

# Assessment of the Risk of Development Accidents in Odontogenic Pyoinflammatory Diseases

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## Abstract

**Aim:** For full-fledged diagnostics and prognosis of the course of odontogenic infectious diseases, we should have information about main pathogenetically significant factors of species and adaptive immunity, and we also need to take into account the characteristics of etiological agents. **The aim of the research:** To reveal the main factors of the complicated course of odontogenic pyoinflammatory diseases of the maxillofacial area. **Results:** The most significant indicators, which were studied in this research, during expectancy of course of the odontogenic pyoinflammatory diseases of the maxillofacial area are as follows: (a) Low level of intracellular production of radicals; (b) low level of antioxidant capacity of blood plasma of patients on the second day of hospitalization; (c) high level of cytokines of the proinflammatory group (interleukin-1 $\beta$  [IL-1 $\beta$ ], IL-6, tumor necrosis factor alpha [TNF- $\alpha$ ]) and low level of IL-10 in the blood plasma of patients during first day of hospitalization, which remaining for 7–10 days against the background of the ongoing therapy; (d) low concentration of TNF- $\alpha$  in the blood plasma of patients with acute odontogenic osteomyelitis on the first day of hospitalization; (e) a considerable proportion of strictly anaerobic pathogens as a part of the mixed microflora of a purulent discharge. **Conclusions:** The most significant risk factors for accidents in odontogenic pyoinflammatory diseases include such as disturbance of effector properties of leukocytes, imbalance of mediator regulation of inflammation, and predominance of strictly anaerobic microflora.

**Key words:** Abscess, antioxidant capacity of plasma, cytokine profile, osteomyelitis, phlegmon, radical formation

## INTRODUCTION

The expectancy of the course of pyoinflammatory processes in the maxillofacial is rather important problem in the dentistry due to the high prevalence and the possibility of developing serious accidents.<sup>[1,2]</sup> According to some authors, the proportion of patients with pyoinflammatory diseases is about 60% in the general structure of disease incidence of maxillofacial in-patient hospitals and, besides, it has a tendency to increase.<sup>[3]</sup> Secondary immunodeficiency in

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inflammatory diseases of the maxillofacial area is not a controversial topic, and it is proved by literary data.<sup>[2,4-7]</sup>

For full-fledged diagnostics and prognosis of the course of odontogenic infectious diseases, it is necessary to have data about main pathogenetically significant factors of species and adaptive immunity, taking into account the characteristics of etiological agents. One of the main functions of leukocytes is the formation of free radicals. Intensive generation of reactive oxygen species is powerful antimicrobial factor in the case of a balance of processes of extracellular and intracellular radical formation. When the balance is shifted to the extracellular side, then radicals damage the organs and tissues of the macroorganism, especially when there is a low level of antioxidant protection.<sup>[8-10]</sup> However, at the same time, insufficient formation of reactive oxygen forms leads to the long persistence of bacterial agents.<sup>[11]</sup> In turn, the activity of neutrophils is regulated by the immunocytokines, such as interleukin-1 $\beta$  (IL-1 $\beta$ ), IL-6, tumor necrosis factor  $\alpha$ , and other.<sup>[12,13]</sup> One of the most progressive directions in predicting the course of the inflammatory process becomes the study of the genes expression of various immunity factors. For example, a close attention is being paid to the search for associations of variants of cytokine genes, which determine the balance of immunoreactivity.<sup>[14]</sup>

As it is known, the features of microorganisms have greatly determined the development of the disease. Problems of therapy of contagious disease are connected with high-persistent potential and multidrug resistance of bacterial agents.<sup>[4,15]</sup>

Using the existing standard methods of examining patients, it is rather difficult to determine character and dynamics of pathomorphological processes in affected tissues, which make difficulty in predicting the course of the disease. Therefore, an assessment of the risk of complications for acute inflammatory diseases is an urgent problem of maxillofacial surgery and surgical dentistry.

The aim of the research is to identify the main factors of the complicated course of odontogenic pyoinflammatory diseases of maxillofacial area.

To achieve this goal, the following tasks were set, as follows:

1. Analyze the frequency and structure of pyoinflammatory diseases of the maxillofacial area in the Kabardino-Balkaria Republic for the period 2010–2015.
2. Research the intensity of the extracellular and intracellular radicals by phagocytes of patients with odontogenic abscesses, with phlegmon of different degrees of prevalence and with acute osteomyelitis.
3. Determine the effectiveness of the phagocytic function of neutrophils of patients with odontogenic abscesses, with phlegmon of different degrees of prevalence and with acute osteomyelitis.
4. Study changes in the total indicator of antioxidant

potential – antioxidant capacity of blood plasma of patients with pyoinflammatory diseases of odontogenic etiology.

5. Study the cytokine profile of the blood and peculiarities of cytokine genes expression of patients with odontogenic abscesses, with phlegmon of different degrees of prevalence and with acute osteomyelitis in the follow-up of the disease.
6. Study the qualitative and quantitative composition of microflora of purulent discharge during odontogenic pyoinflammatory diseases.
7. Identify the most significant indicators for early forecasting of severe course of odontogenic infection.

### The scientific novelty of the research

For the first time, the scientific necessity of complex assessment of activity indicators of effector functions of neutrophils, of antioxidant capacity of blood plasma and cytokine profile as prognostic flow indicators of the pyoinflammatory diseases of odontogenic etiology was proved: Abscesses, phlegmon of different degrees of prevalence, and osteomyelitis. For the first time, a change in the processes of radical formation outside and inside the cell by leukocytes was observed. These leukocytes were isolated from peripheral blood of patients with acute odontogenic osteomyelitis. For the first time, it is defined that the deficiency of intracellular active forms in leukocytes of patients with acute odontogenic osteomyelitis leads to a decrease in the efficiency of intracellular killing of bacteria and the persistence of infectious agents. For the first time, it is revealed a genetic determinism of low cytokine content of the tumor necrosis factor alpha (TNF- $\alpha$ ) in the blood plasma of patients with acute odontogenic osteomyelitis.

## MATERIAL AND METHODS

### Object of the study

The research was conducted at the Department of Surgical Dentistry and Maxillofacial Surgery Federal State Budget Educational Institution of Higher Professional Education “H.M. Berbekov Kabardino-Balkaria State University” in the Department of Maxillofacial surgery of the Republican Clinical Hospital. In the clinic, a comprehensive examination of 274 patients was performed: 70 patients with odontogenic abscesses of maxillofacial area, 140 people with odontogenic phlegmon of different prevalence, and 64 patients with acute odontogenic osteomyelitis. A group of healthy people included 45 donors from the Republican Blood Transfusion Station in Nalchik; 25 men and 20 women of them aged 18 to 40 years.

### Clinical methods of research

General methods of examination (blood pressure, respiratory rate, and pulse rate) and additional methods of examination

(general blood test, general urine analysis, blood sugar level, coagulogram, creatinine, urea, bilirubin and aminotransferase serum, X-ray diagnosis, and electrocardiogram-diagnostics) were used for the patients diagnosis. In the clinical assessment of patient's state was also taken into account such criteria as intensity of suppuration, pain symptom, and body temperature. The course of the wound process was also evaluated by the dynamics of the decrease in the size of the infiltrate and the timing of the appearance of the granulation tissue.

### Laboratory methods of research

The determination of the formation of superoxide radical by neutrophils is based on the reduction of cytochrome with superoxide.

For the determination of the intracellular production of free radicals, the dye hydroethidine was used. Determination of the antioxidant capacity of blood plasma was carried out according to the method developed by G. Klebanov with the use of vitelline environments.

The phagocytic activity of neutrophils was determined in relation to strains of *Staphylococcus aureus*, which were isolated from patients of the researched groups. Determination of the efficacy of bacterial phagocytosis was carried out according to a method developed by Nielsen L.N.

For the studying of the composition of the microflora of the purulent discharge patients of the study groups, smears were made on glass and they were coloured by gram. For the studying the activity of catalase of *S. aureus*, the method of Varvashevich T.N. was used. For the studying the antilizimic activity (AIA), anticomplementary activity (ACA) of bacteria; studying of the level of activity of bacteria against human interferon the methods of Bukharin O.V. was used. Microbiological features of the purulent discharge were studied in the first day of admission to the inpatient hospital.

Antioxidant capacity and effector activity of phagocytes, intra- and extra-cellular production of radicals by leukocytes, cytokine profile was studied in the course of the disease on the 1, 2, 5, 7, 10, and 14 day of hospitalization.

The study of the serum content of IL-1 $\beta$ , IL-6, and IL-10, tumor necrosis factor  $\alpha$  was carried out by the method of

solid-phase enzyme immunoassay ("Biosource," Belgium). The assessment of gene expression of the studied cytokines was carried out by quantitative Real-time PCR using TaqMan technology using the ICycler IQ device (BioRad).

### Statistical processing of the results

For statistical processing of the received results, the methods of calculating the average values and the confidence interval were used. The confidence interval was assessed using the Student's test. Statistical processing and calculation of the Spearman correlation coefficient were carried out using the Microsoft Excel program.

## THE RESULTS OF THE RESEARCH AND THEIR DISCUSSION

### clinical and statistical analysis of incidence of purulent-inflammatory diseases of maxillofacial area in the Kabardino-Balkarian republic for the period 2010-2015

To justify the relevance of the studies, a statistical analysis of the incidence of pyoinflammatory diseases of maxillofacial area in the Kabardino-Balkarian Republic for the period 2010–2015 was made.

Thus, among patients with pyoinflammatory diseases (2,085 persons for the indicated period), the most frequent were patients with phlegmon - they made 23% of the total number of people surveyed; patients with abscesses made 18%; with periostitis of jaws - 13%; with osteomyelitis - 15%, with inflammatory infiltrates - 8%; with lymphadenitis - 7%; with sialoadenitis - 6%; furuncles and carbuncles - 7%; sinusitis - 3%. Ratio of men and women was 57% and 43%, respectively.

The terms of hospitalization of patients with inflammatory diseases of the maxillofacial area made 10.5 bed-days in average.

The longest period of hospital treatment (12–14 bed-days) occurred in patients with odontogenic phlegmon and osteomyelitis [Table 1].

**Table 1:** The distribution of patients with purulent-inflammatory processes of maxillofacial area and neck by age (absol.,%)

Group	Age								Total
	0–15	16–24	25–34	35–44	45–54	55–64	65–74	75 and older	
Abscesses (%)	37 (10)	41 (11)	90 (24)	98 (26)	71 (19)	19 (5)	11 (3)	8 (2)	375 (100)
Phlegmon (%)	67 (14)	125 (26)	86 (18)	129 (27)	43 (9)	10 (2)	10 (2)	10 (2)	480 (100)
Osteomyelitis (%)	41 (13)	75 (24)	81 (26)	53 (17)	34 (11)	17 (5)	9 (3)	3 (1)	313 (100)

Thus, the clinical and statistical analysis of the incidence of pyoinflammatory diseases of maxillofacial area in the Kabardino-Balkarian Republic has showed that abscesses, phlegmon, and osteomyelitis of odontogenic etiology are among the most widespread diseases in the republic. Moreover, the treatment of them takes the greatest number of hospital days. Pyoinflammatory diseases affect groups of young able-bodied population, which emphasizes the socioeconomic importance of the problem.

### Analysis of the clinical examination of patients

From the anamnesis, it was possible to find out, that in a debut of disease all patients marked a pain in a tooth.

Local symptoms of the disease were determined by the localization and depth of the inflammatory process. With interfacial located Phlegmon, a diffuse swelling was defined, painful on palpation; the skin over the focus of inflammation was hyperemic, tense. When localizing an infectious focus in deep cellular spaces changes from the side of skin were insignificant, soft-tissue edema was minimal, a pain syndrome, and impaired functions (mouth opening, chewing, and speech formation) were expressed brightly. During objective examination of patients with osteomyelitis in the area of the affected site of a jaw - infiltration and swelling of tissues were found out. Alveolar portion (Appendix) of jaw was thickened in a spindle-shaped way. In addition, suppuration from under the gingiva is marked. Gingiva and mucosa of transitory fold in the teeth area, which are involved in the process, are rather edematous. Palpation of the transitory fold is very painful. The evidence of inflammatory reaction in the dynamics of the disease we can see in the Table 2.

Thus, in groups with odontogenic phlegmon, spreading on one or two cellular spaces the evidence of the inflammatory process is  $6.3-8.3 \pm 0.4$  points during hospitalization, on 5-7 days the indicators of the course of wound process become much better: Decreases the severity of suppuration, decreases infiltrate size, the wound surface becomes filled with granulation tissue ( $93.5 \pm 3.5\%$  of patients). On the 7<sup>th</sup> day of hospitalization, the intensity of the inflammatory process is  $2.3-4.5 \pm 0.4$  points. In a general, blood test in patients of these groups, there is a slight erythrocytosis ( $6.5 \pm 2.0.1012/L$ ), which indicates hypovolemia. The values

of erythrocytes correlate with a slightly elevated level of hemoglobin ( $146.0 \pm 10.0$  g/L). Leukocytosis ( $15.5 \pm 3.0.109/L$ ) is accompanied by a slight shift toward young forms (6-7% of stab lymphocytes); the sedimentation rate of erythrocytes makes in average  $24.0 \pm 5.0$  mm/h. Normalization of hemodynamic parameters occurs on the 5<sup>th</sup>-7<sup>th</sup> day of observation. In patients with phlegmon of three or more cellular spaces and patients with osteomyelitis, the evidence of the inflammatory process is  $10.5-12.3 \pm 0.4$  points during hospitalization. The course of the disease is characterized by severe symptoms of intoxication, slow wound healing – on the 7<sup>th</sup> day granulation in the wound is formed in 81% of patients, and the intensity of inflammation is  $6.5-7.5 \pm 0.4$  points. On the first day of hospitalization, leukocytosis is expressed ( $18.5 \pm 2.0.109/L$ ), elevated values persist for 7-10 days in hospital. The content of immature forms of leukocytes (8-9%) exceeds the values in other groups; the sedimentation rate of erythrocytes at the time of arrival is on the average  $37.0 \pm 10.0$  mm/h. The parameters of the hemogram on the average become normalized on the 7-10<sup>th</sup> day of hospitalization.

After preoperative infusion preparation an autopsy of a purulent focus is performed and revision of cellular spaces; antibacterial therapy, which includes the prescription of antibiotics of a wide spectrum of action (cephalosporins). A reduction of total intoxication, improvement of rheological features of blood was achieved through the use of direct anticoagulants, parenteral administration of rheopolyglucin, glucose, and saline solutions. The desensibilization therapy (dimedrol, suprastin) was made either.

During research of the intracellular production of free radicals by the phagocytes of patients with odontogenic purulent-inflammatory diseases, it was found out, that the production of active forms of oxygen is significantly less in the leukocytes of patients, comparing to the group of donors ( $P < 0.05$ ) [Figure 1].

In the group of patients with odontogenic abscesses, phlegmon of one and two cellular spaces, the increase of indicator is observed on the 7<sup>th</sup>-10<sup>th</sup> day of hospitalization. In the group of patients with phlegmon of three or more cellular spaces and patients with osteomyelitis, only on the 14<sup>th</sup> day the value of

**Table 2:** The evidence of purulent-inflammatory process in the dynamics of the disease (scores)

Group of patients	Day of research				
	1	2	5	7	10
Abscesses	6.3±0.4	4.7±0.4 <sup>1</sup>	3.3±0.4 <sup>1</sup>	2.3±0.4 <sup>1</sup>	1.5±0.4 <sup>1</sup>
Phlegmon 1 cellular spaces	8.3±0.4	6.5±0.4 <sup>1</sup>	5.3±0.4 <sup>1</sup>	2.5±0.4 <sup>1</sup>	1.2±0.4 <sup>1</sup>
Phlegmon 2 cellular spaces	10.3±0.4	9.5±0.5 <sup>1</sup>	7.3±0.3 <sup>1</sup>	4.5±0.4 <sup>1</sup>	3.3±0.4 <sup>1</sup>
Phlegmon 3 cellular spaces	12.3±0.4	11.5±0.4 <sup>1</sup>	9.2±0.3 <sup>1</sup>	6.5±0.4 <sup>1</sup>	5.5±0.4
Osteomyelitis	12.2±0.4	10.4±0.4 <sup>1</sup>	7.5±0.4 <sup>1</sup>	5.8±0.4 <sup>1</sup>	4.3±0.4 <sup>1</sup>

<sup>1</sup> $P < 0.05$  when compared with the measurement of the previous days

the studied indicator increases by 3–5%. However, to the end of observation in all studied group, the value of intracellular production of radicals do not reach the levels of the norm.

In the study of intracellular killing, it was demonstrated how much the phagocytic function of neutrophils suffers in this case [Table 3]. In groups of patients with phlegmon of the three cellular spaces and osteomyelitis, there is the largest number of surviving bacteria.

That is why, on the one hand, the antimicrobial function of phagocytes suffers, but from the other hand, preconditions for damage to the organs and tissues of the body by excessive production of radicals in the extracellular environment are created. The latter condition is accomplished when there is insufficient level of antioxidant factors of blood plasma protection.

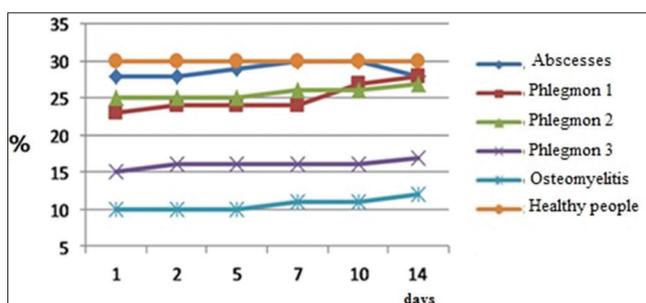
Antioxidant volume of blood plasma (AOA) of patients can be characterize the ratio in the system “pro-oxidants-antioxidants,” that is, it reflects the degree of stress from the effects of free radicals. In patients of all groups during hospitalization, a statistically significant increase of this indicator was revealed ( $P < 0.01$ ) [Figure 2]. Normalization of AOA of plasma level in abscesses and phlegmon patients of one cellular space occurred on the 2<sup>nd</sup> day. However, on the second-third day of the postoperative period, the

antioxidant capacity of blood plasma in patients with phlegmon of two or more spaces turned out to be 15–20% below the norm values. In the group of patients with osteomyelitis on the 5<sup>th</sup> day, the level of AOA reaches values below the normal value ( $55.0 \pm 1.0$ ) and remains like this even on the 14<sup>th</sup> day.

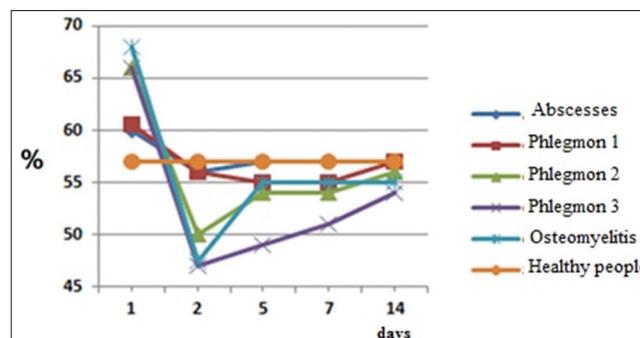
The reduced level of antioxidant plasma of blood, expressed on days 2–5 in patients with the spread of the inflammatory process to three or more cellular spaces and patients with osteomyelitis, is one of the risk factors for radical damage to one’s own organs and tissues.

The ratio of different groups of cytokines in the blood is an important factor in the course of pyoinflammatory diseases. Such reasons can lead to the spread of the inflammatory process as: Low concentration of cytokines of the proinflammatory group and also a prolonged steady increase in their concentration. During the research of concentrations of IL-1 $\beta$ , IL-6, TNF- $\alpha$ , IL-10 in the serum of patients with odontogenic infection, we have received such data. The level of IL-1 $\beta$  on the 1<sup>st</sup> day of hospitalization is much higher than the same donor’s indicator in groups of patients with odontogenic abscesses and phlegmon [Table 4].

The level of IL-1 $\beta$  did not normalize in these patient groups by the end of hospitalization. Patients with diagnosis of acute



**Figure 1:** Dynamics of changes in the intracellular production of radicals by leukocytes of the patients of the examined groups (%)



**Figure 2:** The dynamics of the level of antioxidant capacity blood plasma of the examined patients (%)

**Table 3:** The efficiency of intracellular killing of bacteria by peripheral blood neutrophils of the examined groups of patients (%)

Groups of surveyed	% survivors after phagocytosis				
	1 <sup>st</sup> day	2 <sup>nd</sup> day	5 <sup>th</sup> day	7 <sup>th</sup> day	14 <sup>th</sup> day
Patients with abscesses	8.0±2.5 <sup>1</sup>	8.0±1.5 <sup>1</sup>	7.0±3.5	6.5±3.5	-
Patients with phlegmon of one cellular space	16.0±1.5 <sup>1</sup>	12.0±1.5 <sup>1</sup> 0. <sup>3</sup>	10.0±1.0 <sup>1</sup>	7.5±1.5 <sup>1</sup>	6.5±1.0
Patients with phlegmon of two cellular spaces	21.0±1.0 <sup>1</sup>	18.0±1.0 <sup>1</sup>	14.0±1.5 <sup>1</sup>	7.0±1.0 <sup>1</sup>	6.0±1.5 <sup>1</sup>
Patients with phlegmon 3 or more cellular spaces	27.5±3.0 <sup>1</sup>	25.0±1.5 <sup>1</sup>	20.0±1.0 <sup>1</sup> . <sup>3</sup>	17.5±1.6 <sup>1</sup>	10.0±1.5 <sup>1</sup>
Patients with osteomyelitis	26.0±3.0 <sup>1</sup>	26.0±1.5 <sup>1</sup>	17.0±1.0 <sup>1</sup> 0. <sup>3</sup>	17.5±1.6 <sup>1</sup>	16.0±1.5 <sup>1</sup>
Healthy people	5.0±0.6	-	-	-	-

<sup>1</sup> $P < 0.01$  - respectively to donor indicators; <sup>3</sup> $P < 0.01$  – respectively to the indicators of measurements of the previous days

nidal osteomyelitis on the first day of hospitalization, the donors' concentration of IL-1 $\beta$  also exceeded that of by 295.0  $\pm$  50.0 pg/ml. Note that unlike the purulent-inflammatory process, which does not affect the osteal structure of the jaws, an increase of the mediator level is observed against the background of the therapy. This can be explained by the specific pathogenesis of the disease, that is, the process goes to a subacute stage with continued resorption of bone tissue.

A study of the content of IL-6 and TNF- $\alpha$  in patients bodies with abscesses and phlegmon of varying prevalence revealed a significant increase of the mediators level when patients were admitted ( $P < 0.01$ ) [Tables 5 and 6]. Against the background of the therapy, there is a clear tendency to decrease in the values of the indices. By the time of discharge

from the hospital, normal levels reach the level of IL-6 in the first and second group of patients; the level of TNF- $\alpha$  is not normalized.

Patients with osteomyelitis of the jaws had the level of IL-6 25.0  $\pm$  4.02 pg/ml on the first day of admission and then it did not change significantly. Concentration of TNF- $\alpha$  was 16.0  $\pm$  4.02 pg/ml with a tendency to insignificant growth. A low level of the proinflammatory cytokine is one of the signs of an immunodeficiency state, on the basis of which an osteomyelitis focus is developing.

Of particular interest was the study of the dynamics of IL-10 content against the background of an increased concentration of pro-inflammatory cytokines. It was revealed that in all

**Table 4:** The level of interleukin-1 $\beta$  in the blood plasma of patients with odontogenic abscesses, phlegmon and osteomyelitis in the course of the disease (pg/ml)

Group of patients	Day of observation					
	1 <sup>st</sup> day	2 <sup>nd</sup> day	5 <sup>th</sup> day	7 <sup>th</sup> day	10 <sup>th</sup> day	14 <sup>th</sup> day
Patients with abscesses	810.0 $\pm$ 50.0 <sup>1</sup>	767.0 $\pm$ 86.0 <sup>1</sup>	605.0 $\pm$ 90.0 <sup>1</sup>	267.0 $\pm$ 55.0 <sup>1,3</sup>	95.5 $\pm$ 20.0 <sup>4</sup>	-
Patients with phlegmon of one cellular space	922.0 $\pm$ 45.0 <sup>1</sup>	800.0 $\pm$ 60.0 <sup>1</sup>	710.0 $\pm$ 85.0 <sup>1</sup>	350.5 $\pm$ 50.5 <sup>1,3</sup>	106.5 $\pm$ 25.0 <sup>4</sup>	110.5 $\pm$ 25.0 <sup>4</sup>
Patients with phlegmon of two cellular spaces	985.5 $\pm$ 30.0 <sup>1</sup>	890.0 $\pm$ 55.0 <sup>1,4</sup>	711.0 $\pm$ 45.0 <sup>1</sup>	420.5 $\pm$ 25.0 <sup>2,3</sup>	190.0 $\pm$ 34.0 <sup>2</sup>	146.0 $\pm$ 25.0 <sup>2,3</sup>
Patients with phlegmon of three and more cellular spaces	1135.0 $\pm$ 40.0 <sup>1</sup>	940.0 $\pm$ 40.5 <sup>1,4</sup>	700.0 $\pm$ 55.0 <sup>1,4</sup>	599.5 $\pm$ 24.0 <sup>1,4</sup>	299.0 $\pm$ 39.0 <sup>1,4</sup>	178.0 $\pm$ 20.0 <sup>1</sup>
Patients with osteomyelitis	350.0 $\pm$ 50.0 <sup>2</sup>	320.0 $\pm$ 80.0 <sup>2</sup>	360.5 $\pm$ 95.0 <sup>2,4</sup>	430.5 $\pm$ 60.0 <sup>2</sup>	415.0 $\pm$ 30.0 <sup>2</sup>	450.0 $\pm$ 50.0 <sup>2</sup>
Healthy people	55.0 $\pm$ 2.0	-	-	-	-	-

<sup>1</sup> $P < 0.01$ ; <sup>2</sup> $P < 0.05$  - relative to the indicators of a group of healthy people; <sup>3</sup> $P < 0.01$ ; <sup>4</sup> $P < 0.05$  - relative to the indicators of the previous days of measurements.

**Table 5:** The level of interleukin-6 in the blood plasma of patients with odontogenic abscesses, phlegmon, and osteomyelitis in the course of the disease (pg/ml)

Groups of patients	Days of observation					
	1 day	2 day	5 day	7 day	10 day	14 day
Patients with abscesses	41.0 $\pm$ 9.0 <sup>1</sup>	34.5 $\pm$ 8.0 <sup>1,4</sup>	22.0 $\pm$ 6.0 <sup>2,4</sup>	17.5 $\pm$ 0.5 <sup>2,4</sup>	16.5 $\pm$ 0.5 <sup>2,4</sup>	-
Patients with phlegmon of one cell space	56.0 $\pm$ 10.0 <sup>1</sup>	45.5 $\pm$ 6.0 <sup>1,4</sup>	38.5 $\pm$ 6.0 <sup>2,4</sup>	29.5 $\pm$ 4.5 <sup>2,4</sup>	17.0 $\pm$ 2.0 <sup>4</sup>	15.0 $\pm$ 2.0 <sup>4</sup>
Patients with phlegmon of two cell spaces	58.0 $\pm$ 6.0 <sup>1</sup>	54.0 $\pm$ 3.0 <sup>1</sup>	45.0 $\pm$ 3.0 <sup>1,4</sup>	26.0 $\pm$ 1.0 <sup>2,3</sup>	20.5 $\pm$ 1.5 <sup>2</sup>	19.0 $\pm$ 1.5 <sup>2</sup>
Patients with phlegmon three or more cellular spaces	70.0 $\pm$ 6.0 <sup>1</sup>	64.5 $\pm$ 4.0 <sup>1</sup>	52.5 $\pm$ 5.0 <sup>1,4</sup>	46.0 $\pm$ 3.0 <sup>1</sup>	32.0 $\pm$ 4.0 <sup>2,4</sup>	25.5 $\pm$ 3.0 <sup>2</sup>
Patients with osteomyelitis	25.0 $\pm$ 4.0 <sup>2</sup>	22.0 $\pm$ 3.0 <sup>2</sup>	25.0 $\pm$ 4.0 <sup>2</sup>	25.0 $\pm$ 3.0 <sup>2</sup>	25.0 $\pm$ 4.0 <sup>2</sup>	25.0 $\pm$ 3.0 <sup>2</sup>
Healthy	15.0 $\pm$ 1.5	-	-	-	-	-

<sup>1</sup> $P < 0.01$ ; <sup>2</sup> $P < 0.05$  - regarding the indicators of healthy persons group; <sup>3</sup> $P < 0.01$ ; <sup>4</sup> $P < 0.05$  - regarding the previous measurement days

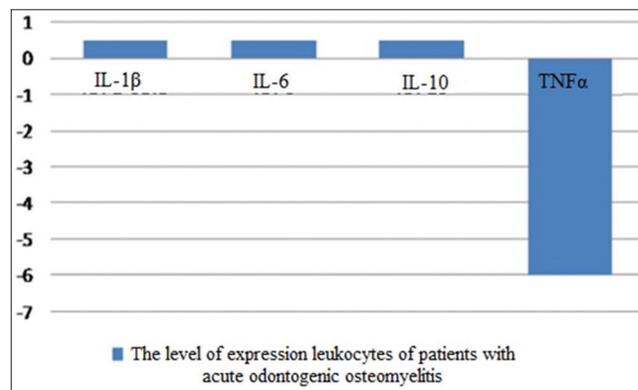
groups of patients the IL-10 content was reduced regarding the donor index ( $P < 0.5$ ) [Table 7]. Positive dynamics of mediator values growth is also observed in all groups of patients, but patients with odontogenic osteomyelitis have it less expressed. The normal level by the end of hospitalization does not reach the value of the indicator in any of the groups studied.

Study of the level of proinflammatory blood cytokines of patients with purulent-inflammatory diseases of the maxillofacial area revealed their significant increase in the acute period of the disease (with the exception of TNF- $\alpha$  of patients with acute osteomyelitis). Significant development of the main elements of the cytokine network over a long period contributes to the depletion of antigen reserves of a specific link of immunity. The latter, in turn, can lead to the spread of the disease (as evidenced by the findings), or its chronization.

Due to the fact that among the investigated pro-inflammatory cytokines, the content of TNF- $\alpha$  in the group of patients with osteomyelitis was lower than healthy donors had, expression of the cytokine genes of patients with osteomyelitis was studied [Figure 3]. The study showed that the expression

of TNF- $\alpha$  genes in leukocytes of patients with odontogenic osteomyelitis is lower than healthy people had, that is, the deficiency of TNF- $\alpha$  in the blood is genetically determined.

The results of a microbiological study of purulent discharge showed that patients with odontogenic abscesses and



**Figure 3:** The level of expression of interleukin-1 $\beta$  (IL-1 $\beta$ ), IL-6, and IL-10, tumor necrosis factor alpha in leukocytes of patients with acute odontogenic osteomyelitis (rel. units)

**Table 6:** The level of tumor necrosis factor- $\alpha$  in the blood plasma of patients with odontogenic abscesses, phlegmon and osteomyelitis in the course of the disease (pg/ml)

Groups of patients	Days of observation					
	1 day	2 day	5 day	7 day	10 day	14 day
Patients with abscesses	60.0 $\pm$ 4.0 <sup>1</sup>	45.5 $\pm$ 6.0 <sup>1</sup>	30.0 $\pm$ 5.0 <sup>1</sup>	21.5 $\pm$ 0.5 <sup>1,4</sup>	22.0 $\pm$ 2.0 <sup>4</sup>	-
Patients with phlegmon of one cell space	65.5 $\pm$ 4.0 <sup>1</sup>	54.0 $\pm$ 6.0 <sup>1</sup>	43.0 $\pm$ 5.0 <sup>1</sup>	31.5 $\pm$ 0.5 <sup>1,4</sup>	23.5 $\pm$ 2.0 <sup>4</sup>	22.0 $\pm$ 0.5 <sup>1,4</sup>
Patients with phlegmon of two cell spaces	71.0 $\pm$ 3.0 <sup>1</sup>	52.0 $\pm$ 3.0 <sup>1,4</sup>	43.5 $\pm$ 4.0 <sup>1</sup>	32.0 $\pm$ 2.0 <sup>2,3</sup>	24.0 $\pm$ 1.0 <sup>2</sup>	23.0 $\pm$ 2.0 <sup>2,3</sup>
Patients with phlegmon three or more cellular spaces	78.0 $\pm$ 3.0 <sup>1</sup>	67.0 $\pm$ 0.5 <sup>1,4</sup>	43.0 $\pm$ 5.0 <sup>1,4</sup>	38.5 $\pm$ 3.0 <sup>1,4</sup>	30.0 $\pm$ 4.0 <sup>1,4</sup>	24.5 $\pm$ 3.0 <sup>1</sup>
Patients with osteomyelitis	16.0 $\pm$ 4.0 <sup>2</sup>	16.0 $\pm$ 3.0 <sup>2</sup>	18.0 $\pm$ 4.0 <sup>2,4</sup>	20.0 $\pm$ 3.0 <sup>2</sup>	20.0 $\pm$ 4.0 <sup>2</sup>	24.0 $\pm$ 3.0 <sup>2</sup>
Healthy	18.0 $\pm$ 2.0	-	-	-	-	-

<sup>1</sup> $P < 0.01$ ; <sup>2</sup> $P < 0.05$  – regarding the indicators of healthy persons group; <sup>3</sup> $P < 0.01$ ; <sup>4</sup> $P < 0.05$  – regarding the the previous measurement days

**Table 7:** The level of interleukin-10 in the blood plasma of patients with odontogenic abscesses, phlegmon and osteomyelitis in the course of the disease (pg/ml)

Groups of patients	Days of observation					
	1 day	2 day	5 day	7 day	10 day	14 day
Patients with abscesses	15.5 $\pm$ 10.0 <sup>1</sup>	15.0 $\pm$ 6.0 <sup>1,4</sup>	16.5 $\pm$ 5.0 <sup>2</sup>	18.5 $\pm$ 0.5 <sup>2,4</sup>	23.5 $\pm$ 3.0 <sup>4</sup>	-
Patients with phlegmon of one cell space	18.0 $\pm$ 10.0 <sup>1</sup>	17.5 $\pm$ 6.0 <sup>1,4</sup>	17.5 $\pm$ 5.0 <sup>2</sup>	20.0 $\pm$ 0.5 <sup>2,4</sup>	25.0 $\pm$ 3.0 <sup>4</sup>	26.0 $\pm$ 2.0 <sup>2</sup>
Patients with phlegmon of two cell spaces	15.0 $\pm$ 3.0 <sup>1</sup>	15.5 $\pm$ 3.0 <sup>1</sup>	15.5 $\pm$ 4.0 <sup>1</sup>	20.5 $\pm$ 2.0 <sup>2,3</sup>	19.0 $\pm$ 1.0 <sup>2</sup>	21.0 $\pm$ 3.0 <sup>2</sup>
Patients with phlegmon three or more cellular spaces	12.5 $\pm$ 6.0 <sup>1</sup>	13.0 $\pm$ 4.0 <sup>1</sup>	14.0 $\pm$ 5.0 <sup>1,4</sup>	16.5 $\pm$ 3.0 <sup>1</sup>	17.0 $\pm$ 4.0 <sup>2,4</sup>	18.0 $\pm$ 3.0 <sup>2</sup>
Patients with osteomyelitis	12.0 $\pm$ 4.0 <sup>2</sup>	12.0 $\pm$ 3.0 <sup>2</sup>	15.0 $\pm$ 4.0 <sup>2</sup>	15.0 $\pm$ 3.0 <sup>2</sup>	15.0 $\pm$ 4.0 <sup>2</sup>	15.0 $\pm$ 3.0 <sup>2</sup>
Healthy	27.0 $\pm$ 1.5	-	-	-	-	-

<sup>1</sup> $P < 0.01$ ; <sup>2</sup> $P < 0.05$  – regarding the indicators of healthy persons group; <sup>3</sup> $P < 0.01$ ; <sup>4</sup> $P < 0.05$  – regarding the previous measurement days

phlegmon as the main representatives of facultative anaerobic pathogens had *S. aureus* and *Streptococcus salivarius*; patients with odontogenic osteomyelitis - *S. aureus* and *Streptococcus* spp. Among representatives of anaerobic bacteria bacteroides, peptococci, fusobacteria were more often detected. The percentage of strictly anaerobic bacteria increased with the prevalence of a purulent disease.

In addition, most strains of staphylococci have resistance factors to components of the nonspecific link of immunity. AIA was detected in 72.5% (90 strains) of 132 bacterial cultures. Anti-interferon activity was detected in 38.7% of cases (47 bacterial cultures). ACA was found in 29 cultures of *S. aureus*. Catalase activity was detected in 85 strains out of 132 (69%) isolated from a purulent discharge. It was found that 2.0% (2 strains) showed high catalase activity (2.5–5 units/20 million); 93.0% (79 strains) had an average level of catalase activity (2.2–2.5 units/20 million); in 5% (4 strains) - a low level of activity (1.5–2.2 units/20 million). Thus, *S. aureus* strains isolated from the wound discharge had an expressed persistent potential, which is one of the factors determining the course of the disease.

The study showed that the studied most important pathogenetic indicators correlate with the prevalence of the purulent-inflammatory process and reflect its clinical picture that is they can be used as criteria that determine the course of the disease.

## CONCLUSIONS

1. In the Kabardino-Balkarian Republic, patients with purulent-inflammatory diseases of the maxillofacial area are most often observed with odontogenic abscesses, phlegmon, and acute osteomyelitis. Patients with phlegmon make up 23% of the total number of people surveyed; patients with abscesses - 18%; patients with osteomyelitis accounted for 15%. Treatment of patients with phlegmon and osteomyelitis of the maxillofacial area requires the longest inpatient treatment.
2. Decrease in the effectiveness of phagocytosis of odontogenic inflammatory diseases is associated with the disruption of the normal ratio of intracellular and extracellular production of free radicals to leukocytes of peripheral blood, which leads to a long-term persistence of bacterial agents.
3. Patients with odontogenic phlegmons of three or more cellular spaces and acute odontogenic osteomyelitis have a low level of antioxidant blood capacity, which is preserved until the end of the hospitalization period and is a factor of radical damage to own tissues that promotes the spread of the inflammatory process.
4. Patients with odontogenic abscesses and phlegmon, had a violation of the ratio of proinflammatory (IL-1 $\beta$ , IL-6, TNF- $\alpha$ ) and anti-inflammatory (IL-10) groups of immunocytokines with a predominant proinflammatory

component. Imbalance is most expressed in the diffuse purulent process and leads to prolonged hospitalization of patients.

5. Low level of TNF- $\alpha$  in the blood plasma of patients with acute odontogenic osteomyelitis is caused by low expression of the genes of this cytokine.
6. In the microflora of purulent discharge of patients with phlegmon of three or more cellular spaces and osteomyelitis, strictly-anaerobic pathogens account for more than 20%. The isolated strains of *S. aureus* have an expressed persistent potential.
7. The most significant risk factors for complications in odontogenic purulent-inflammatory diseases include a violation of effector properties of leukocytes, an imbalance of mediator regulation of inflammation, a predominance of strictly anaerobic microflora.

## Practical recommendations

For the most complete assessment of the flow of odontogenic phlegmon of different prevalence and acute osteomyelitis, it is recommended to measure the level of:

1. Intracellular production of free radicals in leukocytes of patients on the first day of hospitalization. An unfavorable factor in the course of the disease is the level of intracellular production of radicals  $<20 \pm 2.0\%$  of the total production;
2. Antioxidant capacity of blood plasma on the second day of hospitalization, because it is during this period that there is a sharp decline in the level of the indicator. An unfavorable factor in the course of the disease is the AOE level below  $48.5 \pm 1.5\%$ ;
3. The cytokine IL-1 $\beta$ , IL-6, TNF- $\alpha$  in blood plasma on the first day of hospitalization. An unfavorable factor in the course of the disease is the content of:
  - IL-1 $\beta$  more than  $810 \pm 50.0$  pg/ml;
  - IL-6 more than  $58.0 \pm 6.0$  pg/ml;
  - TNF- $\alpha$  more than  $58.0 \pm 4.0$  pg/ml;
4. Cytokine TNF- $\alpha$  in the blood plasma of patients with acute osteomyelitis on the first day of hospitalization. An unfavorable factor in the course of the disease is the level of TNF- $\alpha$   $<16.0 \pm 4.0$  pg/ml.

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