Advances in Science and Education, 2025, 48–51

doi: 10.70728/edu.v01.i08.011
Volume 01, Issue 08
ISSN: 3060-5415
Paper

PAPER

CHANGES IN THE LEVELS OF MATRIX METALLOPROTEINASES IN ORAL FLUID DURING THE DEVELOPMENT STAGES OF PERIODONTITIS

Rustamova S.M. [1] *, Xadjhimetov A.A. [2], Ataxodjayeva M.A. [3], Rejabboyeva N. L. [4]

[1]Doctor of philosophy in biological sciences, PhD, Tashkent State Medical University, Tashkent, Uzbekistan
[2]Doktor of biology, professor, Tashkent State Medical University, Tashkent, Uzbekistan
[3]Candidate of chemistry, Associate professor, Tashkent State Medical University, Tashkent, Uzbekistan
[4]Assistant, Tashkent State Medical University, Tashkent, Uzbekistan

* rustamova31@gmail.com

Abstract

Identifying biomarkers of periodontal diseases and early diagnosis of the disease serves to enhance treatment effectiveness for numerous patients suffering from periodontal diseases worldwide. Starting from gingivitis, which is inflammation of the gum tissues, it can progress to periodontitis, an irreversible condition that leads to the destruction of periodontal tissues, including periodontal pockets and alveolar bones. It is known that during the development of periodontitis, at the gingivitis stage, patients experience gum inflammation without loss of soft and hard tissues. In the initial stages of periodontitis, gum inflammation is observed in patients, while in the subsequent stages of the disease, loss of soft and hard tissues is noted. Therefore, the sequential levels of change in markers across different stages of periodontitis development, along with combinations of biomarkers, provide effective results for diagnosing the disease state.

Key words: saliva, oral fluid, homeostasis, chronic periodontitis, metalloproteinases, gingivitis.

INTRODUCTION

Systematic reviews and meta-analyses have identified five promising biomarkers of oral fluid as effective diagnostic criteria for the early diagnosis of periodontal diseases. At the early stage of development of inflammatory periodontal diseases, patients exhibit gum inflammation accompanied by the destruction of connective tissue, progressing to the destruction of alveolar bone at later stages of the disease. We believe that changes in markers occur sequentially across different phases of periodontitis;

Compiled on: November 1, 2025.

therefore, combinations of biomarkers can be used more effectively for the early diagnosis of this pathology, where a significant role is played by Porphyromonas gingivalis (Pg), interleukins of oral fluid (IL)-1β, and matrix metalloproteinase (MMP)-8, which are closely associated with the development of periodontitis [3,4,7]. Metalloproteinases (MMPs) play no small role in the development of this process, with their inhibitors being tissue inhibitors of matrix metalloproteinases (TIMP) and serum glycoproteins such as α2-macroglobulin. Disruption of the balance between MMP levels and the emergence of inhibitors is considered a decisive factor determining the primary activity of MMPs. During the destruction of periodontal tissues, the synthesis and secretion of MMPs are disrupted, the balance between MMP and TIMP shifts, and levels of neutrophilic MMPs, such as MMP-8 and MMP-9, increase—likely due to a significant rise in the number of macrophages and neutrophils migrating to the site of periodontitis. Enhanced production of pro-inflammatory cytokines in response to microbial products triggers a cascade of reactions, one of which is the stimulation of proteolytic enzyme activation (markers of connective tissue breakdown), where metalloproteinases (MMPs) occupy an important place [1,10]. Given that numerous studies have demonstrated increased expression and activity of MMP-9 and MMP-8 in patients with periodontal diseases, they have been proposed as valid indicators of the disease. An important biological function of MMP-8 in the periodontium is to facilitate the migration of leukocytes, particularly neutrophilic granulocytes, from the bloodstream into the periodontal sulcus by degrading collagen and other components of the extracellular matrix. Additionally, following the onset of inflammation, other cell types (e.g., fibroblasts) may also express MMP-8. It is believed that elevated expression, release, and activation of uncontrolled MMP-8—along with other MMPs and proteinases—induces inflammation associated with tissue destruction in periodontal diseases, as well as in other inflammatory conditions [2,6]. Since type I collagen is the primary component of the periodontal extracellular matrix, particular attention is given to the role of collagenases, especially MMP-8, as one of the most promising biomarkers of periodontitis in oral fluids. MMP-8 and MMP-9 are the most prevalent MMPs in periodontal tissues, and their levels reflect the severity of the disease, its progression, and response to treatment [15].

RESEARCH OBJECTIVE: The purpose of this study was to assess metabolic biomarkers of collagen degradation in oral fluid in patients with periodontal disease.

MATERIALS AND METHODS

Immunological research methods were used in the examination of patients. Under observation were 68 patients with gingivitis and moderate chronic generalized periodontitis (CGP). The control group consisted of 16 somatically healthy individuals aged 30.3±2.1 years, without any nosological forms of acute or exacerbation of chronic periodontal diseases, including those of the oral mucosa, without bad habits or the intake of any medications. The gender distribution in this group was as follows: 45 men (66.1%) and 23 women (33.9%). Levels of metalloproteinase-8 (MMP-8) and pyridinoline cross-linked carboxyterminal telopeptide (ICTP) in oral fluid were determined using commercial enzyme-linked immunosorbent assay (ELISA) kits obtained from the company ”HUMAN”in accordance with the manufacturer’s instructions. Calculations were performed using the SPSS Statistics 21 software package (Statistical Package for the Social Sciences), license №20130626-3, and Microsoft Excel 2007 (Office Professional Plus 2007, license number 45754073) [12,13].

RESULTS OF THE STUDY

Our research demonstrated that the most significant differences were observed in terms of MMP-8 (collagenase-2, neutrophilic collagenase). Neutrophilic collagenase, produced by various cellular elements of the inflammatory focus (neutrophils, epithelial cells, macrophages, plasma cells), is a key enzyme in the degradation of the extracellular matrix, including various types of collagen (I, II, III, V, VII, VIII, X) as well as non-collagenous proteins (aggrecan, elastin, fibronectin, gelatin, laminin, α2-macroglobulin, C1q, angiotensin I, angiotensin II, fibrinogen, bradykinin) [11,14]. Additionally, it participates in dentin demineralization and, upon further

progression, can cause destruction of the alveolar bone.

Table 1. Average Levels of MMP-8 and ICTP in Oral Fluid in Patients with Gingivitis and Periodontitis

Indicator	Healthy Group (Control) n = 14	Gingivitis Group n = 26	Periodontitis Group n = 28
MMP-8 (ng/dL)	4.23 ± 0.41	21.74 ± 3.04*	40.62 ± 2.98*
ICTP (ng/mL)	13.58 ± 1.54	19.24 ± 1.87	48.63 ± 3.91*

Note: * – significantly different compared to the healthy group ($P < 0.05$).

As can be seen from the presented research results (table), the content of MMP-8 in the oral fluid of patients with gingivitis shows an elevated level of metalloproteinase on average 5.1 times compared to healthy patients. The table above also indicates that patients with periodontitis have an elevated level of MMP-8 by 9.6 times when compared to the control group indicators. The observed dynamics of MMP-8 in the oral fluid of the examined patients induce inflammation associated with tissue destruction in periodontal diseases. Pyridinoline cross-linked carboxyterminal telopeptide (ICTP), whose concentration in the oral fluid of the examined patients was elevated, is a product of type I collagen breakdown, specifically the main component of alveolar bone. In inflammatory periodontal diseases, accelerated osteoclastic resorption and degradation of the collagen matrix occur, resulting in the formation of pyridinoline, deoxypyridinoline, and amino- and carboxyterminal cross-linked telopeptides of type I collagen, which then enter the bloodstream [1,5]. In alveolar bone, the dominant form of type I collagen is ICTP (pyridinoline cross-linked carboxyterminal telopeptide of type I collagen). In progressive gingivitis and periodontitis, ICTP degrades and is released under the action of bacterial collagenase or pro-inflammatory mediators of inflammation. Due to this specificity, as a byproduct of alveolar bone destruction, pyridinoline cross-links can be used for the early diagnosis of connective tissue destruction in the periodontium [9].

DISCUSSION OF THE OBTAINED RESULTS

Based on the obtained research results, it can be concluded that MMP-8 and ICTP are currently the most sensitive biomarkers for diagnosing inflammatory processes in the periodontium, as well as indicators of connective tissue and alveolar bone destruction. The elevated levels of MMP-8 and ICTP identified by us, in our opinion, reflect the phase of collagen degradation during the development of inflammatory processes in periodontal tissues and can be useful for monitoring disease activity and appropriate therapy [8].

CONCLUSIONS

1. A complex of oral fluid biomarkers was studied in patients with gingivitis and periodontitis, and the dynamics of periodontal biomarker content in oral fluid were determined in patients with gingivitis and periodontitis.

2. In the context of molecular-destructive disorders in chronic generalized periodontitis and gingivitis, an increase in the content of metalloproteinase-MMP-8 and ICTP in oral fluid was noted, which allows for assessing the degree and dynamics of the inflammatory process and developing treatment tactics for this periodontal pathology.

REFERENCES

1. Вавилова, Т.П., Медведев А.Е. Биологическая химия. Биохимия полости рта. учебник / Вавилова Т.П., Медведев А.Е. – М. : ГЭОТАР-Медиа, 2014. – 560 с.ил.

2. Бельская Л. В., Сарф Е.А., Косенок В. К. Биохимия слюны: методы исследования. // Омск: Омскбланкиздат. - 2015. - 70 с.

3. Бельская Л.В., Сарф Е.А., Косенок В.К, Массард Ж. Антиоксидантная активность смешанной слюны человека в норме // Экология человека. - 2017. - №6. - С. 36.

4. Герасимова Л.П., Кабирова М.Ф., Усманова И.Н., Гадиуллин А.М. Влияние лечебно-профилактических зубных паст на процессы свободнорадикального окисления в модельных системах и ротовой жидкости у пациентов с хроническим гингивитом // Паро-

донтология. – 2016. – Т. 21. – № 2 (79). – С. 53-56.

5. Гончар, Ф.Л. Микрокристаллизация ротовой жидкости как общий показатель гомеостаза организма / Ф.Л. Гончар, И.О. Походенько- Чудакова // Инновационные подходы в практическом решении актуальных вопросов современной ЧЛХ и стоматологии : сб. тр. респ. науч.-практ. конф. - Минск, 2010. - С. 70-72.

6. Григорьев С.С. Диагностические возможности определения цитокинового профиля в сыворотке крови и ротовой жидкости у больных с синдромом Шегрена // Григорьев С.С., Бейкин Я.Б. Уральский медицинский журнал. – 2008. – № 10 (50) С. 24–26.

7. Елендо М.Б., Ломиашвили Л.М., Васильева Н.А. Особенности суточной динамики биохимических показателей ротовой жидкости пользователей ПК // Уральский медицинский журнал. - 2013. - №5 (110).-С. 46-50.

8. Елендо М.Б., Ломиашвили Л.М., Васильева Н.А. Особенности суточной динамики биохимических показателей ротовой жидкости пользователей ПК // Уральский медицинский журнал. – 2013. – № 5 (110). – С. 46–50.

9. Леус, П.А. Диагностическое значение гомеостаза слюны в клинике терапевтической стоматологии : учеб.-метод. пособие / П.А. Леус ; Белорус. гос. мед. ун-т ; 2-я каф. терапевт. стоматологии. - Минск : БГМУ, 2011. - 67 с.

10. Мандра Ю.В. Повышенная стираемость твердых тканей зуба: ранние клинические проявления, морфоструктурные изменения, лечебно-профилактические методы коррекции // Автореферат дисс. на соиск учен. степени д.м.н. – Екатеринбург. – 2011. – 35 с.

11. Рустамова С.М., “Пародонт касалликларини эрта ташхислашда хроматография усулининг самарадорлиги” : услубий тавсияноma. 11.12.2023й. Тошкент 2023. С.5-7.

12. Рустамова С.М., Хаджиметов А.А., Ахмадалиев Н.Н. “Пародонт касалликларини эрта ташхислашда оғиз суюқлиги биомаркерларининг диагностик алгоритмини ишлаб чиқиш” : услубий тавсиянома. 11.12.2023й. Тошкент 2023. С.10-13.

13. Рустамова С.М., Хаджиметов А.А., Ахмадалиев Н.Н. Determining the correlation between the biochemical composition of blood plasma and saliva. “Problems and milestones of immunophysiology development in the new Uzbekistan” International scientific-practical conference. Tashkent Uzbekistan. 10.05.2023 year

14. Рустамова С.М., Хаджиметов А.А., Ахмадалиев Н.Н.,Атаходжаева М.А.,Эргашева В.Ш. Correlation relations of the composition of saliva and blood plasma in the norm. BRITISH VIEW Volume7,Issue 4,2022. С.101-108

15. Сунцов В.Г., Волошина И.М. Особенности состава и свойств в ротовой жидкости у детей при различном уровне интенсивности кариозного процесса // Стоматол. журн. 2010. № 1. С. 12—14.

16. Шаковец Н.В., Лихорад Е.В. Слюна: значение для органов и тканей в полости рта в норме и при патологии // Медицинский журнал.2013.№3.С.7-11