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INFLUENCE OFANTIOXIDANT THERAPY ON THE COURSE OF ADHESIONS IN THE ABDOMINAL CAVITY UNDER THE **EXPERIMENTAL CONDITIONS**

ABSTRACT

In the present work results of influence of antioxidants (emoxypin and mexydol) on formation of adhesions in an abdominal cavity at experimental animals in comparative aspect after modelling of adhesive illness are presented. It is established that in the groups received specified preparations authentic decrease of formation of adhesions is marked with optimization of antioxidant system. The quantity of remezotelizated cells on deserosaled sites of peritoneum in comparison with control group increases.

Keywords: adhesive process, antioxidants, laboratory animals.

In spite of progress of modern medicine, peritoneal adhesions remain one of the unsolved and actual problems of the abdominal surgery at present time. The frequency of the disease, the difficulty of timely recognition, lack of clear criteria of treatment policy and unfavorable outcomes make the problem of adhesions syndrome relevant [3, 4, 7]. Over the past few decades varieties of preventive measures from the formation of adhesions in the abdominal cavity were offered. However, until now there are no fairly effective means for prevention of adhesions in the postoperative period in modern medicine [5, 6, 8].

In recent times, studiers refer to abnormality in pro - and antioxidant balance of the body in the study of the reasons of development of various diseases, including inflammatory conditions [2].

The aim of the research is to determine the potency of drug influence having antioxidant properties: emoxypine and mexidol in comparison, used for prevention and development of adhesion in the abdominal cavity of the laboratory animals after the modeling of the peritoneal adhesions experimentally.

MATERIALS AND STUDY METH-

The research study was carried out on 60 white non-inbred mature rats with initial body weight 230-250 gms, kept under standard vivarium conditions.

The rats were divided into 4 groups of 15 rats in each group for determination the potency of drug influence having antioxidant and antihypoxic properties (emoxypine and Mexidol) at course of adhesion in the abdominal cavity after modeling the process of peritoneal adhe-

Group 1 – the intact group (n = 15). The laboratory animals of this group were not subjected to adhesions and no drugs were administered to them. The lipid peroxidation and antioxidant defense measurements of the rats of this group were investigated for comparative assessment with the laboratory animals of other groups.

The other rats were included into the second, third and fourth groups. They experienced the modeling of the peritoneal adhesions. The midline laparotomy was performed under ether anesthesia in the conditions of experimental operating room. Then the removal of the serous membrane of the visceral peritoneum of the terminal segment of the small intestine situated 2 cm above the ileocecal angle, was performed with the help of gauze turunda up to the slight hyperemia and the capillary hemorrhage occurred over the whole circle of the intestine within 2 cm round. Further, the laparotomy wound

was sutured with the sterile non-absorbable capronic ligatures. All the laboratory animals in pre- and postoperative period were in the vivarium in equal conditions. The laboratory animals were devitalized by etherization's overdosage in 14 days after modeling of the peritoneal adhesions. After mortification the blood for research was taken by decapitation and the visual estimate of the adhesive process in the abdominal cavity was carried out.

Group 2 – the control group (n = 15)was used for comparative assessment of the postoperative therapy effectiveness with groups 3, 4. The laboratory animals were subjected to the modeling of the peritoneal adhesions of the peritoneum. After that during 7 days of the postoperative period the laboratory animals were administered abdominally as a single dose 2 ml of sterile physiological saline (NaCl 0, 89%).

In the third group (n = 15) the rats, after being modeled, were administered Mexidol (60mg/kg) abdominally as a single dose during 7 days of postoperative period.

The fourth group (n = 15) was composed by the rats, modeled to peritoneal adhesions. They were administered emoxypine (60mg/kg) abdominally as a single dose during 7 days of the postop-

In 14 days the laboratory animals after

being modeled to peritoneal adhesions were devitalized by etherization overdosage. On prosection of the abdominal cavity the intensity of the adhesive process was studied macroscopically (pic.1) according to the scoring system [9]: 0 general lack of commissurae; 1 score one commissura between the abdominal cavity organs or between the organs and the abdomen's wall; 2 scores - two commissurae between the abdominal cavity organs or between the organs and the abdomen's wall; 3 scores - more than two commissurae or the adhesive intestine loops, not connected to the abdomen's wall; 4 scores - abdominal cavity organs are directly connected by commissurae with the abdomen's wall despite the quantity of the commissurae.

The condition of the anti-oxidation system and the intensity of the lipidperoxidation reaction were measured in the blood according to the quantitative content of alpha-tocopherol (vit.E) in the blood serum of the laboratory animals under R.Zh.Kiselevich, C.S.I.Skvarko's method. The activity level of lipid-peroxidation process taking into account the quantity of diene conjugates in the blood was determined by I.D. Stalnaya's method (1972). The concentration of hydroperoxide of lipids was determined by L. A.Romanova, I.D. Stalnaya's method (1977) in E.A. Borodin's modification with co-authors (1992).

The segments of the visceral peritoneum of the intestine, earlier proned to the removal of the serous membrane, were taken out and fixed in 10% solution of formalin. Then the histodiagnosis was carried out with blocking in the wax and coloring in hematoxylin and in eosin.

The morphologic picture was supplied by the morphometric investigations which included the complex of criteria proposed by Poroyskiy S.V. and co-authors (2010), permitting to give the objective characteristics in absolute numbers [5].

The statistical processing of the results was carried out according to Student t-test with the use of the software Statistica 6.1.

RESEARCH RESULTS AND DISCUSSION

The results of macroscopical evaluation showed the decrease of the quantity of intra-abdominal commissurae in the laboratory animals which had been administered the named drugs in comparison with the control group (pic.1). However, the most advantageous prophylactic effect to the development of intra-abdominal commissurae was the use of Mexidol (pic.2). There were certain significant differences (p<0,05) between the data of the control group and experimental groups.

Table 1 demonstrates that the control group of laboratory animals (group 2) has

the highest level of adhesion in the abdominal cavity (3,53±0,5) in comparison with the laboratory animals which had been administered abdominally emoxypin (2,6±0,50) and Mexidol (1,8±0,41) at significant difference (p<0,001).

It was revealed that adhesive commissurae are mainly situated in the part of removal of serous membrane of the visceral peritoneum, forming predominantly viscerovisceral commissurae with the loops of the nearby intestines.

As it follows from the findings, significant decrease of the adhesions' intensity in the abdominal cavity is observed in the groups of laboratory animals which had been administered antioxidants after modeling of the peritoneal adhesions. Though the least level of the adhesive process at the macroscopical evaluation was marked in the groups of laboratory animals who had been administered Mexidol in the dosage 60mg/kg at the significant differences (p<0,001).

For studying the changes in the system of lipid-peroxidation and the state of anti-oxidant activity after peritoneal adhesions modeling in the postoperative period, the content of lipid-peroxidation system's constituents (diene conjugates – DC, hydroperoxide of lipids – HL) and antioxidant activity components (α -tocopherol and ceruloplasmin) were investigated on the 14th day in all the four groups of animals (n = 60).

Comparative characteristics of all the groups is observed in Table 3.

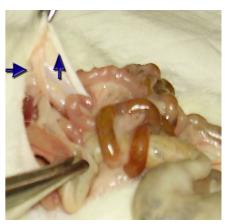
Table 3.

At determining the state of the anti-oxidant activity and the intensity of the lipid-peroxidation reactions on the 14^{th} day of the experiment the highest level of lipid-peroxidation products (p < 0,001) was observed in the blood serum of the control group of the laboratory animals in comparison with other groups: diene conjugates (82,06±10,40 nM/ml), hydroperoxide of lipids (35,40±5,12 nM/ml). At that antioxidant activity, α -tocopherol (43,32 ± 5,05 mcg/ml) and ceruloplasmin (30,58 ± 2,59 mcg/ml) levels were significantly lower than in other groups (p < 0,001).

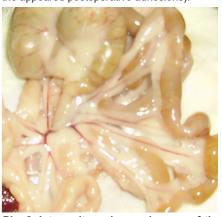
Highly mentioned changes of lipid-peroxidation and anti-oxidant activity proved the intensity of freely proceeding radical reactions and the decrease of the potential of the antioxidant defense of the laboratory animals of the control group in the comparative aspect with other groups of animals.

In the 4th group of rats, which were administered emoxypine 3% abdominally (60mg/kg), the content of lipid-peroxidation products during the postoperative period was significantly less p < 0,001 than in the 2nd group of laboratory animals (control group): diene conjugates (51,39 \pm 2,36 nM/ml), hydroperoxide of lipids (23,63 \pm 1,13 nM/ml).

At estimating the anti-oxidant activity it



Pic. 1. Intraperitoneal commissurae of the animal from the control group (arrows show the appeared postoperative adhesions).



Pic. 2. Intraperitoneal commissurae of the laboratory animal from the group which got Mexidol (insignificant deformity of the intestine in the area of the removal of serous membrane is seen, 14 days after peritoneal adhesions modeling)

Table 1

Characteristics of adhesions in different experimental groups

G	Experimental groups of			
Scores	animals			
	Group 2	Group 3	Group 4	
0 score (abs.)				
1 score (abs.)		3		
2 scores (abs.)		12	6	
3 scores (abs.)	7		9	
4 scores (abs.)	8			
Average (M ± m)	3,53±0,5	1,8±0,4	2,6±0,5	
$p_1 < 0.001;$				
$p_1 < 0.001;$ $p_2 < 0.001;$				
$p_3^2 < 0.001$				

Notes: p1 – significance of differences between the first and the second groups, p2 – significance of differences between the first and the third groups, p3 – significance of differences between the second and the third group

group. Was marked the increase of the alpha-to-copherol level (59,20 \pm 3,37 mcg/ml) and ceruloplasmin (36,56 \pm 1,44 mcg/ml) in the blood serum in comparison with the 2nd (control) group (p < 0,001). It implied

the decrease of activity of freely radical oxidation and the optimization of antioxidant activity after peritoneal adhesions' modeling on the background of emoxypine administration.

In the group of the laboratory animals which were abdominally administered Mexidol 5% in a dose 60mg/kg, the statistical significant (p < 0,001) decrease (in comparison with the animals of the control group) of intensity of free radical oxidation was also investigated, DC (50,94 ± 7,40 nM/ml), HP (21,63 ± 1,82 nM/ml) approximating to the figures of the 1st group of animals (intact): DC $(52,03 \pm 4,40 \text{ nM/ml})$ and HP(20,63 ± 1,84 nM/ml). At comparing the lipid-peroxidant products with the figures of the third experimental group (emoxypine), the significant decrease was marked (p< 0,005) HP (21,63 ± 1,82 nM/ml).

At estimating the antioxidant activity in the 3rd group (Mexidol) the highest increase of the quantitative content of alpha-tocopherol (65,16 ± 4,60mcg/ml) and ceruloplasmin(37,20 ± 1,43 mcg/ml) was observed. At that, alpha-tocopherol level was significantly higher than the same figure of the 1st (intact) and the 4th (emoxypine) groups (p<0,001).

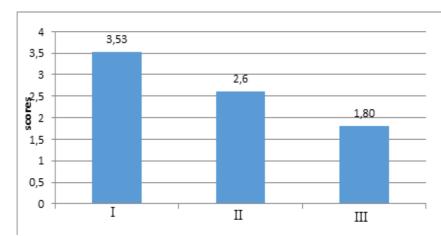
Analyzing the obtained results of the condition of antioxidant defense, it's clearly seen that in all experimental groups in relation to the control group, the lipid-peroxidation level decreases, and the quantitative content of vit.E and ceruloplasmin increases. That indicates the optimization of the antioxidant defense at animals given antioxidant drugs.

At histologic examination in the medicines, the dynamics of morphological changes of the defect of the serosal sheet was evaluated. The morphological pattern was supplied by the morphometric research, which included the complex of criteria proposed by Poroyskiy S.V. and co-authors. These criteria permit to give the objective characteristics in absolute numbers. The results are performed in the table 4.

The animals of the second group (control) had 10 ± 1,60 kl/mm mesothelial cells at the area of the visceral peritoneum subjected to the removal of the serous membrane. Its quantity was accurately less (p< 0,001) than in other experimental groups of animals.

The thickness of the peritoneum amounted up to 60,86 ± 3,27 µm, obtaining the largest value in comparative aspect (p< 0,001) and accompanied by the apparent lymphohysteocytic infiltration.

The above listed changes indicate to more intensive inflammatory process and overdevelopment of the fibrosis of the connective-tissue basis of the abdominal membrane in the postoperative period at the areas of the peritoneum subjected to the removal of the serous membrane in the laboratory animals of this group.



Pic. 3. The results of the macroscopical evaluation (in accordance to the grading scale) of the level of adhesive process strength in the abdominal cavity of the control group (I) at the background use of emoxypine (II), Mexidol (III).

Lipid-peroxidation and antioxidant activity characteristics of different experimental groups

S	Experimental groups of animals (n = 15 in each group)			
Scores (M ± m)	1 st (intact)	2st (control)	3st (Mexidol)	4st (emoxypine)
Diene Conjugates (DC) nM/ml	52,03±4,40	82,06±10,40	50,94±7,40	51,39±2,36
Hydroperoxides (HP) nM/ml	20,63±1,84	35,41±5,12	21,63±1,82	23,63±1,13
Ceruloplasmin mcg/100 ml	40,66±3,57	30,58±2,59	37,20±1,43	36,56±1,44
Vitamin E mcg/ml	51,04±4,17	43,32±5,05	65,16±4,60	59,20±3,37
	$\begin{array}{c} p_1 < 0.001 \\ p_2 = 0.62 \\ p_3 = 0.64 \\ p_4 < 0.001 \\ p_5 < 0.001 \\ p_6 = 0.83 \end{array}$	$\begin{array}{c} p_{1.1} < 0,001 \\ p_{1.2} < 0,001 \\ p_{1.3} = 0,13 \\ p_{1.3} < 0,001 \\ p_{1.5} < 0,001 \\ p_{1.5} < 0,005 \end{array}$	$\begin{array}{l} p_{2.1} < 0,001 \\ p_{2.2} < 0,001 \\ p_{2.3} < 0,005 \\ p_{2.4} < 0,001 \\ p_{2.5} < 0,001 \\ p_{2.5} = 0,21 \end{array}$	$\begin{array}{c} p_{3.1} < 0.001 \\ p_{3.2} < 0.001 \\ p_{3.3} < 0.001 \\ p_{3.3} < 0.001 \\ p_{3.4} < 0.001 \\ p_{3.5} < 0.001 \\ p_{3.5} < 0.001 \end{array}$

Примечание. Достоверность различий уровня ДК между группами: р₁ – 4-й и 1-й, р₂ 1 примечание. Достоверноств различии уровня ДІС между группами. $p_1=4$ -и и 1-и, $p_2=4$ -и и 2-й, $p_3=4$ -й и 3-й, $p_4=1$ -й и 2-й, $p_5=1$ -й и 3-й, $p_6=2$ -й и 3-й; уровня ГП: $p_{1.1}=1$ -между 4-й и 1-й, $p_{1.2}=4$ -й и 2-й, $p_{1.3}=4$ -й и 3-й, $p_{1.4}=1$ -й и 2-й, $p_{1.5}=1$ -й и 3-й, $p_{1.6}=2$ -й и 3-й; уровня церулоплазмина: $p_{2.1}=1$ -между 4-й и 1-й, $p_{2.2}=4$ -й и 2-й, $p_{2.3}=4$ -й и 3-й, $p_{2.4}=1$ -й и 2-й, $p_{2.5}=1$ -й и 3-й, $p_{2.6}=2$ -й и 3-й; уровня витамина Е: $p_{3.1}=1$ -между 1-й и 2-й, $p_{3.2}=1$ -й и 3-й, $p_{3.3}=1$ -й и 4-й, $p_{3.4}=1$ -й и 3-й, $p_{3.5}=2$ -й и 4-й, $p_{4.6}=3$ -й и 4-й.

Table 3

The rates of morphometry of the visceral peritoneum of the small bowel at experimental animals

	Experimental groups of rats ($n = 15$ in each			
Scores	group) 2st 3st 4st			
$(M \pm m)$	2^{st}	3 st	4 st	
,	(control)	(Mexidol)	(emoxypine)	
Thickness of the peritoneum (μm)	60,86±3,27	48,86±1,74	51,36±4,10	
Number of density of mesotheliocytes (1 kl/mm)	10±1,60	18,86±2,50	13,86±1,95	
Average diameter of the mesotheliocytes' cores (um)	7,40±0,55	8,94±0,36	8,07±0,56	
The rate of the shape of the surface	1,64±0,19	$1,32\pm0,18$	1,46±0,16	
$ \begin{array}{c} p_1 < 0.001 \\ p_2 = 0.001 \\ p_3 = 0.05 \end{array} $	$\begin{array}{c} p_{1.1} < 0.002 \\ p_{1.2} = 0.001 \\ p_{1.3} = 0.001 \end{array}$	$\begin{array}{c} p_{3.1} < 0.011 \\ p_{3.2} < 0.001 \\ p_{3.3} < 0.039 \end{array}$	$\begin{array}{c} p_{2.1} < 0.002 \\ p_{2.2} < 0.001 \\ p_{2.3} < 0.001 \end{array}$	

Примечание. Достоверность различий уровня толщины брюшины между группами: р₁ — 2-й и 3-й, р₂ — 2-й и 4-й, р₃ — 3-й и 4-й; р_{1.1} — 2-й и 3-й, р_{1.2} — 2-й и 4-й, р_{1.3} — 3-й и 4-й; р_{2.1} — 2-й и 3-й, р_{3.2} — 2-й и 4-й, р_{3.3} — 3-й и 4-й. The average diameter of the mesotheliocytes' cores was 7,40 \pm 0,55 μm that statistically was less (p< 0,05) than in animals of other groups. This fact pointed out to the hypoactivity of the metabolic processes in the mesothelial cells.

The rate of the shape of the surface at rats of the 1st group was 1,64± 0,19 and it was higher in comparison with other groups of animals (p< 0,05). It is the characteristic of the more intensively proceeding inflammatory process, leading to the deformation of the peritoneum after modeling of the peritoneal adhesions

The laboratory animals of the 4^{th} group which were abdominally administered emoxypine 3% after being modeled to the peritoneal adhesions had the density of mesotheliocytes equal to 13.86 ± 1.95 kl/mm, at the areas of the peritoneum subjected to the removal of the serous membrane. It was 27.5% more (p = 0.000002) than in the 2^{nd} group (control).

The thickness of the peritoneum was $51,36 \pm 4,10 \, \mu m$, that was 15,6% less in comparison with the 2^{nd} (control) group (p < 0,001). Besides, the decrease of lymphogranulecytic infiltration in comparative aspect with the animals of the 2^{nd} group was observed.

The average diameter of the mesotheliocytes' cores was $8.07\pm0.56~\mu m,~13\%$ higher than in the 2^{nd} group of animals (control) (p< 0.05).

The animals of the 2^{nd} group had the rate of the surface shape 11% less in comparison with the 1^{st} group and composed $1,46\pm0,16~\mu m$ (p< 0,05).

Pic.5

The laboratory animals of the 3^{rd} group, which got Mexidol 5% abdominally, had the density of mesothelial cells in the areas with removed serous membrane at an average $18,86 \pm 2,50$ kl/mm. It exceeded 46,9% (p < 0,001) the rates of the 2^{nd} group (control) and 26,5% the rates of the 4^{th} group (emoxypine) of animals (p = 0,001).

The thickness of the area of the peritoneum with the removed serous membrane induced 48,86 \pm 1,74 μ m that 24,5% is less than in the 1st group (p < 0,001) and 5,1% less than in the 4th group (emoxypine) of animals (p < 0,05).

The average diameter of the mesotheliocytes was $8.9 \pm 0.4 \mu m$, 16.8 % higher than un the animals of the 1st group (p < 0,001)and 9,7% larger than the rates of the 2nd group with the 2nd group (p < 0,001).

The rates of the shape of surface was $1,32 \pm 0,2$ and 9,6% less than the results of the 2^{nd} group (p < 0,05) and 19,5% less than the results of the 1^{st} group (p < 0,001).

The resulting data point to the higher reparative potential of the mesotheliocytes, characterized by the rising of the cores' diameter and the density of the cells at the areas with the removed serous membrane within the animals of the 3rd group.

An additional point is that the least observed thickness and deformation on the damaged areas of the abdominal membrane of the animals of the 3rd group may be regarded as the evidence of the low intensively proceeding inflammatory reactions in the areas of the peritoneum subjected to the removal of the serous membrane in the postoperative period.

Pic. 6.

Analyzing the obtained morphometric results, it's evident that the most propitious picture is observed at laboratory animals which got Mexidol abdominally.

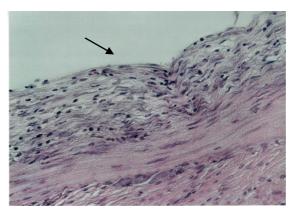
CONCLUSIONS

The administration of the studied antioxidants by the laboratory animals in accordance to our data significantly decreases the appearance of the adhesions in the peritoneum in early operative period.

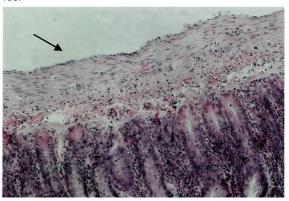
The abdominal administration of the Mexidol in a dose of 60 mg/kg in comparative aspect mainly conduces the regeneration of the mesothelial cells, optimization of the rates of the antioxidant system and the significant decrease of adhesions' degree.

Thus, we demonstrated experimentally the way of excessive adhesion's prevention in the abdominal cavity. In the comparative aspect, it was elucidated that mainly Mexidol 5% (60mg/kg) at abdominal administration conduces the decrease of adhesion level, the decrease of the inflammatory processes, the fall of lipid - peroxidation activity. Antioxidants possess antianginal, anticoagulation, membrane - stabilizing and immunostimulatory activities in varying degrees. Despite the absence of the unified theory of peritoneal adhesions' development, it can be supposed that antioxidative therapy influences

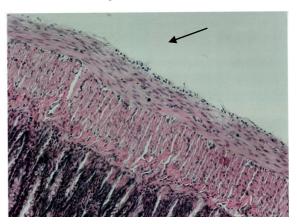
one of the main parts of adhesion. It's the perspective way in the combination therapy and precaution of the peritoneal adhesions.



Pic. 4. Regeneration of the area of the rat's peritoneum subjected to the removal of the serous membrane. The control group. The distorted area of the peritoneum is pointed by the arrow. Hematoxylin and eosin stain. Enlargement: 400.



Pic. 5. Regeneration of the area of the rat's peritoneum subjected to the removal of the serous membrane. Emoxypine was administered. Soft areas of the abdominal membrane's deformation are denoted. The stratum of the mesothelial cells is demonstrated by the arrow. Hemotoxylin and eosin stain. Enlargement: 100.



Pic. 6. Regeneration of the area of rat's peritoneum subjected to the removal of the serous membrane. Mexidol was administered. The stratum of the mesothelial cells is demonstrated by the arrow. Hemotoxylin and eosin staining. Enlargement: 400.

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TRAUMATIC NEUROPATHY OF THE SECOND BRANCH OF THE TRIGEMINAL **NERVE**

ABSTRACT

This research describes the etiology, possible pathogenesis, symptoms and treatment of neuritis of the second branch of the trigeminal nerve which resulted from traumatic damage or postoperative period. To some extent it is bound to the fact that during the last period there are patients with inflammation of the second branch of trigeminal nerve after maxillary sinusotomy, periostitis operation and teethpreserving operations of the upper jaw, especially in the anterior area. At the same time, there are cases of injury of peripheral nerves of the second branch of trigeminal nerve at endodontic treatment of caries complications due to deduction of filling material for the tooth apex in bone tissues and genyantrum. As a rule, the neuritis of the second branch of trigeminal nerve is followed by pain, numbness, paresthesia and sensitivity disorder in the upper lip, lower eyelid, upper cheek part, teeth of the upper jaw, Highmore's sinus, lateral area of the face, etc. Sometimes patients with postoperative or posttraumatic neuropathy of the second branch of trigeminal nerve are taken for simulators or patients with unhealthy state of mind as a clinical picture is rather poor. The desquamation of mucosa epithelium, friability and gingiva bleeding, etc. that indicated trophic frustration in innervation zone take place in the long neuropathy course among some patients.

Authors suggested a complex treatment of this pathology. At the same time the standard treatment of neuritis begins with elimination of the cause of illness: stopping of local inflammatory process, removal of filling material from periapical area, etc. Meanwhile, at this pathology the main thing was weakening or the complete elimination influence of the scar tissue shrouding the nervous trunk (compression, trophy disorder, etc.). Glucocorticosteroid drugs were injected into tissues around the scar on the transitory fold of the upper jaw and also medicinal electrophoresis was done on the scar area. Non- narcotic analgetics were administered for pains. According to indications patients received antihistamine medicines, tranquilizers, neuroleptics, antidepressants, etc additionally. At the same time it was established that the earlier treatment of young scars began, the more successful was therapy of postoperative neuritis.

The research results have testified its effectiveness.

Keywords: neuritis of the second branch of trigeminal nerve, etiology, pathogenesis, symptoms, treatment.

INTRODUCTION

According to ICD-10 the neuritis of trigeminal nerve heads a group of diseases of this pair of craniocereberal nerves. The neuritis of trigeminal nerve is a disease of inflammatory character which af-

fects branches of trigeminal nerve. It is shown by the severe paroxysmal pain in innervation zones and considerably reduces quality of life of the patient.

There are not so many causes of inflammation of trigeminal nerve. Often the neuritis of trigeminal nerve appears as a result of the postponed infectious diseases (meningitis, tuberculosis, flu, syphilis, herpetic infection), frost, trauma, toxic influence, and also can be provoked by inflammatory diseases of teeth