Dynamics of Markers of Bone Resorption in Oral Fluid in Patients with Generalized Parodontitis During its Treatment

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Abstract

One of the promising courses in the clinical dentistry is the use of molecular biological markers in patients with periodontal disease. First of all, this is due to the rising trend in the prevalence and risk factors of the disease, which makes relevant finding effective methods for early detection and preventive treatment. 30 patients diagnosed with generalized periodontitis of the I and II degree of severity were selected for the research. In the experimental groups of patients, an immunoassay was used to determine the marker level of bone marrow metabolism (MMP-8) in the oral fluid, in the dynamics of treatment.

During the study, the content of this enzyme was found to be indicative of the transformation of the inflammatory process in the gums into the destruction of the alveolar bone.

The obtained values of the concentration of MMP-8 in the oral fluid, as well as their dynamics, proved this marker to be indicative of the course of the inflammatory-destructive process in periodontal tissues, and therefore the possibility of its application for the diagnosis and monitoring of the results of treatment of generalized periodontitis

Keywords: generalized periodontitis, matrix metalloproteinase-8, oral fluid, diagnosis

Research background

The problem of diagnosis and treatment of periodontal inflammatory diseases is one of the most significant at present. According to WHO, the prevalence of periodontal disease in people over 40 years old exceeds 95%. The disease often occurs aggressively, has a steadily progressive course and is difficult to treat. At the same time, generalized periodontitis has the first place among periodontal diseases in the prevalence [1]. It should be noted that generalized periodontitis presents a serious socio-economic problem, as it causes the loss of teeth in 21.0% of cases [2]. In turn, the tendency to increase the prevalence of the disease is due not only to socio-economic problems, but also to the growth of risk factors, which makes it relevant to find effective methods for early diagnosis and preventive treatment [3, 4].

The transition of the pathological process from the inflammatory stage to the inflammatory-destructive, which is characterized by the defeat of the bone tissue of the alveolar appendix, is rather complicated and requires additional research methods [5].

The radiographic investigation is widely known to be the most indicative criterion of the efficacy of generalized periodontitis treatment. Based on its results it appears possible to reveal with certainty whether the stabilization of the pathological process in the circulatory tissues was achieved. Nevertheless, the condition of the alveolar bone can be effectively assessed only in 6-12 months period following the treatment which complicates monitoring the process of treatment and correction of therapeutic measures. In this regard, the search for new non-invasive and informative methods of detection is the most urgent task of modern dentistry, which can include biochemical examination of oral fluids [5].

Various studies have proved that the main cause of inflammation in periodontal tissues is the microbial factor, namely, qualitative and quantitative changes in the microflora of the oral cavity, in particular the activation of parodontopathogenic microorganisms. In terms of pathogenesis, periodontitis is one of the causes of the destruction of the connective tissue of the periodontal complex, characterized by collagen and proteoglycan metabolism disorders, and, consequently, resorption of bone and the formation of periodontal pockets [7].

The development of the inflammatory process in the periodontium leads to increased secretion of proinflammatory cytokines such as interleukin-1α, interleukin-1β, interleukin-6, tumor necrosis factor-α. Accordingly, neutrophils produce a large number of enzymes, in particular matrix metalloproteinases, and inflammatory mediators. Increasing the concentration of the latter in saliva is an early diagnostic sign of inflammatory processes in the oral cavity. Thus, special attention, in the context of early detection of destructive processes in the bone component of periodontal disease, should be paid to increasing the concentration of enzymes involved in its destruction of connective tissue due to the development of inflammation, namely collagenases, which include matrix metalloproteinases. Among the last matrix metalloproteinase-8 (MMP-8) is considered the main during periodontitis, because 90-95% of collagenolytic activity falls on it [8].

Generally, matrix metalloproteinases, Zn2 + and Ca2-dependent endopeptidases, are enzymes for the metabolism of most proteins of the extracellular matrix at various stages of the inflammatory process. Matrix metalloproteinase-8 (MMP-8) refers to MMP secretory type (classical, free, soluble), to the class of collagenases. As it was first discovered in neutrophils, therefore it was called "neutrophil collagenase". It accumulates in specific granules of circulating neutrophils. Active in relation to type I collagen, although its effect on other types of collagen is indicated. Activate and stimulate the release of MMP-8 in the inflammatory site of interleukin-1β, interleukin-8, tumor necrosis factor-α [9].

Based on the above-stated level between the level of MMP-8 and collagen-1 degradation products in patients with generalized periodontitis compared with healthy ones, the level of this enzyme in biological fluids is considered as a biomarker of periodontitis [10].

MMP-8 is a promising biomarker in the oral cavity (in ash fluid, peri-implant fluid and saliva), not only to determine the progressive stages of periodontitis and to control the efficacy of the treatment, as well as the peri-implant. Matrix metalloproteinase-8 can be used alone or in combination with other indicators - interleukin-1β and Porphyromonas gingivalis in periodontal pockets. This diagnostic complex is recommended as an alternative in the absence of a comprehensive periodontal examination [10].

In addition to the above-mentioned aspects, the increased level of matrix metalloproteinases, in particular, MMP-8, binds to the active stage of the inflammatory-dystrophic process in periodontal tissues and, accordingly, the rapid destruction of bone tissue [11], which makes it possible to consider it as a marker of the transition of the inflammatory process in the gums, which occurs when gingivitis, to the destruction of the alveolar bone, which is itself a prognostic sign of periodontitis [12].

Parallels between pathogenesis of periodontitis and peri-implant can be typically drawn. However, in an experiment in mice, the greater severity of the inflammatory and dystrophic process was demonstrated around implants rather than around the teeth which was characteristic for a correspondingly higher concentration of MMP-8 [13]. Interestingly, according to the results of a study of

89 patients with 171 intra-skeletal implants, the level of MMP-8 did not differ with mucositis and peri-implant, in contrast to gingivitis and periodontitis [14].

In connection with the above-mentioned goal of our study, the promising use of matrix metalloproteinase-8 (MMP-8) in patients with generalized periodontitis in the dynamics of treatment was revealed.

Materials and methods

The study was conducted among 30 persons in the age between 37 to 45, equal number of men and women, 15 of whom were diagnosed with generalized periodontitis of the I degree of severity, and 15 with the II degree of severity. As the control, results from a group of 8 persons with intact periodontal tissues, selected similarly for the gender and age characteristics of the observation group, were used. To assess the periodontal condition, a traditional clinical examination, supplemented by the results of an X-ray study, was used.

Particular attention was paid to measuring of such clinical parameters as the depth of periodontal pockets, bleeding gums during probing and determining the level of hygiene of the oral cavity. The degree of gingival bleeding was determined using the Muleman Index (SBI). The level of oral hygiene was calculated using the simplified index of oral hygiene in Green-Vermillion (OHI-S). Periodontal index (PI) and index of gingival inflammation (PMA) were also determined. The radiological picture was analyzed on the basis of orthopantomogrammas, taking into account the level of decrease in the height of interalveolar septa and the level of exposure to the roots of the teeth.

All patients with generalized periodontitis received complex treatment in accordance with the protocols of the provision of dental care: removal of dental plaque, smoothing and polishing of the root, immobilization of mobile teeth by splinting. As local therapy, rinsing with antiseptics, gingival treatment, processing of periodontal pockets of anti-inflammatory and antibacterial agents, surgical treatment including curettage according indications was applied.

The content of MMP-8 in the oral liquid was studied through the immune enzyme method (BCM Diagnostics, DMP800, Total MMP8). The research was conducted before and immediately after the treatment (elimination of acute inflammatory events in the peritoneum tissues was considered as a completion of the course).

The data of the conducted clinical and laboratory studies were processed using the MS Excel 2003 software.

Results

As a result of the conducted biochemical studies, an increase in the level of MMP-8 in the oral fluid in patients with generalized periodontitis was proved (0.4 ± 0.1 ng / ml under the I degree of severity, 0.7 ± 0.2 ng / ml – under the II degree against 0.1 ± 0.03 ng / ml of control, $p < 0.05$). At the same time, after a

complex treatment, the level of this indicator decreased to 0.2 ± 0.07 ng / ml under the I degree of severity and to 0.5 ± 0.1 ng / ml – under the II degree (p <0,05).

However, it should be noted that the results obtained after the course of treatment outweighed the control values (p > 0.05) which, in our opinion, suggest only inhibition of the pathological process rather than its complete elimination.

Thus, the study results demonstrated the increase of the level of MMP-8 in the oral fluid increases in comparison with the control values and correlates with the severity of the pathological process in the periodontal tissues. The treatment of generalized periodontitis resulted in a decrease of the MMP-8 in oral fluid.

Conclusion

The level of MMP-8 in the oral fluid increases in comparison with the control values according to the severity of the pathological process in the peritoneal tissues.

Noteworthy that as a result of the treatment of generalized periodontitis, the parameters of MMP-8 in the oral liquid decrease. They approach the values of the control, but do not correspond to them which indicated the stabilization of the pathological process in the periodontal tissues.

The obtained values of the concentration of MMP-8 in the oral fluid, as well as their dynamics, proved this marker to be indicative of the course of the inflammatory-destructive process in periodontal tissues, and therefore the possibility of its application for the detection and monitoring of the results of treatment of generalized periodontitis.

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