The Use of Biomarkers in Planning Prosthetic Rehabilitation in Patients with Periodontium Tissues Disorders

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Abstract

The research is devoted to the current issue of medicine - using of molecular-biological markers in implantation and prosthetic rehabilitation of dental patients with dental defects and periodontal tissue diseases.

Values of such biomarkers as MMP-8, cathelicidin and lactoferrin were estimated in the oral cavity fluid with the employment of enzyme multiplied immunoassay. 40 patients were selected for the present study. Among them, 10 healthy patients comprised observational group, and 30 patients with periodontium tissues diseases formed treatment group. There were 10 patients with first-degree periodontitis, 10 patients with second-degree periodontitis and 10 patients with third-degree periodontitis and defects of dental arches. Level of MMP-8 in oral cavity fluid increased directly depending on periodontitis degree. Values of LL-37 were estimated in inversed relation to MMP-8, i.e. they decreased according to periodontitis degree. Values of lactoferrin increased directly depending on periodontitis degree. Received findings indicates the destruction of connective tissue that points at the intensity of inflammation processes of oral cavity mucous membranes, decreasing of antimicrobial activity and decreasing of tissue immunity in the oral cavity.
Keywords: periodontitis, prosthetic rehabilitation, MMP-8, lactoferrin, cathelicidin ll-37

Research background

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]. According to research information, from 5% to 20% of population suffer from severe form of periodontitis, and the majority of adult population suffers from mild and medium forms of periodontitis [1] [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 informative, minimally invasive, practically applicable methods of estimation of denture base condition at planning implantological treatment and estimating the efficacy of the performed prosthetic rehabilitation.

Applying different laboratory methods of research of oral fluid composition, it is possible to define the activity of those substances that take part in metabolism at inflammatory oral cavity diseases [15].

Such a method is the estimation of the level of biological markers of inflammatory processes in the oral fluid.

At present biological markers are extensively used for more informative definition of treatment efficacy. Study of biomarkers level has clinical value for risk identification, for revealing the disease and its progress, as well as for the estimation of the therapeutic measures undertaken, which, in its turn, is the basis of individual approach establishment in modern clinical practice.[18]
In recent years, owing to numerous researches, biomarkers become more and more available. They complement clinical and radiological picture of a diseases, and allow the doctor to make appropriate decisions. Patients can also use biomarkers in order to get information on their health condition and the necessity of dental treatment. [18]

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) -1α, IL-1β, IL-6 and cachectin α (TNF-α). [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 periodontological 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, such as MMP-8, MMP-13, MMP-2 and MMP-9 at periodontitis [10]. 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 [13]. 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 belonging 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 [16, 17].

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 [16].

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

40 patients were selected for the present study. Among them, 10 healthy patients comprised observational group, and 30 patients with periodontium tissues diseases formed treatment group. There were 10 patients with first-degree periodontitis, 10 patients with second-degree periodontitis and 10 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 (Elabscience®, Human MMP-8 ELISA Kit), cathelicidin (HycultBiotech®, Human LL-37 ELISA Kit) and lactoferrin (HycultBiotech®, Human Lactoferrin ELISA Kit) were estimated in the oral cavity fluid with the employment of enzyme multiplied immunoassay.

The statistical analysis was performed by means of non-parametric statistic methods with the help of software Statistica (version 10.0; Statsoft, USA). Critical significance level at testing of statistical hypotheses was taken on the level p < 0.05.

Data are represented as $M \pm \sigma$, where $M$ is mean value, $\sigma$ is mean squared deviation.

Results

In this research the character of biomarkers composition in juvenile oral fluid prior to prosthetic rehabilitation has been defined. (chart 1)

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 ($0.223 \pm 0.09\text{ng/ml}$). Values at second- and third-degree periodontitis increased 4 and 7 times correspondingly. The increase of MMP-8 level in the oral cavity indicates the destruction of connective tissue that points at the intensity of inflammation processes of oral cavity mucous membranes and at the necessity in periodontological treatment.

Values of LL-37 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 ($4.34 \pm 1.36\text{ng/ml}$). Values at second- and third-degree periodontitis decreased 5 and 12 times correspondingly. Received findings demonstrate the decrease of antimicrobial activity both against Gram-positive and against Gram-negative bacteria. The deficienc of LL-37 in the oral fluid points at the direction of pathological manifestations and reflects the level of periodontium tissues inflammation.

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 ($15.6 \pm 6.4\text{ng/ml}$). Values at second- and third-degree periodontitis increase 5 and 8 times correspondingly. These findings prove the decrease of tissue immunity in the oral cavity.
Use of biomarkers in planning prosthetic rehabilitation

Chart 1. Measures of biomarkers in the oral cavity of patients with dental arches defects and periodontitis of various severity levels.

<table>
<thead>
<tr>
<th>Group</th>
<th>Molecular-biological markers</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MMP-8</td>
<td>LL-37</td>
<td>Lactoferrin</td>
</tr>
<tr>
<td>Observation</td>
<td>0,223±0,09</td>
<td>4,34±1,36*</td>
<td>15,6±6,4</td>
</tr>
<tr>
<td>I-level periodontitis</td>
<td>0,721±0,08</td>
<td>2,15±0,8</td>
<td>31,2±8,2*</td>
</tr>
<tr>
<td>II-level periodontitis</td>
<td>1,015±0,07*</td>
<td>0,868±0,2</td>
<td>78,3±9,1</td>
</tr>
<tr>
<td>III-level periodontitis</td>
<td>1,625±0,09</td>
<td>0,362±0,067*</td>
<td>124,8±10,2*</td>
</tr>
</tbody>
</table>

*the discrepancy is probable for observation group measures (p < 0,05)

It was discovered that values of lactoferrin and MMP-8 demonstrate direct correlational dependence r=0,32 (P < 0,05) which indicates the activity of inflammation processes in periodontium tissues. Values of lactoferrin and cathelicidin demonstrate inverse correlational dependence r=-0,34 (P < 0,05). These findings point at the suppression of tissue immunity, at the increased activity of neutrophils, and at the increase of pathogenic flora level.

Results obtained can be viewed as a potentially high risk for handling dental implantation and prosthetic rehabilitation of patients with periodontium disorders.

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.

References


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