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Original Article

Immunocorrective Therapy in Patients with Limited and Diffuse Purulent-inflammatory Diseases of the Soft Tissues of the Maxillofacial Area and Neck: Research in 132 Patients*

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ABSTRACT

Purpose.
Determine the effectiveness of using the drug Biotroph on the state of local and general nonspecific resistance of the organism in patients with purulent-inflammatory diseases of the soft tissues of the maxillofacial area and neck.
Methods.
Clinical and immunological examination of 132 patients with limited and diffuse purulent-inflammatory maxillofacial and neck area soft tissues diseases identified during hospitalization was carried out.
Results.
Our studies have shown that the using of food supplements Biotroph-4 in the complex treatment of the patients with limited and diffuse purulent-inflammatory maxillofacial and neck area soft tissues diseases allowed eliminate the temporary immunodeficiency completely in the short period of time in all examined patients.
Conclusions.
The complex drug on a natural basis Biotroph-4 is recommended to maxillofacial surgeons and dental surgeons for the treatment of patients with purulent-inflammatory diseases of periomaxillary soft tissues.

Introduction

Purulent-inflammatory diseases of the soft tissues of the maxillofacial area and neck occupy one of the leading places in the clinic of maxillofacial surgery. In recent years, the number of patients with these diseases has increased significantly, the severity of their course has worsened, which can often lead to the development of such severe complications as sepsis, mediastinitis, meningitis, etc. [1, 2]. Held in the Department of Maxillofacial Surgery (Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine) studies have shown that in patients with purulent-inflammatory diseases of soft tissues there is a significant decrease in both local and general nonspecific resistance of the organism, not only during the preoperative period (if there are clinical symptoms of the disease), but also during the first two months after surgical intervention, i.e. in the period of clinical recovery. During the period of rehabilitation of patients with purulent-inflammatory processes of soft tissues, the body of these patients is most susceptible to some forms of inflammatory diseases (acute respiratory viral infection, carbuncles, rhinitis, angina, etc.). The work capacity of these patients is restored only during

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this period of time (two months). For the complete recovery of the patient's body in the postoperative period, it is important to provide him with a full supply of food products that contain not only vitamins, but also the necessary macro- and microelements. In modern conditions it is very difficult to find a full-fledged "set" of everything that a person needs for a quick and complete rehabilitation.

Our attention was attracted by the new series of dietary supplements "Biotroph" (Firma Interpom, LLC, Kyiv, Ukraine). As a preservative in this preparation is one of the most ancient and time-tested, safe and effective preservatives of natural origin – high-quality honey. It is known that honey is an ideal natural preservative, which allows the activity of enzymes to be maintained even during long-term storage. For the manufacture of this drug are used the various organs of healthy, pre-tested animals. A homogenate is prepared from these organs, followed by its magnetic-laser processing, which makes possible to preserve the integrity and activity of natural complexes as much as possible. The source of biologically active substances and enzymes are various internal organs of young healthy animals (calves). The preparations of the Biotroph series contain a unique composition of bioregulators consisting of enzymes, cytomedines, regulatory peptides, amino acids, neurotransmitters, phospholipids, polyunsaturated fatty acids, macronutrient vitamins and microelements. In accordance with the animal organs used for the manufacture of Biotroph preparations, they have a composition that ensures the normal physiological vital activity of the body, and also allows the human body to adapt more effectively to stress.

Regulatory peptides and cytomedines, isolated from immunocompetent organs (lymphatic system, thymus, bone marrow, spleen), contribute to the production of interferon, increase the activity of macrophages, thereby providing antiviral and antibacterial action, form a common and local immunocorrective effect. Cytomedines regulate physiological metabolic processes in organs and tissues, have anti-inflammatory and regenerative effects. Peptides regenerate tissues, normalize blood fibrinolytic properties. Amino acids are a necessary component of metabolism, the normal functioning of cells, organs and systems, play a leading role in the life of the organism. Monosaccharides provide energy to the cells, are an important plastic material, and in complexes with proteins and lipids, they form numerous biologically active compounds. Phospholipids and polyunsaturated fatty acids normalize liver function, regulate lipid metabolism, reduce cholesterol levels, have a cleansing effect on blood vessels, restore elasticity and strength of blood vessel walls, improve blood circulation and metabolism between cells and blood. Vitamins ensure the normal functioning of all body systems, because are accelerators of exchange reactions in the body. Trace elements that make up the composition of these dietary supplements are a necessary condition for maintaining the existence of a living organism; regulate the constancy of its internal environment (homeostasis). Trace elements are part of enzymes, hormones, greatly enhancing their activity, as well as phospholipids and vitamins.

In the choice of postoperative rehabilitation of maxillofacial patients with limited and diffuse purulent-inflammatory diseases, we stopped on the preparation Biotroph-4. The components of the preparation Biotroph-4 increase the immune status of the body (cellular and humoral immunity); regulate the system of homeostasis, blood formation; improve blood supply in organs and tissues; promote removal of toxic metabolic products and radionuclides from the body; stabilize metabolic-dystrophic and metabolic processes in organs and tissues; normalize metabolism; increase adaptation mechanisms under stressful conditions.

Purpose of the research is to study the effect of biologically active dietary supplement Biotroph-4 on the state of local and general nonspecific resistance of the organism in patients with purulent-inflammatory diseases of the soft tissues of the maxillofacial area and neck during the rehabilitation period.

Materials and Methods

The 132 patients with limited and diffuse purulent-inflammatory diseases of the soft tissues of the maxillofacial area and neck (purulent lymphadenitis [7], fununcles, carbuncles [8, 9], odontogenic and non-odontogenic abscesses and phlegmons [10-13]) were examined. All patients were divided into two groups. The first observation group consisted of 62 patients with purulent-inflammatory diseases of the soft tissues, which were treated with traditional (conventional) methods only during the hospitalization of patients. The second group of observation is 70 patients with purulent-inflammatory processes, in the complex of therapeutic measures were additionally included Biotroph-4. Treatment with this drug was started from the first days after the patient was hospitalized. The duration of the use of biologically active additives was 40-45 days. There are no contraindications for taking this drug. 34 practically healthy people served as controls for laboratory tests.

Patients of the first observation group (62 persons) after their hospitalization in the hospital carried out the removal of the causative tooth (with odontogenic processes) and opened abscesses or cellulitis. In the postoperative period, we applied the traditional drug treatment to these patients: intramuscular administration of conventional antibiotics in recommended dosages, sulfanilamide drugs, and also carried out detoxification treatment (as indicated), non-specific hyposensitization therapy (dimedrol, diazolin, suprastin, fenkarol, tavegil, etc.) symptomatic and physiotherapeutic treatment. In the complex treatment of patients of the II group

of observation (70 people), except for the previously listed surgical and drug treatment, the biological dietary supplement Biotroph-4 was used for immunocorrection (from the first days after the patients were hospitalized). For general treatment, Biotroph-4 was applied orally one teaspoon (30 minutes before meals) 3 times a day for 40-45 days. After discharge of patients from the hospital (9-15 days after hospitalization), they continued to take this drug until the end of the recommended period.

All patients during hospitalization and in the process of treatment general clinical examination (clarification of complaints, collecting history of the disease, examination, palpation, percussion of teeth, X-ray, complete blood count, etc.) was carried out, and also determined the local and general non-specific resistance of the organism.

To study the local non-specific resistance of the organism, the functional activity of neutrophils emigrated to the oral cavity through the buccal mucosa was determined. The selection of material was carried out in accordance with the methodology proposed by Dyshlov, and stained the prints for the identification of cationic proteins in neutrophilic leukocytes, who emigrated to the oral cavity through the buccal mucosa according to the method of Pigarevsky [3]. To identify alkaline phosphatase of neutrophilic leukocytes, the azo-combination method was used (modification of Shubich, 1980). The number of emigrated leukocytes and the activity of alkaline phosphatase in them were also determined in prints obtained from the buccal mucosa. To assess the cytochemical reaction, we applied the Kaplow method [4]. Depending on the enzymatic activity of neutrophils, they were divided into 5 types: zero (unstained), the first (with a weak cytoplasm stain), the second (with a moderate cytoplasm stain), the third (with a strong cytoplasm stain) and the fourth (with a very strong cytoplasm stain and diffusion dye to the core region). In a smear, 100 neutrophils were counted and the number of cells belonging to each type was determined. This quantity was multiplied by the type number, the numbers obtained were summed up. The amount was expressed in arbitrary units (standard units).

The study of general nonspecific resistance of the organism [5] was performed using the NBT test according to the Vicksman and Mayansky method. The average neutrophil activation index (mean cytochemical activity index of cationic proteins), the number of activated neutrophils (unstimulated and stimulated), the reserve of neutrophil activation were calculated. Phagocytic activity of blood leukocytes was determined by the method of Chernushenko and Kogosova [6]. The examination was carried out at the hospitalization of patients in the hospital, in the dynamics of treatment, at discharge of the examined from the hospital and in the period of convalescence.

All the numerical data obtained in the course of the study were processed by a mathematical method with the calculation of Student's criterion. Indicators were considered reliable at $P < 0.05$.

Results

The results of the examination of patients with I and II observation groups, showed that the local non-specific resistance of the organism was significantly changed during the hospitalization of the patients (Tables 1-3).

From Table 1 it can be seen that the number of neutrophils that emigrated through the buccal mucosa in patients of group I during hospitalization significantly (<0.001) increased compared to healthy people to 25.9 ± 1.4, and the activity of alkaline phosphatase in them was 64.4 ± 2.3 conventional units (CU) (<0.001). The number of neutrophils that emigrated through the mucous membrane of the cheek in patients of group II observation during hospitalization also significantly (<0.001) increased compared with healthy people to 26.7 ± 1.5, and the activity of alkaline phosphatase in them was 63.6 ± 2.5 CU (< 0.001).

From Table 2 it can be seen that the number of neutrophils that migrated through the buccal mucosa in patients of group I at discharge remained significantly

TABLE 1. Cytological and Cytochemical Indicators in Prints, Taken from the Buccal Mucosa, of Surveyed I and II Observation Groups during Hospitalization.

Observation Group	Number of Persons	Number of Neutrophils (per 100 cells) that Migrated through the Buccal Mucosa	Alkaline Phosphatase Activity in Neutrophils that Migrated through the Buccal Mucosa (CU, conventional units)
		M ± m	M ± m
I observation group	31	25.9 ± 1.4 p < 0.001	64.4 ± 2.3 p < 0.001
II observation group	34	26.7 ± 1.5 p < 0.001	63.6 ± 2.5 p < 0.001
Control group (healthy people)	34	16.9 ± 1.4	40.9 ± 2.1

P (P value) – significance of differences compared with the control group (healthy people).

increased compared with healthy people to 21.1 ± 1.0 (<0.02), and the activity of alkaline phosphatase in them was 54.6 ± 1.2 CU (<0.001). The number of neutrophils that migrated through the buccal mucosa in patients of group II observation at discharge from the hospital was also significantly increased compared with healthy people to 22.0 ± 1.1 (<0.02), and the activity of alkaline phosphatase in them was 55.1 ± 1.8 CU (<0.001).

TABLE 2. Cytological and Cytochemical Indicators in Prints, Taken from the Buccal Mucosa of Surveyed I and II Observation Groups at Discharge from Hospital.

Observation Group	Number of Persons	Number of Neutrophils (per 100 cells) that Migrated through the Buccal Mucosa	Alkaline Phosphatase Activity in Neutrophils that Migrated through the Buccal Mucosa (CU, conventional units)
		M ± m	M ± m
I observation group	31	21.1 ± 1.0 P < 0.02	54.6 ± 1.2 P < 0.001
II observation group	34	22.0 ± 1.1 P < 0.02	55.1 ± 1.8 P < 0.001
Control group (healthy people)	34	16.9 ± 1.4	40.9 ± 2.1

P (P value) – significance of differences compared with the control group (healthy people).

From Table 3 it can be seen that the activity of cationic proteins during hospitalization of patients of group I was significantly reduced to 0.42 ± 0.02 CU (<0.001), and in patients of group II – up to 0.43 ± 0.03 CU (<0.001). At discharge of the examined group I from the hospital, the activity of cationic proteins of neutrophils remained at significantly low numbers – 0.47 ± 0.02 CU (<0.001), as in group II of observation – 0.48 ± 0.03 CU (<0.001).

TABLE 3. The Activity of Cationic Proteins in Prints, Taken from the Mucous Membrane of the Cheek of Surveyed I and II Groups of Observation.

Observation Group	Number of Persons	Activity of Cationic Proteins (CTP) in Neutrophils that Migrated through the Buccal Mucosa (CU, conventional units)	
		At Hospitalization	On Discharge
I observation group	29	0.42 ± 0.02 P < 0.001	0.47 ± 0.02 P < 0.001
II observation group	31	0.43 ± 0.03 P < 0.001	0.48 ± 0.03 P < 0.001
Control group (healthy people)	28	0.67 ± 0.02	

P (P value) – significance of differences compared with the control group (healthy people).

Thus, the number of neutrophilic leukocytes that emigrated through the buccal mucosa in patients with purulent-inflammatory diseases of the soft tissues in both observation groups significantly increased and the activity of alkaline phosphatase in them also significantly increased compared with healthy people. This indicated the presence of inflammations in the oral cavity of the subjects when they were discharged from the hospital. The activity of cationic proteins in neutrophilic leukocytes in patients of both observation groups significantly decreased at all stages of inpatient treatment, which indicated a low local nonspecific resistance of the organism. Based on the indicators we obtained, we can conclude that patients with purulent-inflammatory diseases of soft tissues had low local nonspecific resistance of the organism both during their hospitalization and during their discharge from the hospital (for 9-15 days).

The indicators of general nonspecific resistance of the organism were studied in patients with purulent-inflammatory diseases (Tables 4 and 5). Indicators of phagocytic activity of peripheral blood neutrophils (percentage of phagocytic activity and phagocytic number) in patients of group I of the observation during hospitalization were significantly reduced compared with healthy people and, accordingly, were: 66.1 ± 1.2% (P < 0.001); 4.7 ± 0.2 (P < 0.001), and at discharge from the hospital: 68.2 ± 1.0% (P < 0.001); 5.2 ± 0.2% (P < 0.001).

Phagocytic activity of peripheral blood neutrophils in patients of group II observation with hospitalization were also significantly reduced compared with healthy people and, respectively, equal: 65.4 ± 1.4% (P < 0.001); 4.6 ± 0.2 (P < 0.001), and at discharge from the hospital: 69.3 ± 1.3% (P < 0.01); 5.5 ± 0.3 (P < 0.05).

TABLE 4. Indicators of Changes in the Phagocytic Activity of Peripheral Blood Leukocytes in Patients with Purulent-Inflammatory Diseases in the Dynamics of the Treatment.

Observation Group	Number of Persons	Indicators of Phagocytic Activity of Blood Leukocytes			
		At Hospitalization		On Discharge	
		Percentage of Phagocytosis (M ± m)	Phagocytic Number (M ± m)	Percentage of Phagocytosis (M ± m)	Phagocytic Number (M ± m)
I group	30	66.1 ± 1.2 P < 0.001	4.7 ± 0.2 P < 0.001	68.2 ± 1.0 P < 0.001	5.2 ± 0.2 P < 0.001
II group	30	65.4 ± 1.4 P < 0.001	4.6 ± 0.2 P < 0.001	69.3 ± 1.3 P < 0.01	5.5 ± 0.3 P < 0.05
healthy people	27	74.5 ± 1.6	6.4 ± 0.3	74.5 ± 1.6	6.4 ± 0.3

P (P value) – significance of differences compared with the control group (healthy people).

Indicators of general nonspecific resistance of the organism in patients of the first group of observations according to the nitroblue tetrazolium test (NBT-Test) (Table 5) during hospitalization differed significantly from the norm and were as follows: Non-active neutrophils (NAN) (unstimulated) – 18.1 ± 0.7 (P < 0.001), at discharge – 16.2 ± 0.8 (P < 0.001), 1 month after discharge – 19.8 ± 0.9 (P < 0.001), 2 months after discharge – 24.4 ± 0.4 (P > 0.05), with a norm of 25.4 ± 0.9. Non-active neutrophils (NAN) indicators (stimulated) at hospitalization – 29.3 ± 0.8 (P < 0.001), at discharge – 27.6 ± 0.8 (P < 0.001), 1 month after discharge – 34.2 ± 0.9 (P < 0.001), 2 months after discharge – 40.3 ± 1.2 (P < 0.05), with a norm of 40.7 ± 1.2. The average cytochemical indicator of the activity of neutrophil cationic proteins (INA) during hospitalization was 0.23 ± 0.01 CU (P < 0.001), at discharge – 0.22 ± 0.01 CU (P < 0.001), after I month after discharge – 0.26 ± 0.01 CU (P < 0.001), 2 months after discharge – 0.29 ± 0.01 CU (P > 0.05), with a norm – 0.31 ± 0.01 CU. The activation reserve was at hospitalization of 20.1 ± 0.3 CU (P < 0.001), at discharge from the hospital – 17.2 ± 0.4 CU (P < 0.001), 1 month after discharge – 27.2 ± 0.5 CU (P < 0.001), 2 months after discharge – 36.6 ± 0.5 CU (P > 0.05), with a norm of 37.0 ± 2.1 CU (Table 5).

Indicators of general nonspecific resistance of the organism in patients of group II observation by the NBT-test (Table 5) during hospitalization also differed significantly from the norm and were as follows: NAN (unstimulated) – 17.6 ± 0.6 (P < 0.001), at discharge – 17.8 ± 0.9 (P < 0.001), 1 month after discharge – 25.1 ± 0.9 (P > 0.05), 2 months after discharge – 25.5 ± 0.9 (P > 0.05), with a norm of 25.4 ± 0.9. NAN indicators (stimulated) at hospitalization – 28.8 ± 0.7 (P < 0.001), at discharge – 31.6 ± 0.9 (P < 0.001), 1 month after discharge – 38.9 ± 0.9 (P > 0.05), 2 months after discharge – 40.8 ± 1.0 (P > 0.05), with a norm of 40.7 ± 1.2. The average cytochemical indicator of the activity of neutrophil cationic proteins (INA, indicator of neutrophils` activity) during hospitalization was 0.22 ± 0.01 CU (P < 0.001), with discharge – 0.24 ± 0.01 CU (P < 0.001), after 1 month after discharge – 0.29 ± 0.01 CU (P > 0.05), 2 months after discharge – 0.32 ± 0.01 CU (P > 0.05), with a norm – 0.31 ± 0.01 CU. The activation reserve was at hospitalization of 20.0 ± 0.4 CU (P < 0.001), at discharge from the hospital – 25.2 ± 0.3 CU (P < 0.001), 1 month after discharge – 35.9 ± 0.5 CU (P > 0.05), 2 months after discharge – 38.6 ± 0.9 CU (P > 0.05), with a norm of 37.0 ± 2.1 CU (Table 5).

When comparing the obtained immunological parameters of patients with limited and diffuse purulent-inflammatory processes (groups I and II), it was found that when they were hospitalized and when they were discharged from the hospital, these figures practically did not differ, but were significantly lower than in healthy people. When the drug Biotroph-4 was included in the medical treatment, the immunological indices of general nonspecific resistance of the organism were normalized 1 month after discharge from the hospital in group II, and in group I, the observations remained significantly reduced and normalized only 2 months after discharge hospital.

Conclusions

Studies have shown that the inclusion in the complex treatment of the biological food additive Biotroph-4 allowed in a short time completely eliminate the temporary immunodeficiency identified during hospitalization in all examined patients with limited and diffuse purulent-inflammatory processes of the soft tissues of the maxillofacial area and neck.

TABLE 5. Dynamics of Changes in the General Nonspecific Resistance of the Organism According to the Nitroblue Tetrazolium Test (NBT-Test) in Patients with Purulent-Inflammatory Diseases of Soft Tissues Before and After Their Clinical Recovery.

Observation Group	Studied Blood Parameters	Time of Examination			
		During Hospitalization	On Discharge	1 Month After Discharge	2 Months After Discharge
I group (46 patients)	NAN (unstimulated)	18.1 ± 0.7 P > 0.001	16.2 ± 0.8 P > 0.001	19.8 ± 0.9 P > 0.001	24.4 ± 0.4 P > 0.05
	NAN (stimulated)	29,3 ± 0,8 P > 0,001	27,6 ± 0,8 P > 0,001	34,2 ± 0,9 P > 0,001	40,3 ± 1,2 P > 0,05
	INA	0,23 ± 0,01 P > 0,001	0,22 ± 0,01 P > 0,001	0,26 ± 0,01 P > 0,001	0,29 ± 0,01 P > 0,05
	Activation reserve	20.1 ± 0.3 P > 0.001	17.2 ± 0.4 P > 0.001	27.2 ± 0.5 P > 0.001	36.6 ± 0.5 P > 0.05
II group (53 patients)	NAN (unstimulated)	17.6 ± 0.6 P > 0.001	17.8 ± 0.9 P > 0.001	25.1 ± 0.9 P > 0.05	25.5 ± 0.9 P > 0.05
	NAN (stimulated)	28.8 ± 0.7 P > 0.001	31.6 ± 0.9 P > 0.001	38.9 ± 0.9 P > 0.05	40.8 ± 1.0 P > 0.05
	INA	0.22 ± 0.01 P > 0.001	0.23 ± 0.01 P > 0.001	0.29 ± 0.01 P > 0.05	0.32 ± 0.01 P > 0.05
	Activation reserve	20.0 ± 0.4 P > 0.001	25.2 ± 0.3 P > 0.001	35.9 ± 0.5 P > 0.05	38.6 ± 0.9 P > 0.05
Healthy people (27 persons)	NAN (unstimulated)	25.4 ± 0.9			
	NAN (stimulated)	40.7 ± 1.2			
	INA	0.31 ± 0.01			
	Activation reserve	37.0 ± 2.1			

P (P value) – significance of differences compared with the healthy people.
NAN – non-active neutrophils.
INA – indicator of neutrophils` activity.

Thus, the complex drug on a natural basis Biotroph-4 should be recommended to maxillofacial surgeons and dental surgeons for the treatment of patients with purulent-inflammatory diseases of soft tissues around jaws.

Conflict of Interest

The authors declare no conflict of interest.

Role of the Co-authors

All authors are equally contribute to that paper.

Ethical Approval

Approval was obtained from the Medical Ethics Committee of the Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine.

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