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## Dynamics of the secretory immunoglobulin a concentration in the oral fluid of the patients with generalized periodontitis

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### Abstract

The article shows the data of the completed clinical randomized, controlled, double-blind, parallel, longitudinal research of 96 somatic healthy people, aged from 18 to 35 years, including 68 patients with generalized periodontitis, who formed the main group (group A) and the comparison group (group C) and 28 persons without generalized periodontitis (control group N). We investigated the effect of the combined treatment on changes in the concentration of the secretory immunoglobulin A in the oral fluid. The quantification of SIgA in the oral fluid was conducted by the method of solidphase immunosorbent analysis. In the combined treatment of the patients of the group A except the basic initial periodontal therapy (removal of soft and hard dental plaque, detoxification and polish of roots, closed curettage) the additional drug therapy was applied: for the general treatment – synbiotic and vitamin and mineral complex, and for the local treatment - antibacterial gel, and also antiseptic preparation. The patients from the group C were treated similarly, excluding synbiotic. The Wilcoxon signed rank test (T - test) was used to assess the statistical significance of indicators difference in groups in different periods of observation for dependent samples, and to compare independent samples (groups N, A, C) – the Mann-Whitney test (U- test) was used. It was found that in the patients with chronic GP of I degree concentration of SIgA in oral fluid is reduced, or is within healthy parameters in comparison with healthy people. Under the influence of the combined treatment in patients of both groups (regardless of synbiotic) significantly increased the concentration of SIgA in the oral fluid immediately after the treatment. In the later periods of observation there was found the steady increase of SIgA level in group a (treated using synbiotic) and decrease in group C (treated without using synbiotic).

**Keywords:** generalized periodontitis, combined treatment, synbiotic, oral fluid, secretory immunoglobulin A.

### 1. Introduction

The condition of organism reactivity occupies a significant place in the genesis of periodontal diseases. Activity of dystrophic and inflammatory processes in periodontium (as a response to bacterial factors) cause local and general immunological mechanisms<sup>[1, 2]</sup> It is established that the development of generalized periodontitis (GP) occurs against a significant level reduction of antimicrobial systems of oral cavity, and reduction of nonspecific body resistance of patients correlates with the severity and duration of the pathological process in the periodontium<sup>[3, 4]</sup>.

An essential role in antimicrobial protection play all classes of immunoglobulins and, in particular, the secretory immunoglobulin A (SIgA), which is recognized as the most effective among many famous humoral protective factors of mucous membranes<sup>[5, 6]</sup>.

In the natural environment the SIgA effect may depend on the antibacterial substances of external secretion (lactoferrin, lactoperoxidase and lysozyme etc.) as well as on the state of microbiocenosis of mucous membranes, stress, speed of salivation, hormonal state, smoking, and others<sup>[7, 8, 9]</sup>.

Number of SIgA in a healthy body considerably surpasses this indicator for all classes of serum immunoglobulins<sup>[7]</sup>. It is believed that antibacterial protection in case of caries and periodontal diseases is provided by induction of IgA-antibodies by stimulating the immune system of the mucosa<sup>[5, 10, 11]</sup>. Deviation (usually reduction) in concentration of the main forms of immunoglobulins, as well as changes in the ratio between representatives of individual classes of immunoglobulins and other protective proteins can be the basis for the diagnosis of immune deficiency (secondary immunodeficiency) and the reason for the appointment of appropriate treatment<sup>[7]</sup>.

In recent years an interest to the infections treatment by using bacterial therapy increased

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Significantly [12, 13]. Scientists believe that supporting the natural balance of microflora and microbiological therapy are the main conditions to reduce the burden on the immune system. Special importance has the favorable local effect which probiotics make on the immune system of the intestinal mucosa, and through it - on the entire immune system [14]. The therapeutic potential of probiotic agents depends on the functionality of probiotic strains and their ability to survive. These conditions are satisfied by synbiotics - complex drugs that include optimal combination of probiotics and prebiotics. Since probiotic drugs have non-specific immunomodulatory effect, the research of changes in immune parameters under their influence is relevant [15, 16].

The purpose of this research was study of the influence of treatment method using synbiotic on concentration changes of SIgA in oral fluid of patients with GP.

## 2. Materials and methods.

The research was conducted on the basis of the Dental Center of University Hospital of Ivano-Frankivsk National Medical University. The article contains data of the completed research of 96 people, aged from 18 to 35 years, somatically healthy, among them - 68 patients with chronic GP of I degree, who formed the experimental group (group A) and group the comparison group (group C) and 28 healthy people (without GP), who formed the control group (group N). The development degree and the state of disease was determined by classification of M.F. Danilevskiy (1994), which is recommended as a working classification in educational and medical institutions of the country [17].

Research design: clinical, randomized, controlled, double-blind, parallel, longitudinal. The examination was carried out before, immediately after and 6 and 12 months after the treatment. The stratification by an age and a sex was conducted to form the homogeneous groups. The randomization was performed by the envelopes method. The masking was carried out by assigning a code to the patients, the researchers and the patients didn't know to which groups the last one belong. Due to requirement of concealment the results, one of the authors performed randomization code, that wasn't broken until the completion of all data were acquired and all analysis was finished. The research is non-interventional, was conducted without the participation of the pharmaceutical companies, and all the medicines, duly registered in Ukraine, were appointed by usual way under the terms of the registration dossier.

The work was conducted in accordance with the ethical principles of biomedical research involving human, which were adopted by the Helsinki Declaration of Human Rights and approved by the local ethics committee.

The criteria for inclusion were: age 18-35 years, GP of I degree, treated carious teeth, signed informative consent for participation in the research. The exclusion criteria were: tobacco smoking, alcohol and drug usage, pregnancy and lactation in women, acute and chronic diseases of internal organs, complicated caries, loss of more than two teeth, violation of the clinical controlled research terms.

The quantitative determination of SIgA in the oral fluid was conducted by the method of the solidphase immunosorbent analysis using commercial set of the firm, "Vector BEST" (Russia) on the enzyme-linked immunosorbent analyzer „Sunrise" (Tecan, Austria). The saliva for the research was taken in the morning, fasting, without morning oral hygiene in sterile tubes, frozed and stored for research at a temperature of

-20 °C.

In the combined treatment of the patients of the group (A) except the basic initial periodontal therapy (removal of soft and hard dental plaque, detoxification and polish of roots, closed curettage) the additional drug therapy was applied: for the general treatment – symbiotic "Atsydolak", one sachet (3 g of powder) of witch contains probiotics (lyophilized bacteria *Laktobacillus acidofilus* about 1,95 per 10<sup>9</sup> CFU, lyophilized bacteria *Bifidobakterium* about 1,95 per 10<sup>9</sup> CFU) and raftilose prebiotic; (2 sachets per day; course - 10 days); vitamin and mineral complex "Olihovit", containing vitamins (A, E, D, group B, PP, C), macronutrients (iron, magnesium, potassium, calcium), minerals (zinc, fluoride, copper, manganese, molybdenum, cobalt); (1 tablet 1 time a day; course - 20 days); for the local treatment - antibacterial gel "Metrodent" (containing metronidazole and chlorhexidine gluconate) for applications on gums under individually manufactured periodontal mouth guard (twice a day for 30 min.; course - 10 days), and also antiseptic and anti-inflammatory medication "Septofit-diet" (containing 0.1 mg of sodium usninat) for resorption (1 table 4 times a day, keeping in mouth to complete resorption, course - 10 days). The patients of the group (C) were treated similarly, excluding medication "Atsydolak".

The Wilcoxon signed rank test (T-test) was used to assess the statistical significance of indicators difference in groups in different periods of observation for dependent samples, and to compare independent samples (groups N, A, C) – the Mann-Whitney test (U-test) was used. The mathematical processing of the data was performed using the program Microsoft Office Excel 2007 and specialized computer environment of statistical data processing R (R Core Team (2014)). The description of quantitative indicators is presented in the format: median (Me) and interquartile swing (25-th (Q1); 75-th (Q3) percentile). The critical meaning of the statistical significance was considered equal to 0.05.

## 3. Results of the investigation and their discussion

SIgA concentration in the oral fluid of healthy individuals was 3.002 (2.219, 4.697) g / l in terms of me and was higher for such concentration in patients with to GP (see. Table 1). However, the statistical significance of indicators' differences for U-test was set at level  $p_{N-1A}=0,094$  ( $p_{N-1A}>0,05$ ) for group A and at level  $p_{N-1C}=0,028$  ( $p_{1A-1C}>0,05$ ) for the group C, and the difference between groups A and C at this stage was not detected ( $p_{1A-1C}>0,05$ ). This can be explained by the fact that according to the data of other studies the content of SIgA in oral fluid is affected by many different factors [7, 8, 9] and immunity tension is observed with periodontal diseases, which promotes multidirectional changes of SIgA concentration [10, 18], and insufficient capacity of nonparametric statistical criterion. Thus, our research found that in patients with GP of I degree without concomitant somatic pathology the SIgA concentration in oral fluid is slightly lower or ranges within indicators in healthy individuals.

Immediately after treatment SIgA levels increased in both groups. T-test revealed a statistically significant difference between the indices before and after treatment ( $p_{1A-2A}<0,001$ ;  $p_{1C-2C}<0,001$ ). It is not established statistically significant difference between the groups according to U-test at this stage of the study ( $p_{N-2A}> 0,05$ ,  $p_{N-2C}>0,05$ ,  $p_{2A-2C}>0,05$ ). Thus, complex therapy of GP promotes an increase of SIgA concentration in the oral fluid of patients of both groups.

After 6 months of treatment it was observed a content increase

of SIgA in group A and decrease - in Group C according to median index, but according to T-test a statistically significant

difference between the indicators after treatment and after 6 months is not set ( $p_{2A-3A} > 0,05$ ;  $p_{2C-3C} > 0,05$ ).

**Table 1:** The estimation of the SIg A (g/l) in the oral fluid concentration in the different observation periods Me (Q1; Q3))

Observation periods	Observation groups			Mann Whitney U-test
	control group (N), n=28	main group (A), n=33	comparison group (C), n=35	
before the treatment (1)	3,002 (2,219; 4,697)	2,798 (1,302; 3,357)	1,825 (1,169; 3,832)	$p_{N-1A} > 0,05$ $p_{N-1C} < 0,05$ $p_{1A-1C} > 0,05$
after the treatment (2)		2,931 (2,076; 4,265)	2,684 (2,150; 4,035)	$p_{N-2A} > 0,05$ $p_{N-2C} > 0,05$ $p_{2A-2C} > 0,05$
6 months after the treatment (3)		3,272 (2,180; 4,026)	2,245 (1,460; 3,700)	$p_{N-3A} > 0,05$ $p_{N-3C} > 0,05$ $p_{3A-3C} > 0,05$
12 months after the treatment (4)		3,262 (2,164; 3,943)	2,253 (1,290; 3,498)	$p_{N-4A} > 0,05$ $p_{N-4C} < 0,05$ $p_{4A-4C} < 0,05$
Wilcoxon T-test		$p_{1A-2A} < 0,001$ $p_{1A-3A} < 0,05$ $p_{1A-4A} < 0,05$ $p_{2A-3A} > 0,05$ $p_{2A-4A} > 0,05$ $p_{3A-4A} > 0,05$	$p_{1C-2C} < 0,001$ $p_{1C-3C} > 0,05$ $p_{1C-4C} > 0,05$ $p_{2C-3C} > 0,05$ $p_{2C-4C} < 0,05$ $p_{3C-4C} < 0,05$	

Note. Probability of p indicators difference:

N – indicators of the control group (healthy persons), 1A – indicators before the treatment in the group A, 2A – after the treatment in the group A, 3A – 6 months after the treatment in the group A, 4A – 12 months after the treatment in the group A, 1C – before the treatment in the group C, 2C – after the treatment in the group C, 3C – 6 months after the treatment in the group C, 4C – 12 months after the treatment in the group C.

On the tendency to SIgA level decrease in Group C indicates that there is no statistically significant difference between the indexes before treatment and after 6 months at this stage of observation ( $p_{1C-3C} > 0,05$ ), while in the group A a statistically significant difference between similar indicators remained ( $p_{1A-3A} < 0,05$ ). According to U-test a statistically significant difference between the groups after treatment was not revealed ( $p_{N-3A} > 0,05$ ;  $p_{N-3C} > 0,05$ ;  $p_{3A-3C} > 0,05$ ).

After 12 months a statistically significant difference of SIgA content with an indicator before treatment remained in group A ( $p_{1A-4A} < 0,05$ ) and it was not revealed a statistically significant difference between the indicators immediately after treatment and in 6 months ( $p_{2A-4A} > 0,05$ ), which indicates a steady increase of SIgA level in oral fluid of patients in this group. At this stage of research a statistically significant difference of indicators before treatment has not already been revealed in group C ( $p_{1C-4C} > 0,05$ ) and a statistically significant decrease in the concentration of SIgA compared to rates after treatment and after 6 months was observed ( $p_{2C-4C} < 0,05$ ;  $p_{3C-4C} < 0,05$ ). According to U- test no statistically significant difference has not been revealed between the group of healthy and group A at this stage of observation ( $p_{N-4A} > 0,05$ ). In this case a statistically significant difference is defined when comparing the indicators of group N and group C ( $p_{N-4C} < 0,05$ ) and group A and group C ( $p_{4A-4C} < 0,05$ ).

Thus, the downward trend of SIgA level in group C and consistently high indicators in Group A in the remote terms of observation (after 6 and 12 months) and also a detected statistically significant difference between the main group and group of comparison in 12 months may indicate a pronounced positive effect of the applied in group A complex therapy using the synbiotic medications on SIgA concentration in oral fluid and is consistent with the results of other researchers who have studied the effect of probiotic therapy on immune parameters [19, 20].

#### 4. Conclusions

It was discovered, that in the patients with chronic GP of I degree concentration of SIgA in the oral fluid was reduced or was within the healthy parameters in comparison with healthy people.

Under the influence of the combined treatment in the patients of both groups (regardless of synbiotic) significantly increased the concentration of SIgA in the oral fluid immediately after the treatment.

In the later periods of observation there was discovered a steady increase of SIgA level in the group A (treated using synbiotic) and a decrease in the group C (treated without using synbiotic).

The perspective of further research is to study the influence of the applied methods of treatment on the other immunological and biochemical parameters in oral fluid of the patients with GP.

#### 5. Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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