination of patients with severe fractures of the zygomatic-orbital complex showed that the indicators of the general conjunctival index, such as the perivascular change index (control - 2.4 ± 0.3 points; the main group - 1.6 ± 0.1 points), the vascular change index (control - 4.7 ± 1.6 points; the main group - 3.8 ± 1.3 points), the intravascular change index (control - 9.1 ± 2.1 points; the main group - 7.4 ± 1.4 points), the capillary change index (control - 2.7 ± 0.8 points; the main group - 2.9 ± 0.4 points) were less pronounced in the patients of the main group already on the 7th postoperative rehabilitation day, than in patients of the control group.

Table 1. Biomicroscopy data of eye conjunctiva in fractures of the zygomatic-orbital complex with displacement of fragments during postoperative rehabilitation

Biomicroscopic indicators	day	Clinical group	
		Control	Main
Perivascular change index, as points	7	2.4±0.3	1.6±0.1 p<0.05
	14	1.7±0.1	1.2±0.1 p<0.05
Vascular change index, as points	7	4.7±1.6	3.8±1.3 p>0.05
	14	3.7±1.1	2.9±0.3 p>0.05
Intravascular change index, as points	7	9.1±2.1	7.4±1.4 p>0.05
	14	8.5±1.9	5.1±1.1 p>0.05
Capillary change index, as points	7	2.7±0.8	2.9±0.4 p>0.05
	14	2.2±0.4	2.5±0.4 p>0.05
General conjunctival index, as points	**7**	**18.9±1.2**	**15.7±1.0** p<**0.05**
	14	**16.1±1.8**	**11.7±1.1** p<**0.05**

* Note: p is the statistical significance between the control and main groups

When assessing sensitivity disorders in patients with fractures of the zygomatic-orbital complex on the 7th and 14th day after repositioning and fixation of fragments in the correct position, it was found out that the most persistent sensitivity of the anatomical areas occurs at the separation zone of the cheekbone from the neighboring anatomical structures (temporal and frontal bones, upper jaw). The positive effect of the proposed complex of conservative treatment on the restoration of conduction and sensitivity of nerve fibers was statistically established, as reflected in the number of patients with impaired sensitivity in these anatomical areas, which is much smaller in the main group (Table 2).

Table 2. Anatomical areas of the head, diagnosed with sensory disorders in fractures of the zygomatic-orbital complex during postoperative rehabilitation

Anatomical areas of sensory disorders	Clinical group	Number of patients	
		Day 7	Day 14
Soft tissues of the infraorbital area, lower eyelid, nasal wing, upper lip (on the affected side)	Control	15	8
	Main	8	3
Soft tissues of the zygomatic area	Control	12	5
	Main	5	1
Soft tissues of the frontal temporal area	Control	7	4
	Main	3	0
Frontal group of the upper jaw teeth (incisors, canines) (on the affected side)	Control	10	6
	Main	5	1
Small angular teeth of the upper jaw (on the affected side)	Control	3	0
	Main	1	0
Large angular teeth of the upper jaw (on the affected side)	Control	0	0
	Main	0	0

Electrical sensitivity of nerve fibers in fractures of the zygomatic bones on the 7th day after surgery established that no signs of neuromesis (severe damage) were present in any patient (Table 3). Axonotmesis of the infraorbital nerve (moderate degree of damage) was found only in the patients of the control group - 68.4 ± 5.2 μA on the affected side. In patients of the main group, the threshold of electrical excitability of the infraorbital nerve on the 7th day of postoperative rehabilitation made up 48.1 ± 5.3 μA. The pulp sensitivity of the frontal group of teeth and premolars had a slight degree of damage on the 7th day in both clinical groups - control -28.1 ± 2.7 μA; basic - 20.9 ± 2.1 μA.

Re-examination on the 14th day after surgical rehabilitation showed that, in all patients of the main group, the electrical sensitivity of the infraorbital, zygomatic nerves and dental pulp was within normal limits. In patients with fragment displacement in the area of the maxillary suture on the 14th day, neuropraxia of the infraorbital nerve was diagnosed in the control group - 52.9 ± 4.8 μA. The results of electroodontometry of teeth showed that hypoaesthesia was observed in patients of the control group (Table 3).

Table 3. Indicators of electrical sensitivity of infraorbital and zygomatic nerves and teeth of the upper jaw in fractures of the zygomatic-orbital complex

Indicators of electrical sensitivity	Day	Control group	Main group
Threshold of electrical excitability of the infraorbital nerve (mkA)	7	68.4±5.2	48.1±5.3 p<0.05
	14	52.9±4.8	33.2±3.4 p<0.05
Threshold of electrical excitability of the zygomatic nerve (mkA)	7	40.2±4.3	30.6±3.7 p>0.05
	14	32.5±3.6	28.4±3.5 p>0.05
Threshold of electrical excitability of frontal group of upper jaw teeth (mkA)	7	28.1±2.7	20.9±2.1 p<0.05
	14	20.3±3.4	14.4±1.9 p<0.05
Threshold of electrical excitability of small angular teeth of upper jaw (mkA)	7	23.1±2.6	20.4±3.2 p>0.05
	14	18.7±2.2	14.5±1.7 p>0.05

* Note: p is the statistical significance between the control and main groups

Determination of the content of neuron-specific enolase in the venous blood of postoperative rehabilitation (Table 4) showed that, in patients with mild traumatic brain injury and severe trauma, the rate exceeded the norm on the 7th day in both study groups (control - 24. 5 ± 1.5 ng / ml; main group - 15.6 ± 1.4 ng / ml), indicating processes of neurodegeneration of the infraorbital and zygomatic nerves, due to injury.

Examination on the 14th day showed that, in patients of the control group, the content of neuron-specific enolase continued to exceed the norm (19.4 ± 1.3 ng / ml). In patients receiving transcranial therapy and parabulbar injections of fibrinolytic drug on the 14th day, the marker of nerve fiber damage decreased and did not exceed the norm - 15.1 ± 1.5 ng / ml (Table 4).

Table 4. Dynamics of the content of neuron-specific enolase in the blood of patients with fractures of the zygomatic-orbital complex

Clinical group	Content of neuron-specific enolase (ng / ml)	
	7 day	14 day
Control	24.5±1.5	19.4±1.3
Main	15.6±1.4 p<0.05	15.1±1.5 p<0.05

*** Note: p is the statistical significance between the control and main groups.**

Discussion. Changes in microcirculation in the bulbar conjunctiva vessels between the control and main group were detected on the 7th day, but a more pronounced difference was detected on the 14th day. Thus, the general conjunctival index in the control group corresponded to the following values: 18.9 ± 1.2 points on the 7th day and 16.1 ± 1.8 points on the 14th day.

For the sake of comparison, the indicators obtained in the main group patients, *i.e.* those whose treatment was supplemented by injection of the fibrinolytic drug into the parabulbar tissues, were 15.7 ± 1.0 points (p <0.05) and 11.7 ± 1.1 points (p <0.05), respectively. The results show that injections of «Hemase» help the reduction of perivascular edema, the disappearance of retrograde blood flow, aneurysms and vascular anomalies, erythrocyte aggregation and blood flow blockages.

One of the manifestations of compression by bone fragments and hematomas in the area of the maxillofacial suture and the bottom of the orbit is the development of neuropathy, which is subjectively manifested by sensory disorders in the maxillofacial area. In patients with fractures of the zygomatic-orbital complex, such disorders were characterized by impaired sensitivity in the form of paresthesia of the soft tissues of the infraorbital region, lower eyelid, nose wings, upper lip and upper jaw teeth. Introduction in the conservative postoperative treatment of parabulbar injection of fibrinolytic drug contributed to a statistically faster recovery of nerve fiber conduction.

Determination of electrical excitability of nerve fibers statistically confirmed the presence of a higher violation in patients who used the traditional scheme of postoperative rehabilitation. Thus, the threshold of electrical excitability of the hyoid nerve in fractures of the zygomatic-orbital complex in the control group on the 7th day was 68.4 ± 5.2 μA, while in the main - 48.1 ± 5.3 μA (p <0 , 05). On day 14, the difference in the excitability threshold was even more pronounced: in the control - 52.9 ± 4.8 μA, in the main group - 33.2 ± 3.4 μA (p <0.05), with a healthy side index at 27.1 ± 1.9 μA.

The dynamics of the content of neuro-specific enolase in venous blood also fully confirmed the effectiveness of the proposed conservative treatment. In patients of the control group, on both the 7th and 14th day, it exceeded the values obtained during the examination of the main group: 24.5 ± 1.5 ng / ml to 19.4 ± 1.3 ng / ml and 15, 6 ± 1.4 ng / ml to 15.1 ± 1.5 ng / ml. This data indicates that the processes of neuroregeneration occur faster in the patients of the main group than in the control.

The obtained data allows to state that application of the proposed course of postoperative rehabilitation helps restore the conduction of nerve trunks, has an anti-edematous effect on the soft tissues of the infraorbital area and improves the hemodynamics of the infraorbital artery and vein.

4. CONCLUSIONS

The results obtained show that injection of the fibrinolytic drug into the parabulbar tissues helps the reduction of perivascular edema, and disappearance of the effects of retrograde blood flow, aneurysms and vascular anomalies, erythrocyte aggregation and blood flow blockade, and the full recovery of blood flow in the infraorbital artery basin necessary for the comlete elimination of compression by hematomas and inflammatory exudate of the suborbital and zygomatic nerve fibers.

The positive effect of the proposed method of treatment was statistically and significantly confirmed by the data of electrical excitability of nerve fibers: the threshold of electrical excitability of the infraorbital nerve in fractures of the zygomatic orbital complex in the control group patients on the 7th day was 68.4 ± 5.2 μA, while in the main one - 48.1 ± 5.3 μA ($p < 0.05$). On day 14, the difference in the excitability threshold was even more pronounced: in the control - 52.9 ± 4.8 μA, while in the main group - 33.2 ± 3.4 μA ($p < 0.05$).

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