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CLINICAL AND IMMUNOLOGICAL FEATURES OF GINGIVAL EPITHELIUM AND THEIR CORRECTION IN CORONARY HEART DISEASE PATIENTS WITH PROLONGED USE OF ACETYLSALICYLIC ACID

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ABSTRACT

A great number of dental research is devoted to the studies on pathogenetic mechanisms of periodontal complex lesions in various pathological conditions and diseases of the human body. The study on changes in the oral cavity of patients with somatic diseases, who regularly take or have taken drugs for a long time, is of particular interest.

The present article is devoted to an urgent challenge in dentistry: alterations in the oral cavity of patients with coronary heart disease, who have to undergo the approved standard therapy taking acetylsalicylic acid at a dose of at least 75 mg per day.

Administration of even low doses of acetylsalicylic acid is associated with the 2-4 times increase of gastrointestinal bleedings risk. Regular intake of drugs by patients cannot but affect the health of the oral cavity organs and tissues.

The article presents comparative analysis of dental and immunological status of patients with different duration of acetylsalicylic acid intake. It is proved that above 50% acetylsalicylic acid taking patients with coronary heart disease have dental complaints (bleeding gums and enhanced sensitivity of hard dental tissues), while more than 70% suffer from pathological changes of hard dental tissues (wedge-shaped defects) and periodontal tissues.

It is shown that patients taking acetylsalicylic acid for less than 1 year have more expressed changes of hard dental and periodontal tissues regarding the prevalence rate and severity of clinical symptoms, as evidenced by index numbers.

Treatment efficiency was evaluated in the dynamics of clinical observation. Prescribing the local immunocorrective therapy and development of individual algorithms of oral hygiene lead to a more expressed normalization of immunological and clinical indicators in the oral cavity.

Based on data obtained it is possible to assert that patients taking acetylsalicylic acid during one year need additional preventive and therapeutic dental procedures no less than once in 3 months.

Thus, the need is justified for interaction of physicians – internists and dentists – for early detection of possible abnormalities in the oral cavity, as well as the need for development of algorithms on prevention and treatment of the specified impairment.

Keywords: coronary heart disease, acetylsalicylic acid, periodontium, CD-markers.

INTRODUCTION

Changes of hard and soft tissues of the oral cavity in various diseases of the human body, particularly in cardiovascular lesions, attract the interest of researchers during the last years [*Liu P. et al., 2006; Bahekar A. et al., 2007; Cronin A., 2009; Duan J. et al., 2009*].

Changes in the oral cavity of patients with somatic diseases, which are obliged to take drugs regularly or for a long time, are of particular inter-

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est [*Omarova H., 2003; Urakov A. et al., 2008*].

The current literature highlights specific changes in the oral cavity occurring against the background of periodical administration of various drugs [*Omarova H., 2003*]. However, the item of possible reactions to dental therapy, including a long-term administration of antiaggregatory drugs, has not been highlighted up to the present day [*Duan J., 2009*]. Thus, it often stays unknown, whether there is a connection between the pathological changes in the oral cavity and the impact of physical illness, or they are manifestations of side effects of the drugs [*Holmlund A. et al., 2006; Demmer R., Desvarieux M., 2006; Persson G., Persson R., 2008*].

Patients with coronary heart disease have to take antiaggregatory drugs for the prevention of recurrent ischemic attacks for a long time or even until the end of life [*Cardiovascular morbidity and mortality, 2009*].

Acetylsalicylic acid (ASA) is the "gold standard" and is widely used as a therapeutic and prophylactic agent for cardiovascular diseases in recent years [*Netyazhenko V., Malchevskaya T., 2005*].

The main mechanism of ASA action is an irreversible inhibition of cyclooxygenase-1 (COX-1) platelet enzymes that reduces thromboxane A2 precursor synthesis (inducer of platelet aggregation and a strong vasoconstrictor). In addition to reducing thromboxane A2 synthesis, ASA reduces the formation of vasodilators with de-aggregative properties − prostacyclin [*Shumakov V., 2011*].

However, it is the inhibition of COX-1 platelets that determines its anti-aggregative effect, since its re-synthesis is not possible in case of a nuclear-free platelet structure. ASA brings forth a loss of platelet aggregation properties over the entire period of their life (7-10 days).

In addition to reducing platelet aggregation, ASA indirectly, besides COX-1 and COX-2 enzyme inhibition, inhibits the synthesis of prostaglandins. It is known that in healthy tissues COX-1 causes the synthesis of prostaglandins, which are responsible for physiological cytoprotection in the digestive canal, including oral cavity. Prostaglandins promote the synthesis and secretion of mucus and sodium bicarbonate in mucous membranes and also promote endothelial cell proliferation. The decrease of prostaglandins synthesis reduces cytoprotective properties of mucous membranes of the upper gastrointestinal tract, which can lead to ASA side effects-induced inflammatory and destructive lesions of the mucous membranes and hemorrhagic complications, in particular: disorders of organs and tissues of oral cavity. Prostaglandins involved in inflammation are synthesized due to COX-2, which is activated in the inflamed tissues [*Brin V. et al., 2007; Mazur I. et al., 2010*].

The study objective was evaluation of dental status and immunological parameters of gingival epithelium in the dynamics of the clinical observations and their correction in patients with coronary heart disease after myocardial infarction with different duration of ASA treatment.

MATERIAL AND METHODS

To achieve the stated goals 90 patients aged 35 to 60 years with a verified diagnosis of coronary heart disease after myocardial infarction and receiving an outpatient and inpatient treatment at the State Institution "L.T. Malaya Therapy Institute of NAMS (Ukraine)" were chosen. At the time of examination, all patients were regularly taking antiaggregatory ASA therapy within 1 to 5 years (Aspirin, Cardiomagnyl − 75 *mg* per day), which was prescribed by the doctor-cardiologist based on international criteria and standards for diagnosis and treatment stated by the Ministry of Health of Ukraine. Depending on the ASA treatment duration, all patients were divided into groups: Group 1 − 1-47 patients taking ASA from 1 to 4 years, and Group 2 − 43 patients taking ASA for less than 1 year.

The study did not involve patients with active inflammatory processes in the oral cavity, endocrine disorders (diabetes mellitus), diseases of the gastrointestinal tract and women of postmenopausal age. All exceptions were due to the fact that the abovementioned pathological conditions directly affect the condition of periodontal tissues, as well as the fact that such patients are usually treated for comorbidities that may influence the clinical picture in the oral cavity during the study. None of the patients had medical history of data for surgical intervention on the heart. It should be also added that the study did not involve patients with evidence of aspirin-resistance.

Patients underwent clinical dental examination with determination of CFE index (C – carious

teeth, F – filled teeth, E – extracted teeth), Simplified Oral Hygiene Index (OHI-S) by J.C. Green, J.R. Vermillion (1964) and periodontal tissues state: papillary-marginally-alveolar index (PMA, in %) according to C. Parma (1960), complex periodontal index (CPI) as modified by P.A. Leus (1988), bleeding index according to H.R. Müchlemann (1971). All the indexes were presented in points [*Yudina N., Azarenko V., 2006*].

Changes in periodontal tissues were diagnosed based on systematics of M.F. Danilevsky (1994), gum recession was evaluated according to Miller classification (1970) [*Yudina N., Azarenko V., 2006*].

Cytological and morphometric studies were performed on scrapings of gingival epithelium. After rinsing the oral cavity with normal saline solution the gingival mucosa surface was scraped with light pressure using the end of a sterile dental spatula, and it was transferred onto a glass slide and dried for 2-3 minutes with open air access. Cytological preparations were stained with azure-eosin. Preparations were viewed in the light microscope "Micros" (Germany). A digital video camera "CAM 2800" (Germany) under light microscopy (optical train x40, ocular lens x10) was used to make photos of the cell. Fifty cell images with clear boundaries were selected for studies. The morphometric determination of the area and the perimeter of cell nucleus and cytoplasm and percent volume of cellular elements in cytological preparations of gingival mucosa was carried out using morphometric computer program "BioVision". The frequency of cells with abnormalities was determined based on 1000 cells.

Correlation analysis was performed for all morphometric parameters to identify the possible connection of these changes on the duration of ASA treatment.

The relative number of immune cells with CD4+, CD8+, CD4+/CD8+, CD16+, CD54+, CD95+ surface markers was evaluated by indirect immunocytochemical peroxidase method using the panel of monoclonal antibodies to CD4, CD8, CD16, CD54, CD95 white blood cell surface antigens, and also the index of immunoreactivity: CD4/CD8 ("Sorbent", Russia). Diaminobenzidine was used for detection of peroxidase. Preparations were viewed using light microscope ("Micros", Germany). The number of antigen-positive cells was determined as percent of stained by diaminobenzidine (brown) per 1000 cells in 5 fields of vision taking into account the percentage of stained cells in the preparations of negative control (negative control: incubation with buffer without using antibodies followed by peroxidase staining). Detailed description of the method: poly-L-lysine application to the slide with ripening and drying at room temperature, then applying a smear, fixing the cells in vapours of 4% solution of paraformaldehyde for 5 minutes to obtain cytological preparations; applying 1% bovine serum albumin (BSA) on phosphate buffered saline (PBS) with incubation for 30 minutes to block nonspecific binding of antibodies; application of 5 μl of studied monoclonal antibodies on cytological preparation with incubation for 45 minutes at 4°C; washing off not bonded monoclonal antibodies with the following gradual application of 50 µl of solution of the other antibodies F(ab)2 and 50 μl of freshly prepared mixture of 3,3-diaminobenzidine tetrachloride to cytological preparation with incubation. Further preparations are stained and washed and analyzed using light microscope.

Patients of Group 1 underwent professional tooth brushing followed by recommendations on hygienic care of the oral cavity. The follow-up visit of this group of patients was conducted after 6 months in order to study the further course of already existing changes and diagnostic evaluation of oral cavity alterations in dynamics.

Patients of Group 2 (taking ASA for less than 1 year) were randomly divided into subgroups: Subgroup 2A was represented by 22 patients, for which treatment and individual algorithm of oral hygiene were recommended after professional oral hygiene. Only the individual algorithm of oral hygiene was recommended to Subgroup 2B (21 patients) after professional oral hygiene. For local treatment Subgroup 2A patients used immunomodulator Derinat, which contains sodium deoxyribonucleate – a drug activating processes of cellular and humoral immunity. The drug was administered in the form of oral baths three times a day for 6 days.

The oral hygiene algorithm was recommended according to the following scheme: after meals in the morning and evening – mouthwashing using ½ cup of water, cleaning of dental gaps (toothpaste,

floss, superfloss), tongue cleaning, proper teeth cleaning; toothpastes (in case of dental hyperesthesia – Colgate for sensitive teeth "Complex Protection"; in case of absence of dental hyperesthesia – "Colgate Total 12") and finger gum massage with toothpaste rubbing ("Colgate Propolis", "Colgate with sea buckthorn", "Parodontax"), intensive rinsing using conditioners (according to indications – "Colgate Plax", "Herbs", "Refreshing Mint"). After each meal throughout the day – mouthwash using ½ cup of water and cleaning of dental gaps.

Re-examination of Group 2 patients was also performed after 6 months for comparison of preventive and treatment measures effectiveness.

The study was conducted as part of the scientific-research work of the Department of atherosclerosis and coronary heart disease, approved by the NAMS of Ukraine and approved by the ethics committee of the State Institution " L.T. Malaya Therapy Institute of NAMS (Ukraine)".

Statistical processing was conducted using computer programs "Statistica 5 for Windows". Compliance analysis of achieved data with the law of normal distribution of random quantities was performed for data processing. The results are shown as M±m (M – arithmetic mean, m – error of the arithmetic mean). Comparison of average values was performed using Student's *t* criteria. Statistical analysis of data was conducted at given reliability (0.95), obtained results were considered significant at $p<0.05$.

Results

The average age of the patients was 45-55 years. Patients of this age made 85.0% of all cases, while the age of 35-45 years was represented in 15.0% of patients.

It is known that the incidence of coronary heart disease increases among patients belonging to older age groups. The same pattern was observed among the studied cohort of patients. Registered distribution can be explained by atherosclerotic changes in vessels of patients from older age groups due to the loss of interaction of cellular and neurohumoral factors of blood with the artery walls. Among the patients of the study, men made the majority in Group 1 achieving 35 (74.5±1.25%) subjects, while the number of women was 12 (25.5±0.73%). As for Group 2, here the number of men was also higher: 34 (79.1%), whereas the number of women made 9 (21.0%). Male prevalence in the surveyed cohort of patients, in our opinion, can be explained by the increased percentage of men in the middle age category of Ukrainian population that is fully consistent with the literature data.

According to medical history data, gums bleeding upon teeth brushing was stated by 11 (23.4±6.2%) patients of Group 1 and 12 (27.9±6.8%) patients of Group 2. The ratio of bleeding when taking solid food for patients of Group 1 and 2 was 2 (4.3±2.9%) to 9 (20.9±6.2), respectively. Patients taking ASA for a long time stated teeth sensitivity significantly more often ($p<0.05$) than patients in Group 2. Thus, hypersensitivity to thermal stimuli troubled 8 (17.0±5.5) patients of Group 1; 2 (4.3±2.9%) patients mentioned increased sensitivity to the action of chemical factors, and mechanical stimuli evoked hyperesthesia in 3 (6.4±3.6) patients of this group. However, only 3 (7.0±3.9%) patients in Group 2 stated increased teeth sensitivity of the 1st degree, and 4 (9.3±4.4%) stated that of the 2nd degree.

Oral hygiene state in all patients was rated as satisfactory and Green-Vermilion index (OHI-S) in Group 1 was 1.43±0.11 and did not differ significantly from the index in Group 2 (1.24±0.13).

The CFE index in patients with long-term ASA treatment reached 10.65±0.56 ($p<0.05$) reliably differed from Group 2, the rate of which corresponded to 8.51±0.57. It should be noted that the number of filled teeth did not differ between groups of patients, while the prevalence of extracted teeth in patients of Group 1 was significantly higher.

A typical feature of these patients was the presence of non-carious teeth lesions, namely the V-shaped defects, the mean appearance value of which in Group 1 was 2.6 times higher than in Group 2, i.e. in patients recently receiving ASA.

In 23 (48.9±7.3%) patients of Group 1 gum recession was registered, the average value of which was 1.4 *mm* that was 5.7 times higher than the value in patients taking ASA for less than 1 year.

In the structure of periodontal diseases the incidence of inflammatory changes (gingivitis, periodontitis) was observed in 92.0±4.1% of patients

in Group 2 and only in 51.0±7.3% of Group 1 patients having not only inflammatory, but also atrophic changes in the periodontal tissues. All registered changes of periodontal complex were confirmed by index numbers (Table 1).

The morphometric analysis of gingival epithelial cells showed that both groups experienced changes of nuclear-cytoplasmic ratio, but the test group showed markedly significant decrease of this index due to the increase of the epithelial cells nuclei area in patients without significant changes in the area of cell cytoplasm.

TABLE 1.

The index assessment of periodontal tissues of the investigated patients

Indices	Group 1	Group 2
Simplified Oral Hygiene Index	1.4 ± 0.131	1.24 ± 0.13
Papillary-marginally-alveolar index,%	2 0.0 ± 0.02	21.0 ± 0.02
Complex periodontal index by Leus	0.92 ± 0.11	1.35 ± 0.14 *

NOTE: * - $p<0.05$.

Correlation analysis was carried out taking into consideration stated data, the purpose of which was to reveal a possible link between changes in the cell-nuclear ratio and the duration of ASA treatment (Figures 1-2). Correlation analysis revealed the presence of a moderate strength positive correlative relationship between the ratio of cell perimeter to the nucleus and the duration of ASA treatment. Changes in the nucleus, namely the increase of its size, can be associated with a reduction of the nucleus "shelf life" upon exposure to exogenous factors, which may include intake of medications.

In conducting gum white blood cell typing on expression of clusters of differentiation (CD-markers) on their surface it was found that all patients with coronary artery disease had significantly increased specific content of CD4+ cells (T-helper-inductors) and CD8+ cells (cytotoxic T-lymphocytes) compared with known normal range parameters. Immunoregulatory ratio of CD4/CD8 (the ratio of the major subpopulations of lymphocytes) in the examined patients was significantly reduced due to more significant growth of CD8 cells number.

The content of cells bearing a marker of natural killer cells (CD16+) significantly increased in both groups of patients, but during the long-term ASA therapy this increase ($p<0.05$) was significantly less expressed (22.09±0.60 and 37.14±0.61, respectively).

According to our data, the most pronounced expression of ISAM-1 (CD54+) was observed in Group 2 patients, who have recently taken ASA (49.09±0.74). It should be noted that on the background of long-term use of the drug this index was slightly lower (36.64±0.82; $p<0.05$).

The number of cells with the cell death programming receptor (CD95+) also increased in the groups of studied patients. The most marked increase in CD95 expression was noted in Group 2 (40.05±0.63) in contrast to those patients, who underwent long-term ASA therapy and had significantly decreased index equal to 31.98±1.35 ($p<0.05$).

Carrying out cytology studies revealed a significant increase in the number of white blood cells in the preparations of the patients not only in comparison with the normal range, but also between groups of patients (Table 2). However, white blood cells infiltration in patients receiving long-term ASA therapy was significantly lower than in other study group.

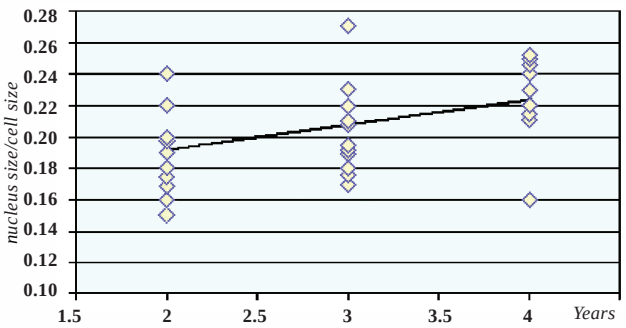

FIGURE 1. *Correlation of nucleus size/cell size and duration of ASA treatment in patients of Group 1.*

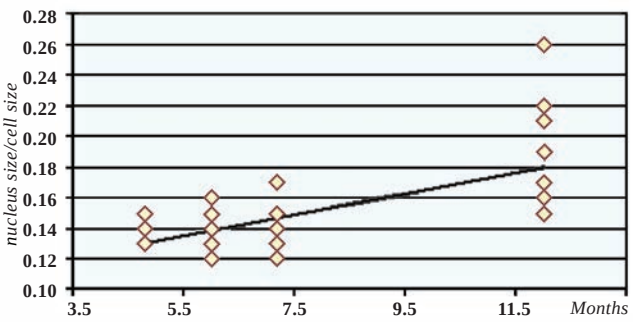

FIGURE 2. *Correlation of nucleus size/cell size and duration of ASA treatment in patients of Group 2.*

TABLE 2.

The composition of immune cells in scrapes from the gingival epithelium of study groups patients

Index	Group 1	Group 2
White blood cells	17.26 ± 1.28	34.26 ± 1.79 *
Neutrophils (%)	91.79 ± 0.44	85.12 ± 0.47 *
Lymphocytes (%)	4.28 ± 0.31	8.56 ± 0.40 *
Monocytes (%)	4.02 ± 0.22	6.26 ± 0.28 *

NOTE: * - $p<0.05$.

At the second visit (after 6 months) patients of Group 1 had reduced incidence of complaints for bleeding and discomfort in the gums. Thus, if at the first visit 23.4±6.2% of patients complained of bleeding during teeth brushing, then at the repeated examination the prevalence of complaints decreased 2.2 times. In addition, the number of complaints related to tooth sensitivity, especially those due to the impact of thermal stimuli, was 1.3 times higher.

The CFE index was significantly increased up to 11.8±0.47, and the frequency of occurrence of non-carious teeth lesions increased from 27.7±6.5% to 38.3±7.1% in the study of hard tissues. In addition, we recorded the 0.6 times increase in the frequency of the 1st degree gingival recession occurrence.

The changes in the structure of periodontal diseases were also observed: decrease in the number of catarrhal symptoms of gingivitis from 19.1±5.7% to 10.6±4.5%, though there was more than 2 times increase of atrophy propagation in periodontal tissues; this latter was reliably supported by a reduction of all periodontal index numbers.

In patients of both subgroups, 2A and 2B, no significant differences in the frequency of complaints related to gums bleeding were observed: neither at the first, nor at the second visit. However, the incidence of bleeding at hard food intake significantly decreased after the treatment course in subgroup 2A, while spontaneous bleeding was recorded in two patients of the subgroup 2B (Table 3).

If initially 7 (32.0±9.9%) cases of tooth sensitivity occurrence due to the action of different stimuli were registered in subgroup 2A before treatment, then after 6 months, although this parameter increased 1.4 times, it was still not significantly different from data of the first visit. No cases of hyperesthesia were recorded in the subgroup 2B before treatment, but after half a year, 10 patients (48.0±10.9%) mentioned this complaint.

Oral hygiene state for all patients was assessed as satisfactory and did not significantly differ not only between the two groups before treatment, but also within subgroups during the first and second visits. It should be noted that CFE index significantly increased from 8.81±0.91 to 9.48±0.87 in the subgroup 2B due to extracted teeth.

The changes in the structure of periodontal disease were also noted during the second visit. Thus, the frequency of catarrhal gingivitis occurrence significantly decreased from 50.0±10.7% to 4.5±4.4% in the subgroup 2A. Significant differences were also observed in the subgroup 2B, but there was only 2.6 times decrease in the frequency of diagnosis for catarrhal gingivitis. Moreover, a dental examination of subgroup 2A patients revealed no new cases and no exacerbation cases of existing degenerative inflammatory periodontal diseases; this latter differed from data of subgroup 2B, where aggravation of periodontitis and its conversion from the first to the second severity degree was reported.

Despite the stabilization of inflammatory and destructive processes, both groups showed signs of atrophy symptoms of periodontal complex disease (in subgroup 2A the index was 9.1%, while in the

TABLE 3.

The distribution of gingival bleeding in patients of subgroups 2A and 2B according to medical history

Bleeding degree	Subgroup 2A (n=22)					Subgroup 2B (n=21)				
	Before treatment	%	After treatment	%	*p*	Before treatment	%	After treatment	%	*p*
First	6	27.3	9	40.9	0.357	6	28.6	3.0	14.3	0.277
Second	5	22.7	0	0.0	0.022	4	19.0	4.0	19.0	1.000
Third	0	0.0	0	0.0	1.000	0	0.0	2.0	9.5	0.163

subgroup 2B it made 28.6% of cases). Dynamics of changes in the index numbers of periodontal tissue is presented in Table 4.

Both subgroup 2A and subgroup 2B tended to normalize immunological parameters (CD4+, CD8+, CD95+), but the values in subgroup 2A were significantly closer to the numerical values of the normal range. These values of the basic differentiation markers are shown in Table 5.

DISCUSSION

The clinical picture of patients with coronary heart disease taking ASA is in most cases characterized by development of dental disorders. More than 70.0% of CHD patients taking ASA have pathological changes of hard tissues of the teeth and periodontal tissues [*Demmer R., Desvarieux M., 2006; Holmlund A., 2006*].

The incidence and nature of complaints, the prevalence of non-carious pathology, changes of index numbers of periodontal tissues were significantly different in patients with different duration of ASA treatment. The vast majority of patients (77.0±1.6%) undergoing ASA treatment for less than one year have significant clinical changes in the periodontal tissues of an inflammatory nature, as opposed to patients taking ASA for a long period of time. Furthermore, the presence of gums recession and atrophic effects in periodontal tissues are typical feature of patients receiving long-term ASA treatment. It is known that there are changes not only in the blood vessels of the heart, but also in the microvasculature of the periodontal tissues in coronary heart disease. The ASA affects COX-1 and COX-2 synthesis by initially reducing the physiological synthesis of prostaglandin E2, and then the inflammatory prostaglandin [*Shumakov V., 2011*]. There is only a partial restoration of periodontal microvasculature during constant ASA intake, and part of the vessels are likely to undergo atrophy that further leads to atrophic changes in these tissues [*Brin V. et al., 2007*].

The morphometric analysis revealed a significant reduction in nuclear/cytoplasmic ratio in patients of the main (treatment) group due to the increase of epithelial cells nucleus area ($p<0.05$) on the background of the absence of significant changes in the area of the cell cytoplasm. Changes in the nuclei, namely the increase in its size, can be associated with a reduction in the duration of cell shelf life due to the impact of exogenous factors, among which medicines might be as well.

Furthermore, it is known that natural killers (NK-cells) with immunophenotypic markers CD16 exhibit cytotoxic activity and the ability to produce cytokines. Despite the fact that their number is very low in healthy gums, their content may increase with the severity of the disease. The protec-

TABLE 4.

The index assessment of periodontal tissues of the patients

Indices	Subgroup 2A (n=22)			Subgroup 2B (n=21)		
	Visit 1	Visit 2	*p*	Visit 1	Visit 2	*p*
Papillary-marginally-alveolar index(%)	22.0 ± 0.03	16.0 ± 0.02	0.0002	21.0 ± 0.02	18.0 ± 0.02	0.0023
Complex periodontal index	1.36 ± 0.19	1.09 ± 0.15	0.0148	1.33 ± 0.20	1.15 ± 0.15	0.0382
Müchlemann index	1.03 ± 0.17	0.80 ± 0.14	0.0130	1.02 ± 0.16	0.85 ± 0.13	0.0020

TABLE 5.

Changes of differentiation markers in scrapings from the gingival epithelium in the 6-month dynamics

Differentiation markers	Subgroup 2A (n=22)			Subgroup 2B (n=21)		
	before treatment	after treatment	*p*	before treatment	after treatment	*p*
CD4	42.55 ± 1.30	44.36 ± 1.01	0.0019	43.38 ± 1.14	43.95 ± 1.00	0.0192
CD8	29.73 ± 1.04	25.32 ± 0.52	0.0000	30.05 ± 1.25	27.95 ± 0.92	0.0006
CD4/CD8	1.44 ± 0.03	1.76 ± 0.04	0.0000	1.48 ± 0.05	1.59 ± 0.04	0.0001
CD95	39.77 ± 0.86	33.00 ± 0.57	0.0000	40.33 ± 0.93	37.81 ± 0.81	0.0000

tive function of the gums is provided by the immune competent cell system, dysfunction of which – in the progression of inflammatory processes – captures all the components of periodontium and underlies the pathogenesis of a number of dental diseases. The increase in number of monocytes and lymphocytes in the periodontal tissues is important since these cells play an essential role in induction and maintenance of inflammatory and destructive processes in periodontal issues. Lymphocytes are constantly found in gums epithelium of healthy person, but their number is not significant and they do not form clusters. Upon gums inflammation, and especially during the chronic process, the number of these cells dramatically increases. Monocytes/macrophages in normal range provide nonspecific and specific defense reactions, contributing to the effective destruction of foreign antigens. In studied cohort of patients, particularly those undergoing ASA treatment for no less than one year, local changes in the cellular composition of the gums are marked by increasing the number of polymorphonuclear white blood cells, as well as mononuclear cells. The immune competent cells are activating, enhancing further infiltration and contributing to the maintenance of the chronic inflammatory process. The reduction of white blood cell infiltration and a certain decrease in immune cells activity during prolonged ASA treatment may indicate suppression of inflammation and induction of periodontal tissues regeneration.

The growth of specific content of all researched CD-markers was revealed through gums white blood cells typing by their expression on the surface of differentiation clusters in patients, who undergo ASA treatment for less than one year, not only compared with the normal range, but also in comparison with the Group 1.

Thus, patients, especially during the first year of prescribed standard ASA therapy, need immediate dentist attention 2-3 times per year for early diagnosis and implementation of preventive and therapeutic measures to prevent the occurrence of abnormalities in the oral cavity.

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