CLINICAL AND IMMUNOLOGICAL ASSESSMENT OF SYSTEMIC ENZYME THERAPY EFFICIENCY IN THE TREATMENT OF MAXILLOFACIAL FURUNCLES AND CARBUNCLES

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In this article Furuncles and carbuncles are described, which are one of the most common diseases of maxillofacial region. In this regard, searching and testing of the new methods of furuncles and carbuncles treatment of maxillofacial region, problem of decrease in side effects of therapy is very actual. The modern, quickly developing therapy method at the immunopathological states and diseases connected with violation of immunity and a hemostasis is the systemic enzyme therapy of pyo-inflammatory processes including internal organs. The system and combined application of wobenzym for patients with maxillofacial region furuncles and carbuncles were followed in dynamics of treatment unlike antibacterial therapy by quantity increase of lymphocytes CD4+, by decrease of the complement activity and quantity of soluble fibrin-monomeric complexes.

Keywords: furuncles and carbuncles, pyo-inflammatory pathology, fibrin-monomeric complex, lymphocyte, wobenzym, therapy, leucocytes migration

Furuncles and carbuncles are one of the most common diseases of maxillofacial region, ranking the first place among neodontogenic pyo-inflammatory pathologies of maxillofacial region [4]. The high frequency of furunculosis and its recurrent course are largely due to immune deficiency which contributes to the rapid development of bacteremia with maxillofacial furuncles and carbuncles [6].

Numerous works are devoted to research of cellular and humorial immunity at furunculosis [5]. Considering the leading role of the immune system reactions in furunculosis pathogenesis, its antibacterial therapy, a use of immunomodulators in this disease is proved.

In furunculosis the positive effects of specific immune preparations are noted: staphylococcal anatoxin, antifagin, anti-staphylococcal plasma, antibacterial antilimpholine, staphyloprotectin, tomycidum [1]. Also immunomodulators, sorbents and proteolytic enzymes are effective: Tactivin, myelopidum, tagansorbent, differin, galavit, polyoxidonium, imosimasum [2]. However, action of immunoactive preparations is studied insufficiently in pyo-inflammatory diseases of maxillofacial region where owing to person's anatomical topographical features the disease quickly progresses and the risk of development of complications is high.

In this regard, searching and testing of the new methods of furuncles and carbuncles treatment of maxillofacial region, problem of decrease in side effects of therapy is very actual. The modern, quickly developing therapy method at the immunopathological states and diseases connected with violation of immunity and a hemostasis is the systemic enzyme therapy of pyo-inflammatory processes including internal organs. The preparation of the systemic enzyme therapy with wobenzym has anti-inflammatory, antiedematous, immunomodulatory and fibrinolytic effects [3].

Due to the above, in pyo-inflammatory diseases of maxillofacial region the carrying out of the researches allowing to assess the clinical and immunological efficiency of enzyme therapy of maxillofacial region furuncles and carbuncles is proved.

Examination and treatment results of 244 patients, from them with abscessed boils – 96 (39,3%), with recurrent boils (RB) – 86 (35,3%) and carbuncles – 62 patients (25,4%) are reflected in work. Patients aged from 18 till 65 years, including from 20 to 30 years (32,1%) and from 31 to 40 years (42,0%), from them 149 men (61,1%) and 95 women (38,9%) were observed.

Clinical examination of patients with maxillofacial region furuncles and carbuncles was being carried out from 2012 to 2015 on the basis of Maxillofacial Surgery Department of JSC «Astana Medical University» and further in out-patient conditions during clinical supervision of patients.

The examined patients taking into account the treatment methods have been divided into 3 groups (Table 1). Traditional therapy included prescription of an antibiotic after determination of sensitivity to it (gentamycinum of 120 mg a day), vitamins (Vit. B1, B6), deintoxication (haemodesum, saline) and desensibilizing therapy, local treatment by opening of an abscess, processing of a wound by an antiseptic, introduction of a drainage and daily

bandages with hypertensive solution. The systemic enzyme therapy (SET) assumed administration of wobenzym on 5 dragees 3 times a day within 2 weeks to the patient with maxillofacial region furuncles and carbuncles. The patients with recurrent boils in an aggravation stages were administered wobenzym on 5 dragees 3 times a day within 2 weeks and further on 3 dragees 3 times a day up 2 months.

Table 1

Distribution of patients depending on the carried-out therapy

Clinical form	Antibiotic therapy (ABT)	ABT + systemic enzyme therapy (SET)	ABT + SET and local enzyme therapy
Abscessed furuncle	33	35	28
Carbuncle	20	21	21
Recurrent furuncle	32	23	31

Local treatment of patients with the complicated course of disease assumed opening of an abscess, processing of a wound with antiseptic and introducing wobenzym in the form of powder on 240 mg. The wound was closed with the sterile napkin moistened with saline. Bandaging was carried out daily in the presence of purulent discharge from wound.

30 healthy people were examined for control. Primary examination was carried out on the first day of hospitalization, further in 10–12 days, the third was during process subsiding (in 1,5 months).

The indicators of total of T- and V-lymphocytes in peripheral blood were determined at all patients by the Jondal et.al method. (1972); subpopulations of T-lymphocytes (T_x, T_c) were defined by Limatibul et.al. (1978), and also with use of monoclonal antibodies to CD3+, CD4+, CD8+, CD20+ lymphocytes, a cages coloring technique in the immunofluorescent test of Sorbent LLP, the immunoregulatory index (CD4+/CD8+), the results were compared and they were more exact in determination with the use of monoclonal antibodies, but clinical manifestations of process reflected the changes of laboratory indicators, the content of A, M, G immunoglobulins (Mancini G., 1965), the circulating immune complexes (CIC) by Haskowa (1972). A factor level of the braking migration of leucocytes (BML) in leucocytes migration inhibiting reaction with staphylococcal allergens (Artyomova A.G., 1973), hemolytic activity of a complement on 50 % to hemolysis, phagocytosis and phagocytic number were also considered (Stenko M.I., 1975). The system indicators of a hemostasis were estimated on fibrinolysis research (Eremin G.F., et al. 1982), ristomycin induced aggregation of platelets (RIA) according to A.S. Shitikova (1982), fibrinogen (Rutberg R.A., 1984), the maintenance of soluble fibrin-monomeric complexes (SFMC) in using the phenanthroline test (Hawigen J., 1970).

Statistical processing of material was carried out by means of the software package of "Statistic 5.7" by the standard techniques of variation statistics with an assessment of results reliability, a confidential interval by Student criterion and by the method of the correlation analysis according to Pearson.

Research results and their discussion:

The indicators analysis of immune system of patients with maxillofacial furuncles and carbuncles has shown that they have reduced absolute quantity of CD3+ of lymphocytes in comparison with control (Table 2), at the same time the lymphopenia was characteristic of patients with recurrent furuncle ($p < 0,05$). The absolute quantity of CD4+ of lymphocytes has been authentically reduced in comparison with control at patients with recurrent furuncle ($p < 0,05$).

Sensibilization study to a specific antigen has revealed strengthening of the phagocytes migration factor (PMF) – producing activity of cells in response to staphylococcal allergen at patients with carbuncle and recurrent furuncle, at the same time the most expressed sensibilization was at recurrent furuncle ($p < 0,01$).

Research of humoral immunity indicators has revealed relative increase in quantity of CD20+ of lymphocytes at patients with carbuncle and IgG content increase in comparison with control at patients with maxillofacial region furuncles ($p < 0,05$). The CIC maintenance was reliable above control irrespective of a clinical form of a disease, at the same time increase of the CIC concentration happened in weighting process and synchronization process.

Phagocytosis indicators authentically exceeded control at patients with furuncles on

the face whereas the phagocytic cells quantity was 1,3 times lower than control at patients with carbuncle and recurrent furuncle. Phagocytic number increase was also registered at patients with furuncles ($p < 0,05$), at the same time at patients with recurrent furunculosis it authentically decreased. At patients with carbuncle and recurrent furuncle the increase of complement activity was noted in comparison with control, at the same time the highest rates were registered at patients with recurrent furunculosis.

Platelets increase was noted at patients with furuncles in comparison with control group whereas its decrease was observed at patients with recurrent furunculosis. Fibrinogen concentration increase was the highest in comparison with control at patients with recurrent furunculosis ($p < 0,05$). In the same group of patients the lowest level of ristomin induced aggregation of platelets was noted ($p < 0,05$). Blood concentration of soluble fibrin – monomeric complexes at patients with maxillofacial region furuncles and carbuncles was high irrespective of a clinical form of a disease. Time lengthening of fibrinolysis was noted at patients with maxillofacial carbuncle and recurrent furunculosis.

Table 2

Indicators of immunity and hemostasis system of patients with maxillofacial region furuncles and carbuncles

Options	Healthy people	Furuncules	Carbuncules	RF
Lymphocytes, $\cdot 10^9$/l	1850 ± 59,9	1902 ± 19,2	1736 ± 27,1	1649 ± 18,6*
$CD3^+$ lymphocytes, %	40,10 ± 1,63	31,70 ± 0,49**	34,87 ± 0,77*	39,68 ± 0,57
exam. p. $\cdot 10^9$/l	742 ± 23,0	604 ± 5,74**	606 ± 8,93**	654 ± 7,00**
$CD4^+$ lymphocytes, %	21,79 ± 1,37	21,37 ± 0,42	22,54 ± 0,68	22,63 ± 0,48
exam. p. $\cdot 10^9$/l	403 ± 11,6	407 ± 3,69	391 ± 5,44	373 ± 3,71*
$CD8^+$ lymphocytes, %	10,70 ± 2,62	10,77 ± 0,32	11,39 ± 0,47	11,95 ± 0,34
exam. p. $\cdot 10^9$/l	198 ± 4,64	205 ± 2,52	198 ± 4,53	197 ± 3,41
$CD4^+/CD8^+$	2,03 ± 0,47	1,98 ± 0,10	1,97 ± 0,13	1,89 ± 0,14
LIR, migration index	0,91 ± 0,07	0,96 ± 0,06	0,71 ± 0,06*	0,54 ± 0,05**
$CD20^+$ lymphocytes, %	11,18 ± 0,41	11,14 ± 0,21	12,50 ± 0,20*	11,46 ± 0,96
exam. p. $\cdot 10^9$/l	207 ± 10,2	212 ± 12,0	217 ± 14,2	189 ± 11,0*
IgA g/l	1,92 ± 0,45	1,55 ± 0,12	1,36 ± 0,18	1,21 ± 0,12
IgM g/l	1,86 ± 0,45	2,04 ± 0,14	1,78 ± 0,21	1,45 ± 0,13*
IgG g/l	12,40 ± 1,09	14,89 ± 0,37*	13,50 ± 0,56	10,32 ± 0,35
CIC, conven.units	72 ± 9,10	136 ± 12,3*	163 ± 14,2**	220 ± 23,0**
Phagocytosis, %	49,8 ± 1,67	58,0 ± 0,51**	38,9 ± 0,79**	39,4 ± 0,57**
Phagocytosis numbers	4,12 ± 0,67	5,84 ± 0,24*	3,52 ± 0,30	2,32 ± 0,18*
Complement, %	40 ± 1,63	40 ± 0,51	45 ± 0,80*	50 ± 0,58**
Thrombocytes $\cdot 10^9$/l	253 ± 6,56	278 ± 2,31*	261 ± 3,30	231 ± 2,02*
IAR	16,7 ± 1,24	15,5 ± 0,38	14,7 ± 0,58	13,3 ± 0,40*
Fibrinogen, g/l	2,88 ± 0,56	4,09 ± 0,20*	4,11 ± 0,32	4,41 ± 0,23*
SFMC, mcg/ml	37,3 ± 1,61	46,4 ± 0,51**	47,2 ± 0,80**	47,0 ± 0,57**
Fibrinolysis,min	4,50 ± 0,70	5,30 ± 0,10	7,30 ± 0,41*	8,80 ± 0,32**

Note. * – reliability of distinctions with control ($p < 0,05$), ** ($p < 0,01$).

Thus, at the examined patients irrespective of a clinical form of a disease the low maintenance of CD3+ of lymphocytes, increase of soluble fibrin-monomeric and circulating immune complexes were registered. At the same time, sensibilization dependence to staphylococcal allergen from the number of the CIC (respectively $r = 0,4$ and $r = 0,5$), from the maintenance of CD3+ of lymphocytes ($r = –0,39$ and $r = –0,41$) and from phagocytic number is revealed ($r = –0,37$ and $r = –0,39$) only at patients with carbuncle and recurrent furunculosis. Number feedback of the CIC from PN ($r = –0,43$ and $r = –0,41$), positive correlation of the CIC level from activity of a complement is revealed ($r = 0,36$ and $r = 0,43$) in the same groups of patients.

Clinical efficiency of wobenzym at maxillofacial furuncles and carbuncles was estimated on terms of decrease in symptoms of intoxication, body temperature, time of an epithelization of furuncles and carbuncles (decrease in hypostasis and hyperaemia, clarification of a wound from purulent separated wound); on development frequency of the next complications and remote recurrence, at the same time indicators of ESR and quantity of leucocytes in peripheral blood were considered.

System and local application of a wobenzym for patients with maxillofacial region furuncles and carbuncles provided reliable reduction of intoxication symptoms in comparison with traditional therapy. So, after a wobenzym therapy of patients with maxillofacial furuncles and carbuncles, duration of symptoms, intoxications were authentically less in comparison with antibiotic treatment, temperature was normalized on average for 2 days in comparison with traditional treatment earlier ($p < 0,05$). Epithelization of a wound at the patients treated with wobenzym happened earlier than at the patients who have received traditional therapy (Table 3).

Combined (system and local) application of wobenzym has yielded the best immediate results of treatment in comparison with an antibacterial and systemic enzyme therapy (wobenzym per os).

Phlebitis of a facial vein (Table 4) was the most frequent complication developing at the examined patients. The patients treated by wobenzym had a phlebitis frequency considerably less than at the patients who have received antibiotic treatment ($p < 0,05$), and the smallest number of phlebitis is registered at the patients who have received combined (system and local) treatment of wobenzym ($p < 0,05$ in comparison with a systemic enzyme therapy).

After three months examination the frequency of recurrence in group of the patients treated with a systemic enzyme therapy and with the combined method of treatment (Table 5) was respectively 1,62–1,75 times less than in group of the patients who have received antibacterial therapy ($p < 0,05$). In 2 years examination results of the combined (system and local) treatments with wobenzym were much better than the results of one systemic enzyme therapy and antibacterial treatment ($p < 0,05$).

Clinical efficiency of wobenzyn was confirmed by assessment results of the immune status and system of a hemostasis in treatment dynamics of patients with maxillofacial region furuncles and carbuncles.

The cellular immunity study at patients with maxillofacial region furuncles and carbuncle has revealed the quantity increase of CD3+ of lymphocytes after systemic enzyme therapy and combined (system and local) applications of wobenzym ($p < 0,05$). The maintenance of CD4+ of lymphocytes increased in dynamics of treatment with wobenzym at patients with carbuncles and recurrent furunculosis ($p < 0,05$), after antibiotic treatment the quantity of CD4+ of lymphocytes authentically didn't change or, on the contrary, decreased at patients with maxillofacial carbuncle ($p < 0,05$).

Table 3

Wound epithelization terms (in days) at patients with maxillofacial region furuncles and carbuncles

	Group of patients depending on therapy		
	Antibiotic therapy (ABT), $n = 85$	ABT + SET, $n = 79$	ABT + SET + local Wobenzym, $n = 80$
Furuncle	7,7 ± 0,43	6,1 ± 0,31*	5,2 ± 0,32#
Carbuncle	10,8 ± 0,60	8,4 ± 0,42*	7,1 ± 0,45#
RF	9,2 ± 0,62	6,7 ± 0,54*	5,3 ± 0,34#

Note.* – difference with ABT ($p < 0,05$), # – difference with a group of patients who took antibiotics and systemic enzyme therapy ($p < 0,05$).

Table 4

Development frequency of phlebitis at maxillofacial region furuncles and carbuncles depending on a way of treatment

Clinical form	Group of patients depending on therapy								
	Antibiotic therapy (ABT), *n* = 85		ABT + SET, *n* = 79				ABT + SET + local enzyme therapy, *n* = 80		
	Total	Number of rec. exam. p.	Total %		Number of rec. exam. p.	%	Total	Number of rec. exam. p.	%
Furuncle	33	6	18,2	35	3	8,57	28	1	3,57
Carbuncle	20	4	20	21	3	14,2	21	2	9,52
RF	32	4	12,5	23	2	8,69	31	1	3,22

Table 5

Repeated development frequency of furuncles in patients with RF within the 3rd month and 2 summer supervision depending on the carried-out therapy (%)

Recurrence time	ABT, *n* = 32		ABT + SET, *n* = 23		ABT + SET + local enzyme therapy, *n* = 31	
	exam. p.	%	exam. p.	%	exam. p.	%
In 3 months	9	28,2	4	17,4	5	16,1
In 2 years	14	43,7	5	21,7	4	12,9

A decrease in the PMF – producing activity of leucocytes in response to staphylococcal allergen after systemic enzyme therapy and combined (system and local) applications of wobenzym was noted ($p < 0,05$) at patients with carbuncle and recurrent furunculosis. Reliable increase of lymphocytes CD20+ quantity and activity of a complement is revealed in treatment dynamics by antibiotics at patients with maxillofacial region furuncles. Complement activity increased after antibacterial treatment at patients maxillofacial region carbuncles. The system and combined enzyme therapy irrespective of a clinical form of an illness caused decrease of the complement activity ($p < 0,05$).

Application of wobenzym led to decrease in level of the CIC ($p < 0,01$) at the examined patients. Increase of phagocytosis and decrease in the CIC were reliable at the patients treated by combined (system and local) application of wobenzym irrespective of a clinical form of an illness.

The indicator of intravascular blood clotting (SFMC) authentically decreased after the combined enzyme therapy irrespective of a clinical form of an illness. Decrease in time of a fibrinolysis has been noted in group of patients with maxillofacial region carbuncles and recurrent furunculosis, accepting wobenzym ($p < 0,05$).

Thus, the system and combined application of wobenzym for patients with maxillofacial region furuncles and carbuncles were followed in dynamics of treatment unlike antibacterial therapy by quantity increase of lymphocytes CD4+, by decrease of the complement activity and quantity of soluble fibrin-monomeric complexes. Decrease in fibrinolysis and the PMF – producing activity of leucocytes on staphylococcal allergen were noted at patients with carbuncle and recurrent furunculosis after treatment with wobenzym.

In the conclusion, the combined (system and local) treatment with wobenzym unlike system and antibacterial therapy led to decrease in the CIC and increase of phagocytosis irrespective of a clinical form of a disease. These changes of the immune status and a hemostasis at the patients who have received wobenzym contributed to reliable improvement of the next and further outcomes of therapy in comparison with antibacterial treatment.

References

1. Akhtamov M.A., Bystritskaya T.F., Katkhanov A.M., Sultanova N.K., Samgin M.A., et al. The positive effects of specific immune preparations staphylococcal anatoxin, antifagin, anti-staphylococcal plasma, antibacterial antilimpholine, staphyloprotectin, tomycidum. – 2002.

2. Golshmid V.K., Karibayeva A.T., Davletbayev M.Zh., Monakhov S.A., Sherbakova O.A. Immunomodulators, sorbents and proteolytic enzymes are effective: Tactivin, myelopidum, tagansorbent, differin, galavit, polyoxidonium, imosimasum. – 2003.

3. O'Dell M.L., Nouza Z., et al. The preparation of the systemic enzyme therapy with wobenzym. –1999.

4. Robustova T.G. Neodontogenic pyo-inflammatory pathologies of maxillofacial region. – 2000.

5. Savitskaya, L., Setdikova N.H., Oliferchuk N.S. et al. Cellular and humorial immunity at furunculosis. – 2005.

6. Shargorodskiy N.T., Nau G. Development of bacteremia with maxillofacial furuncles and carbuncles. – 2002.