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CORRECTION OF THE SYSTEMIC IMMUNITY HUMORAL COMPONENT PARAMETERS IN PATIENTS WITH GENERALIZED PERIODONTITIS

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Dynamics of indicators of humoral arm of systemic immunity using complex therapy with the inclusion of immunomodulators in patients with chronic generalized periodontitis of I and II grades of development on giardiasis background was studied. It is established that the developed treatment regimen has a pronounced normalizing effect on the activity of humoral immunity. Under its influence, IgE and CIC levels in blood serum return to normal and the affinity of antimicrobial IgG antibodies increases. The obtained data give grounds to assert that the developed treatment regimen of complex therapy in patients with chronic generalized periodontitis of I and II grades of development on giardiasis background was more effective than conventional treatment.

Key words: chronic generalized periodontitis, giardiasis, humoral immunity.

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Despite significant advances in the study of etiology and pathogenesis of periodontal diseases, as well as current considerable arsenal of dental drugs, the problem of treatment of these diseases, in particular generalized periodontitis (GP), remains unresolved. Therefore, studies aimed at finding new pathogenetically substantiated methods of treatment and prophylaxis of GP are relevant to this day. As known, GP development is often combined with concomitant diseases or occurs as a consequence of human somatic illnesses. [1, 2]. One of many such diseases is parasitosis. Conducted research showed that GP that develops on giardiasis background, has a long chronisity and is often resistant to conventional treatment [3].

In Ukraine up to 30-40 thousand cases of giardiasis is recorded annually, and, according to researchers, giardiasis contributes to the emergence of somatic and exacerbation of existing chronic diseases, affecting various systems of human body, including immune system. [4, 5]. In view of this, questions related to the immune system condition in patients with GP with parasitosis required a careful study.

In accordance with the results of the conducted research, it was established that GP development is closely related not only to the elements of immune deficiency, but also to the autoimmune process [6], which greatly complicated the selection of optimal treatment regimen. Identifying features of the immune response in patients with I and II grades GP against the background of giardiasis required focus on developing methods of correcting immune system functions by means of immunomodulators, which opens a posibility to influence the body's immunoreactivity, thereby contributing to increase in the effectiveness of conventional treatment. The research interest in the study of applied therapy effectiveness, in particular its ability to positively influence the immunological status of the organism of patients is quite understandable.

The purpose of the study was to determine the effect of applied complex therapy on the indicators of humoral arm of systemic immunity in patients with chronic generalized periodontitis of I and II grades of development on giardiasis background.

Materials and methods. The studies conducted by the Department of Dentistry of Kharkiv National Medical University together with the Department of Parasitic and Tropical Diseases of Kharkiv Medical Academy of Postgraduate Education were carried out under conditions of voluntary informed consent of patients. 180 patients with giardiasis invasion at the age of 20-40 with chronic GP of I and II grades were examined. They formed the main group (24 patients with GP of I grade and 66 patients with GP of II grade of development) and the comparison group (24 patients with GP of I grade and 66 patients with GP of II grade of development). To compare the data of patients with GP, 30 practically healthy individuals (PHI) without pathology of periodontal disease and without parasitosis and chronic pathology of other organs and systems for the period of examination were involved in the study. They formed a group PHI.

The dental diagnosis of patients was made on the basis of a survey, review, definition of simplified oral hygiene index OHI-S (Green JC, Vermillion JR, 1964) [7], index assessment of periodontal tissues state (intensity of periodontal tissue inflammation - PMA (Parma G., 1960) [7], periodontal index - PI

(Russell A., 1956) [7], sulcus bleeding - bleeding index Muhlemann-SBI (Muhlemann, 1971) [8], measurement of dentogingival junction loss level (mm), gingival pockets depth (mm), gum recession height (mm) and X-ray examination according to the classification of periodontal diseases (Danylevskyi M.F., 1994).

Selective teeth grinding was carried out for all patients of the main and comparison groups and, if any - elimination of traumatic occlusion and removal of supra gingival and sub gingival dental deposits. Non-surgical or surgical debridement of gingival pockets was performed and, if necessary - removal of loose teeth. Permanent or temporary teeth splint, rational dental prosthetics, oral cavity sanitation were carried out. 0.05%- 0,2% Chlorhexidine bigluconate solution was used for the medical treatment of periodontal tissues. The main group patients treatment was carried out in two stages.

Table 1

Suggested treatment and prevention complex for patients with GP in the presence of giardiasis infestation

№No.	Drug	Dosage	Terms	Mechanism of action
StageI: GP development stage I and II against giardiasis infestation				
Locally				
1.	«Decasan»	Irrigations and instillations into periodontal pocket (p/p)	GP st. I – 10 days; GP st. II – 14 days.	Antimicrobial, virucide, fungicide and antiprotozoal actions; exhibits desensitizing and anti-inflammatory properties
2.	«Catomas»	Instillations into p/p and fpplications on gums	GP st. I – 10 days; GP st. II – 14 days.	Antioxidant, immunomodulatory, anti-microbial, anti-inflammatory and epithelizing effects
On the system level				
3.	«Erbisol	Intramusculary (i/m), in the evening. GP st. I – 4 ml – 10days; GP st. II – 4 ml - 10 days and 2 ml additionally 10 days.		Immunomodulatory, detoxifying, anti-inflammatory, antioxidant, membrane-stabilizing, reparative, hepatoprotective action; capable of inhibiting autoimmune and allergic processes, restoring the balance of Th1-lymphocytes and Th2-lymphocytes activity
4.	«Sage oil»	Consistently, according to instruction	GP st. I – 1 month; GP st. II – 2 months.	Herbal adaptogen. Has anti-inflammatory, antimicrobial, hemostatic, anti-inflammatory properties.
5.	«Kvertulin»	Consistently, according to instruction	GP st. I and II – 1 month.	Dysbacteriosis prevention; antioxidant, membrane and capillary-stabilizing action.
StageI: GP development stage I and II against giardiasis infestation				
Locally				
1.	«Abigel» periodontal gel	Instillations into p/p and fpplications on gums.	GP st. I – 10 days; GP st. II – 14 days.	Anti-inflammatory, astringent, antiseptic, fixative and hemostatic action
2.	Toothpaste «Lacalut flora»	In the morning and in the evening	GP st. I and II – during treatment: After treatment. GP st. I – 1 month; GP st. II – 2 months.	Has high cleansing, periodontium protective, antihalitosis effects
3.	Oral rinse «Listerine Total Care»	In the morning and in the evening	GP st. I and II – during treatment. After treatment: GP st. I – 1 month; GP st. II – 2 months.	Anti-inflammatory, antioxidant, antimicrobial, hemostatic, antihalitosis properties; reduces the rate of tartar formation
On the system level				
1.	«Pumpkin seed oily extract»	Consistently, according to instruction	GP st. I – 1 month; GP st. II – 2 months.	Adaptogen, normalizes metabolism, has choleretic, hepatoprotective, anti-sclerotic, regenerating, antioxidant action.

Depending on the severity of GP the following treatment-and-prophylactic operations were performed for the patients of the main group: local use of drugs with complex antimicrobial, anti-inflammatory, fungicidal and antiprotozoal effect (Decasanum irrigations), antimicrobial, anti-inflammatory, antioxidant and immunomodulatory effect (Katomas instillations and applications)

according to the degree of GP (I or II) for 10 or 14 days, respectively. On a systemic level Erbisolum immunomodulator was prescribed intramuscularly according to the treatment regimen (10 or 20 days depending on the severity), as well as Salvia Oil or Pumpkin Seed Oil Extract vegetative adaptogen (1 or 2 months according to severity) and Kvertulin antioxidant (10 or 14 days depending on the severity). The obligatory component of treatment-and-prophylactic complex for patients with GP on giardiasis background was a dualfold daily use of Lacalut flora toothpaste and Listerine Total Care oral rinse for 1 or 2 months, depending on the severity.

Patients of the comparison group were treated according to the conventional treatmen regimen, which provided for local use of instillations and applications of Metrogyl Denta gel with antimicrobial and antiseptic effect, Aecol ointment with antioxidant, anti-inflammatory and reparative effect (10 or 14 days according to GP severity), and systemic use of Echinacea Compositum S – a drug with complex immunomodulatory, anti-inflammatory and detoxification effect (intramuscularly for 10 days according to the treatment regimen) and Linex probiotic for 10 days. The treatment regimen was supplemented by the hygiene algorithm consisting of dualfold daily use of Forest Balsam toothpaste and oral rinse for 1 or 2 months, depending on the severity.

The impact of the proposed and conventional therapy on humoral immunity was assessed by the dynamics of changes in IgA, IgM, IgG, IgE, CIC levels in blood serum, complement activity, antibodies level to etiological infectious agents and common antigenic determinant (CAD), affinity of antibodies produced by IgG. IgA, IgM, IgG in blood serum were determined spectrophotometrically with PEG-6000 [9]. The level of IgE was determined using ELISA according to the instruction. Complement activity was evaluated by means of 50% hemolysis of sheep erythrocytes according to the method of Chudomels in modification of N.I. Kondrashova. The concentration of circulating immune complexes (CIC) in blood serum was determined by the method of selective presipitation of PEG - 6000 (V.M. Frolov, 1991) [10]. Affinity of antimicrobial IgG - antibodies was estimated using relative number by the method of R. Luxton and E. Tompson [11], Telnyuk Y.I. and co-writers [12]. Statistical processing of materials was carried out using mathematical statistics methods for analysis of the data obtained [13]. In particular, methods of evaluation, by means of which, with a certain probability, conclusions regarding distribution parameters were drawn. To determine the difference between mean values, the parametric Student's t-test and non-parametric - Wilcoxon signed-rank test were used. The verification of found differences was carried out at the level of significance < 0,05. In addition, statistical processing of results was performed using Microsoft Excel 2007 and MedStat program, according to the recommendations for the statistical processing of biomedical data [14].

Results of the study and their discussions. The results of the study indicate that after conducted therapy all indicators of humoral immunity in patients of main group with both I and II grades of disease development experienced positive changes. Already on the first day of the end of treatment (table 1, 2) reduction of increased values of IgE, CIC to the values of the norm was observed and normalization of complement activity in patients with GP of II grade of disease development occurred in this period.

Table 2

IgA IgM, IgG, IgE, CIC and complement concentration in blood serum in patients with GP of I grade of development on giardiasis background after the course of therapy.

Indicators	Before treatment 24 ppl./24 ppl.	After treatment			Group PHP 30 ppl.
		1 day	30 days	6 months	
IgA, g/l	1.31±0.19 1.31±0.19	1.50±0.19 1.35±0.19	1.52±0.15 1.41±0.18	1.51±0.14 1.42±0.16	1.51±0.14
IgM, g/l	1.28±0.14 1.27±0.14	1.38±0.17 1.30±0.16	1.24±0.16 1.27±0.16	1.22±0.14 1.24±0.15	1.22±0.13
IgG, g/l	12.1±1.32 12.0±1.32	12.6±1.43 12.1±1.44	12.83±1.33 12.0±1.36	12.45±1.20 12.3±1.36	12.41±1.11
IgE, IU	127.3±13.7* 127.3±13.7*	77.9±8.8** 115.6±13.1*	70.5±8.4** 91.4±10.9*,**	68.9±7.9** 96.8±11.3*,**	67.50±7.62
CIC, g/l	1.88±0.20* 1.87±0.20*	1.59±0.20 1.81±0.20*	1.42±0.19** 1.67±0.18	1.42±0.16** 1.67±0.18	1.41±0.12
Complement CH_{50}	71.0±6.38* 71.0±6.38*	65.91±6.79 68.53±7.01	60.86±6.18 63.26±6.31	60.59±5.18 63.84±6.32	60.52±4.51

Notes. Above the line - indicators of patients of the main group; under the line - patients of the comparison group; * - p<0.05 between the indicators of patients with GP and group PHI; ** - p<0.05 between the indicators of patients before and after treatment; *** - p<0.05 between the indicators of patients of main and comparison group.

Table 3

IGA IGM, IGG, IGE, CIC AND COMPLEMENT CONCENTRATION IN BLOOD SERUM IN PATIENTS WITH GP OF II GRADE OF DEVELOPMENT ON GIARDIASIS BACKGROUND AFTER THE COURSE OF THERAPY

Indicators	Before treatment 66 ppl. / 66 ppl.	After treatment			Group PHP 30 ppl.
		1 day	30 days	6 days	
IgA, g/l	1.33±0.19* 1.32±0.19*	1.44±0.20 1.40±0.20	1.50±0.18 1.42±0.18	1.52±0.18 1.46±0.18	1.51±0.14
IgM, g/l	1.29±0.14 1.29±0.14	1.39±0.17 1.31±0.16	1.26±0.17 1.28±0.17	1.22±0.15 1.28±0.17	1.22±0.13
IgG, g/l	12.53±1.51 12.53±1.51	12.59±1.60 12.55±1.60	12.56±1.51 12.46±1.56	12.55±1.36 12.90±1.57	12.41±1.11
IgE, IU	130.6±13.9* 130.7±13.9*	81.4±.9**.*** 119.6±13.9*	72.9±8.8**.*** 94.3±11.8*.**	68.7±7.9**.*** 98.3±11.9*.**	67.50±7.62
CIC, g/l	2.5±0.27* 2.4±0.27*	1.71±0.22** 2.0±0.24*	1.49±0.18** 1.81±0.21*	1.42±0.16**.*** 1.82±0.19*	1.41±0.12
Complement, CH50	79.3±6.73* 79.3±6.73*	68.7±6.83 70.7±6.91	62.1±6.82** 66.3±6.84	60.9±6.11** 67.6±6.73	60.52±4.51

Notes. Above the line - indicators of patients of the main group; under the line - patients of the comparison group; * - p<0.05 between the indicators of patients with GP and group PHI; ** - p<0.05 between the indicators of patients before and after treatment; *** - p<0.05 between the indicators of patients of main and comparison group.

Positive effect of treatment on these indicators remained throughout the entire observation period (6 months).

During the observation significant changes in immunoglobulins IgA, IgM, IgG levels in patients did not occur, with the exception of just a slight correction of their level to the average values of the norm.

However, reduction of increased values of IgE happened slowly in patients who were treated using the conventional therapy (comparison group), reliable differences in comparison with the values before the treatment were registered beginning only from the thirtieth day of the end of treatment (table 1, 2).

IgE level in blood of patients of the comparison groups remained significantly higher than values of the norm throughout the entire observation period. Concentration of circulating immune complexes (CIC) in blood of patients with GP of I grade of disease development of the comparison group did not differ significantly from the values of the norm only from the thirtieth day of the end of treatment. However, during all observation periods (1 day, 30 days, 6 months) significant differences occurred in the indicators of the CIC in patients with GP of II grade of disease development of the comparison group. Conducted studies showed that the activity of the complement before the treatment was not significantly different from the values of the norm in patients with GP of II grade of disease severity of the main group and the comparison group. On the 1st day of the end of treatment complement activity indicators in patients with GP of II grade of development of main and comparison groups returned to the value of the norm.

Under the influence of the developed therapy, a dynamic increase in the affinity of antimicrobial IgG antibodies occurred. The affinity of IgG antibodies in patients with chronic generalized periodontitis of I and II grades of main groups was recorded at the level of PHI group on the 1st day of the end of treatment and remained the same throughout the observation period (6 months) (table 3). Some increase in the affinity of IgG occurred in patients with GP of I and II grades of disease development of comparative groups after the end of treatment, but the restoration of the affinity to the values of norm did not occur during the entire observation period.

Table 4

Affinity of IgG antibodies to common antigenic determinant of bacteria in patients with GP of I and II grades of development, which progressed on parasitosis background before and after the course of therapy

Groups of patients	Before treatment	After treatment		
		1 day	30 days	6 months
CGP of I gr. + giardiasis	602,8±70,6*; n=24 602,8±70,6*; n=24	903,9±92,4**,*** 701,5±83,4*	>1000 **,*** 730,9±83,4*	>1000 **,*** 727,8±83,1*
CGP of II gr. + giardiasis	601,1±70,3*; n=66 601,1±70,3*; n=66	896,7±93,2**,*** 691,6±84,5*	>1000 **,*** 716,3±84,1*	>1000 **,*** 710,1±84,1*
Group PHP	>1000			

Notes. Above the line – indicators of patients of subgroups 2A, 2B, 2C; below the line – patients of subgroups 3A, 3B, 3C; * - p<0.05 between the indicators of patients with GP and group PHI; ** - p<0.05 between the indicators of patients before and after treatment; *** - p<0.05 between the indicators of patients of main and comparison group.

During all the observation periods the affinity of antimicrobial IgG antibodies in patients of comparison groups significantly differed from patients of main groups who received complex immunocorrective treatment.

The nature of the humoral systemic immunity component's response in patients with GP before and after treatment in the works of various authors [4, 7, 9, 12, 15,] has common tendencies, although the data regarding the concentration of individual immunoglobulins are sometimes controversial.

The results obtained by us are in general agreement with the opinion of other researchers [1, 2, 5, 7, 10]. Thus, Trigolos N.N. and co-authors [15] noted that the concentration of all three immunoglobulins (IgA, IgM, IgG) classes in the serum of patients with GP is significantly higher than in healthy persons. However, the authors noted a particularly high content of IgG in patients: (23.78 ± 0.61) g / l [control (13.97 ± 0.18) g / l, $p < 0.05$], emphasizing that its amount always grows with inflammation. Laktionov A.L. [12] also indicates the greatest increase in the concentration of IgG and IgM while reducing the level of IgA in patients with generalized periodontitis. Krainov SV [11] in the course of treatment for patients with GP follows a tendency to reduce the level of SIgA, IgA, IgG and IgM pointing out that the normalization of these indices occurred more dynamically in the group where immunomodulatory therapy was applied.

The author also notes that the stage of immunomodulation, included in the scheme of complex treatment in chronic generalized periodontitis, is able to provide a higher rate of recovery and stable normalization of immunological reactivity in patients. But there is another opinion. For example, Dirik V.T. [4] notes that the serum content of IgG in major groups patients with GP is lower than in the control group.

Conclusion

The obtained data indicate that the developed therapy for patients with chronic generalized periodontitis of development grades I and II against the background of giardiasis had a pronounced normalizing effect on the activity of humoral immunity. Under its influence IgE and CIC levels in blood serum normalize and the affinity of antimicrobial IgG antibodies grows.

Comparing the indices of immunological status in two experimental groups (the main and comparison groups) during all the observation period, it can be stated that the developed complex therapy with the use of immunomodulators is more effective and clinically promising than the conventional therapy.

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Реферати

КОРЕКЦІЯ ПАРАМЕТРІВ ГУМОРАЛЬНОЇ ЛАНКИ СИСТЕМНОГО ІМУНІТЕТУ У ХВОРИХ НА ГЕНЕРАЛІЗОВАНИЙ ПАРОДОНТИТ

Савельєва Н.М., Соколова І.І.

Досліджено динаміку показників гуморальної ланки системного імунітету при застосуванні комплексної терапії з включенням імуномодуляторів у хворих на генералізований пародонтит (ГП) хронічного перебігу I і II ступеня розвитку на тлі лямбліозу. Було обстежено 180 пацієнтів з лямбліоз у віці 20-40 років, хворих на ГП хронічного перебігу I і II ступеня розвитку (основна група і група порівняння). Пацієнти основної групи отримували розроблену комплексну терапію із застосуванням імуномодуляторів, пацієнтів групи порівняння лікували за традиційною схемою. Встановлено, що розроблена схема лікування має виражену нормалізуючу дію на активність гуморального імунітету. Під її впливом нормалізується вміст в сироватці крові IgE і і циркулюючих імунних комплексів (ЦІК), підвищується спорідненість антимікробних IgG-антитіл. Отримані дані дають підставу стверджувати, що схема розробленої комплексної терапії у хворих на ГП на тлі лямбліозу виявилася більш ефективною, ніж традиційне лікування.

Ключові слова: хронічний генералізований пародонтит, лямбліоз, гуморальний імунітет.

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КОРРЕКЦИЯ ПАРАМЕТРОВ ГУМОРАЛЬНОГО ЗВЕНА СИСТЕМНОГО ИММУНИТЕТА У БОЛЬНЫХ ГЕНЕРАЛИЗОВАННЫМ ПАРОДОНТИТОМ

Савельева Н.Н., Соколова И.И.

Исследована динамика показателей гуморального звена системного иммунитета при применении комплексной терапии с включением иммуномодуляторов у больных генерализованным пародонтитом (ГП) хронического течения I и II степени развития на фоне лямблиоза. Было обследовано 180 пациентов с лямблиозом в возрасте 20-40 лет, больных ГП хронического течения I и II степени развития (основная группа и группа сравнения). Пациенты основной группы получали разработанную комплексную терапию с применением иммуномодуляторов, пациентов группы сравнения лечили по традиционной схеме. Установлено, что разработанная схема лечения обладает выраженным нормализующим действием на активность гуморального иммунитета. Под ее влиянием нормализуется содержание в сыворотке крови IgE и ЦИК, повышается сродство антимикробных IgG-антител. Полученные данные дают основание утверждать, что схема разработанной комплексной терапии у больных ГП на фоне лямблиоза оказалась более эффективной, чем традиционное лечение.

Ключевые слова: хронический генерализованный пародонтит, лямблиоз, гуморальный иммунитет.

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PREDICTION OF HEPATIC FIBROSIS PROGRESSION RATE IN CHRONIC HEPATITIS C ON THE BASIS OF CLINICAL AND GENETIC SIGNS

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A cross-sectional study of 166 patients with chronic hepatitis C was carried out. As a result of the analysis, among the 35 possible factors of rapid progression of hepatic fibrosis in chronic hepatitis C, 10 most informative ones were identified: male gender (p=0.005), 1 genotype of HCV (p=0.040), alanine aminotransferase above 3 upper limits of normal (p=0.015), the levels of aspartate aminotransferase, γ-glutamyltranspeptidase and total bilirubin exceeding the upper limit of normal (p=0.000, p=0.000 and p=0.001, respectively), alcohol consumption >40 g/day (p=0.033), chronic cholecystitis and/or pancreatitis (p=0.000), type II diabetes mellitus (p=0.007) and a carriage of the normal genotype (Gln/Gln, Gln/-) of the TLR7 gene (p=0.001). In order to optimize the prognostication of the affiliation of a patient with chronic hepatitis C to the risk group of rapid progression of hepatic fibrosis there were proposed the highly effective mathematical model, developed on the basis of multiple discriminant analysis, exact forecast of which was 82.5 %.

Key words: chronic hepatitis C, the rate of fibrosis progression, prognostic model, discriminant analysis.

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At present, the hepatitis C virus (HCV) is the primary cause of chronic liver diseases [7]. HCV infection remains one of the most important problems of world health care due to its high prevalence, a constant tendency to an increase in the number of patients, a high level of chronic diseases development, the risk of hepatic cirrhosis and hepatocellular carcinoma, the complexity of treatment, and the lack of specific prevention [3, 11]. According to official data, there are 130-150 million patients with chronic hepatitis C (CHC) in the world, 700 thousand annually die of complications of this disease, and in the next 20 years, a further increase in mortality is predicted [11, 13].

Continuous progress is typical of CHC and now hepatic fibrosis (HF) is considered as a process by which a certain number of external factors interact with a unique combination of host factors, which causes significant differences in the natural course of the disease. There are virus factors (genotype and HCV quasispecies, the level of viral load) and host factors (male gender, duration of disease, age over 40 years