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USE OF BIOMARKERS IN PLANNING PROSTHETIC REHABILITATION IN PATIENTS WITH PERIODONTIUM TISSUES DISORDERS

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According to WHO, about 75 % of population in different regions of the world suffer from partial adentia. Clinical observations demonstrate that in the majority of cases the cause of adentia is generalized periodontitis which is an inflammatory and destructive disease of periodontium tissues that is characterized by inflammation of gums, formation of periodontal pockets and progressing destruction of alveolar ridge which requires dental implantation and prosthetic rehabilitation.[1] Periodontitis is considered one of the most globally spread diseases, with the incidence of 15-20 %. [2] Moreover, periodontitis is connected to other serious diseases such as ischemic heart disease, head and neck carcinoma, and chronic obstructive pulmonary disease. [3-5] At present there are no standard criteria for prosthetic treatment efficacy. In practical work, only functional and aesthetic properties of dentures are estimated which gives their general characteristics alone. Present methods of more detailed estimation of dentures and their impact of periodontium tissues (electromyography, Doppler sonography, rheography, polarography, functional tests) are still under investigation and do not allow to use them in practical sphere. At the same time, the estimation of the prospective results of prosthetic rehabilitation and the analysis of complications, connected with implanting and teeth replacement, allow to assess risk factors, typical of different kinds of dental prostheses, to justify reasonability of their employment and to predict treatment results. In the context of the mentioned above data, there is strong necessity in the introduction of new enlightening, minimally invasive, practically applicable methods of estimation of denture base condition at planning implantological treatment and estimating the efficacy of the performed prosthetic rehabilitation. One of these methods is estimation of the level of biological markers of inflammation processes in oral fluid. The main task of biomarkers is early identification of a disease and conclusive estimation of treatment efficacy. Employing different laboratory methods of oral fluid analysis, it is possible to estimate the activity of the substances that are involved in metabolism at inflammatory diseases of the oral cavity [18]. During recent years the research for the introduction of molecular and biochemical markers analysis into dental practice at various oral cavity diseases has been actively conducted. It is commonly known that periodontitis is an inflammatory reaction; inflammatory process will lead to intensification of the secretion of anti-inflammatory cytokines, such as interleukin (IL) -1a, IL-1β, IL-6 and cachectin a (TNF-a). [6]. After this neutrophils release various enzymes, such as matrix metalloproteinases (MMP) and inflammation mediators. The detection of biomarkers in oral fluid is non-invasive, easily accessible and cost effective. Some clinical researches have revealed that some kinds of oral cavity biomarkers are connected either with the dento-facial system disorders or with systemic diseases [7]. The study of medical literature has confirmed considerable pathogenic role of some biomolecules, namely of matrix metalloproteinases of lactoferrin and cathelicidin, in the development of periodontium tissue diseases. Matrix metalloproteinases are the main proteases that contribute to periodontitis and are connected with periodontologial status. [8, 9] Type I collagen forms bulk of extra-cellular matrix of periodontium, that is why special attention was given to collagenases and gelatinases, suh as MMP-8, MMP-13, MMP-2 and MMP-9 at periodontitis [13]. Among them MMP-8 is the main collagenase at periodontitis; besides, from 90 to 95 % of collagenolytic activity in gum fluid is caused by MMP-8. Thus, at present MMP-8 is considered one of the most prospective biomarkers for diagnosing periodontitis in oral cavity fluid [10]. Though some studies have shown high level of MMP-8 of oral cavity fluid in patients with

periodontitis in comparison with healthy people [11,12]; other studies have demonstrated contrastive or ambiguous results [13,14]. Lactoferrin (Lf) is a multifunctional protein that belongs to transferrins that are synthesized by epithelial cells and are contained in different secretory fluids – oral cavity fluid, nasal glands discharge, breast milk – as one of the components of immune system. In modern practice Lf is used as organo-specific marker of pathogenic process activation for the purpose of diagnosis and prediction of diseases of mucous membrane and periodontium [15, 16]. Antimicrobial peptide cathelicidin (LL-37) is localized in neutrophils, skin, mucous membranes, and oral cavity fluid. Strong connection with the level of LL-37 in oral cavity fluid and oral cavity diseases has been estimated. The decrease of LL-37 concentration in saliva of compromised patients correlates with inflammatory diseases of periodontium tissues [17]. Taking into account everything mentioned above, the purpose of the present research was to estimate prognostically valid criteria at planning implantological and prosthetic treatment of patients with periodontium tissues disorders and defects of dental arches.

Materials and Methods. 80 patients were selected for the present study. Among them, 20 healthy patients comprised observational group, and 60 patients with periodontium tissues diseases formed treatment group. There were 20 patients with first-degree periodontitis, 20 patients with second-degree periodontitis and 20 patients with third-degree periodontitis and defects of dental arches. Diagnosis was grounded on the information obtained from patients' complaints, life histories, case histories, as well as from the results of objective examination (general and additional methods). Special attention was given to measuring such clinical parameters as the depth of periodontal pockets, ulaemorrhagia at probing, and sanitary state of the oral cavity. Values of such biomarkers as MMP-8, cathelicidin and lactoferrin were estimated in the oral cavity fluid with the employment of enzyme multiplied immunoassay.

Results. Obtained data are represented as M±σ, where M is mean value, and σ is mean-square deviation. Level of MMP-8 in oral cavity fluid increased directly depending on periodontitis degree. At first-degree periodontitis, values of MMP-8 increased 3 times in comparison with the observation group (0,223±0,09ng/ml). Values at second- and third-degree periodontitis increased 4 and 7 times correspondingly. Values of cathelicidin were estimated in inversed relation to MMP-8, i.e. they decreased according to periodontitis degree. At first-degree periodontitis, values of cathelicidin decreased 2 times in comparison with the observation group (4,34±1,36ng/ml). Values at second- and third-degree periodontitis decreased 5 and 12 times correspondingly. Values of lactoferrin increased directly depending on periodontitis degree. At first-degree periodontitis, values of lactoferrin increased 2 times in comparison with the observation group (15,6±6,4ng/ml). Values at second- and third-degree periodontitis increase 5 and 8 times correspondingly. It was discovered that values of lactoferrin and MMP-8 demonstrate direct correlational dependence $r=0,32$ ($P < 0,05$), while values of lactoferrin and cathelicidin demonstrate inversed correlational dependence $r= -0,34$ ($P < 0,05$).

Conclusion. Estimation of level of biomarkers in oral cavity fluid is a prospective diagnostic method which is minimally invasive, does not require specific qualification of a dentist, and gives an opportunity to estimate the present state of denture base tissues, which allows rational planning of prosthetic rehabilitation of dental patients and controlling the process of adaptation.

Further research prospective is the elaboration of scientifically grounded protocol of using molecular-biological markers in implantology and prosthetic rehabilitation of dental patients.

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Key words: periodontitis, MMP-8, lactoferrin, cathelicidin, prosthetic rehabilitation

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STATE OF CONNECTIVE TISSUE ELEMENTS OF THE DENTAL-MAXILLARY SYSTEM IN CHILDREN WITH DIFFUSE NONTOXIC GOITER

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The dental-maxillary human system consists of tissues, the majority of which is a kind of the connective tissue. The osseous alveolus, periodontium, gums, pulp, and dentine – all of them contain the main structure-forming elements as fibers and extracellular matrix. The latter one is presented by proteoglycans, heterogeneous proteins covalently bound with glycosaminoglycans (GAG) playing a crucial role in biochemistry of the connective tissue [1,2,3]. Changes of the connective tissue in case of pronounced functional disorders of the thyroid gland are described in endocrinology. For example, in case of hypothyroidism hydrophilic GAG and the products of their breaking down are accumulated causing mucous swelling of the interstitial tissues [4]. Meanwhile, scientific literature practically does not contain the information concerning disorders in GAG system and preclinical stages of the disease. Due to this fact we have conducted examination of biochemical markers of the connective tissue intercellular matrix metabolism in the oral cavity of children in case of the most spread thyroid pathology – diffuse nontoxic goiter (DNG).

Materials and Methods. 60 children suffering from DNG and 60 somatically healthy children aged from 12 to 15 years were examined. The following groups of observation were formed: IA – somatically and dentally healthy children (n=30); IB – somatically healthy children suffering from chronic catarrhal gingivitis (CCG) (n=30); IIA – dentally healthy children suffering from DNG (n=30); IIB – children suffering from DNG and CCG (n=30). The following biochemical indices were determined in the oral fluid of children: crude protein level by O.H. Lowry's method; glycoproteins level by E.G. Romanenko's method [5]; GAG level and their fractions by E.V. Kariakina's method [6]. The results obtained were statistically processed applying variation statistics methods.

Results. Changes of proteoglycans metabolism are reflected in changes of quantitative and qualitative GAG content in biological fluids of the human body. Due to this fact we consider it to be reasonable to determine general and fractional GAG content of the oral fluid in children under conditions of periodontal tissue pathology and comorbid pathology of the thyroid gland. The results of the study showed that in children under conditions of DNG general GAG level in the oral cavity is reliably higher than that of the somatically healthy children. Particularly, in case of clinically intact periodontium the difference between the indices was found to be approximately twice as much: IA group – (0,16±0,01) g/L, IIA – (0,31±0,03) g/L ($p<0,05$). In children suffering from CCG a reliable difference between the indices was found as well: IB group – (0,22±0,02) g/L, IIB – (0,38±0,01) g/L ($p<0,05$). Attention is drawn to the fact that GAG content in the oral fluid of children with underlying DNG without pathology of the periodontal tissue was (0,31±0,03) g/L, which is 42 % more than that of somatically healthy examined children with CCG – (0,22±0,02) g/L ($p<0,05$). An increased amount of free GAG is known to be in direct relation with the processes of the main substance degradation. Considering this nature of mucopolysaccharides origin it can be suggested that even when clinical signs of inflammatory processes are absent, certain metabolic disorders occur in the gums of children under conditions of DNG, which mostly promote development of periodontal tissue pathology. It is evidenced by the results of clinical examinations which determined reliably higher spread and intensity of periodontal tissue damage in children with the examined thyroid pathology. In GAG structure in children from all the groups of observation the fraction of sulfated GAG (SGAG) prevailed. The variants of it are the following compounds: chondroitin-4-