DYNAMICS OF SECRETORY IGA IN PATIENTS WITH GENERALIZED CHRONIC PERIODONTITIS

Sashkina TI, Runova GS, Abdullaeva AI, Bozhedomov AYu ✉, Saldusova IV, Zaychenko OV, Faskhutdinov DK, Sokolova SI

Pirogov Russian National Research Medial University, Moscow, Russia

Generalized chronic periodontitis (GCP) is a widespread disease. It has a serious negative impact on the quality of a patient's life, posing a challenge to dentists all over the world. At present, standard therapy regimens for GCP adopted in the Russian Federation do not account for the mucosal barrier state, which is determined by a number of various factors, including the levels of secretory immunoglobulin A (sIgA). In our study, we attempted to assess the functional state of the mucosal barrier in patients with GCP and to provide a rationale for using immunotherapy aimed at restoring the effective barrier function of the oral mucosa. SIgA concentrations, which served as an indicator of the mucosal barrier state, were measured with ELISA. We found that patients with GCP had significantly lower sIgA concentrations in the oral fluid in comparison with healthy individuals. Although therapeutic procedures did help to increase sIgA levels, they still were much lower after therapy than in healthy volunteers (54.6 ± 30.5 μg/ml vs 151.2 ± 105.2 μg/ml). Increased permeability of the mucosal barrier caused sIgA to leak into the peripheral blood serum, where its concentration grew from 0.21 ± 0.28 μg/ml to 0.35 ± 0.47 μg/ml during the treatment course, suggesting damage to the mucosal integrity. This fact needs to be accounted for when treating patients with GCP.

Keywords: generalized chronic periodontitis, mucosal barrier, sIgA

Author contribution: Sashkina TI, Runova GS — study design, data processing, manuscript revision; Abdullaeva AI — data acquisition, manuscript draft preparation; Bozhedomov AYu — data processing, statistical analysis, manuscript revision; Saldusova IV, Zaychenko OV, Faskhutdinov DK, Sokolova SI — data processing, manuscript revision.

Compliance with ethical standards: the study was approved by the Ethics Committee of Moscow State University of Medicine and Dentistry (Protocol № 23 dated May 26, 2011). The patients gave informed consent to participation in the study and publication of its results.

✉ **Correspondence should be addressed:** Alexey Yu. Bozhedomov
Ostrovityanova 1, Moscow, 117997; alecso_84@mail.ru

Received: 19.05.2019 **Accepted:** 04.06.2019 **Published online:** 14.06.2019

DOI: 10.24075/brsmu.2019.039

ДИНАМИКА СЕКРЕТОРНОГО IGA У БОЛЬНЫХ ХРОНИЧЕСКИМ ГЕНЕРАЛИЗОВАННЫМ ПАРОДОНТИТОМ СРЕДНЕЙ ТЯЖЕСТИ

Т. И. Сашкина, Г. С. Рунова, А. И. Абдуллаева, А. Ю. Божедомов ✉, И. В. Салдусова, О. В. Зайченко, Д. К. Фасхутдинов, С. И. Соколова

Российский национальный исследовательский медицинский университет имени Н. И. Пирогова, Москва, Россия

Хронический генерализованный пародонтит (ХГП) широко распространен во всем мире. У больных снижается качество жизни, поэтому лечение данного заболевания является актуальной проблемой стоматологии. В настоящий момент терапию ХГП в Российской Федерации проводят по стандарту, не учитывающему важнейшую составляющую пародонта — мукозный барьер. Его состояние зависит от многих факторов, в том числе уровня секреторного иммуноглобулина А (s-IgA). Целью исследования было оценить состояние мукозного барьера для обоснования применения методов терапии, позволяющих восстановить его эффективность. В качестве инструмента для оценки эффективности слизистого барьера мы использовали уровень s-IgA, который определяли методом иммуноферментного анализа. Мы показали, что в ротовой жидкости у больных ХГП уровень s-IgA значительно снижен по сравнению со здоровыми. Проведенная стандартная терапия повышает его уровень, но он остается достоверно ниже, чем у здоровых (54,6 ± 30,5 мкг/мл; 151,2 ± 105,2 мкг/мл соответственно). Увеличение проницаемости слизистого барьера приводит к появлению s-IgA в сыворотке периферической крови, причем его концентрация возрастает после проведенной терапии с 0,21 ± 0,28 мкг/мл до 0,35 ± 0,47 мкг/мл, что свидетельствует о значительных нарушениях целостности мукозного барьера у больных ХГП и о необходимости учитывать эти нарушения при проведении терапевтических мероприятий.

Ключевые слова: хронический генерализованный пародонтит, мукозный барьер, s-IgA

Информация о вкладе авторов: Т. И. Сашкина и Г. С. Рунова — планирование исследования, обработка полученных данных, редактирование рукописи; А. И. Абдуллаева — сбор данных, написание черновика рукописи; А. Ю. Божедомов — обработка полученных данных, статистическая обработка данных, редактирование рукописи; И. В. Салдусова, О. В. Зайченко, Д. К. Фасхутдинов и С. И. Соколова — обработка полученных данных, редактирование рукописи.

Соблюдение этических стандартов: исследование одобрено этическим комитетом Московского государственного медико-стоматологического университета (протокол № 23 от 26 мая 2011 г.), все пациенты подписали добровольное информированное согласие на участие в исследовании и публикацию результатов.

✉ **Для корреспонденции:** Алексей Юрьевич Божедомов
ул. Островитянова, д. 1, г. Москва, 117997; alecso_84@mail.ru

Статья получена: 19.05.2019 **Статья принята к печати:** 04.06.2019 **Опубликована онлайн:** 14.06.2019

DOI: 10.24075/vrgmu.2019.039

A healthy oral mucosal barrier is critical for protecting periodontal tissue against inflammation. Its functional state is determined by a variety of specific and nonspecific humoral and cellular factors including those that promote continuous renewal of the epithelial surface. Periodontitis is characterized by the loss of integrity and abnormal blood flow in periodontal tissue. The tissue gets infiltrated by immune cells and pathogenic bacteria, which eventually causes damage to the mucosal barrier, affects its protective properties and promotes inflammation. Secretory immunoglobulin A (sIgA) is one of the crucial components of the mucosal barrier. This immunoglobulin is synthesized in lymphoid tissue associated with salivary glands and lymphocytes underlying the epithelium in the *lamina propria*. There are a few factors that interfere with tissue healing and can be observed in patients with periodontal pathology: hypoxia, immune imbalance, abnormal neutrophil activity, elevated proinflammatory cytokines, and aberrant sIgA levels. The barrier function of the oral mucosa can be

assessed by measuring sIgA concentrations. Such tests are particularly relevant in dentistry and other medical fields that involve the study of oral mucous membranes. According to recent publications, local immunity is compromised in patients with congenital or acquired susceptibility to chronic periodontitis. This refers to sIgA levels in the first place. Therefore, adding immunotherapy to the treatment regimens would be beneficial for such patients [1–7]. The aim of the present work was to assess the dynamics of sIgA levels as an indicator of the mucosal barrier state in patients with generalized chronic periodontitis (GCP) and to provide a rationale for using immunotherapy aimed at restoring the effective barrier function of the oral mucosa.

METHODS

The study was conducted at the facilities of the Department of Clinical Pathophysiology of Pirogov Russian National Research Medical University. We examined 178 patients with GCP and identified those suffering from a moderate form of the disease. The age of the selected patients was 37 to 52 years. Severity of periodontitis was graded according to the criteria of Russian Dental Association (RDA, 2012). SIgA was measured in the samples of oral fluid collected from 25 participants. Oral fluid samples collected from healthy volunteers aged 25 to 49 years were used as a control.

The following inclusion criteria were applied: voluntary consent to participate, no decompensated conditions, no severe occlusal diseases, arch integrity (except for single dental crowns), and no removable dentures.

The study excluded patients with other types of pathological inflammation of the oral cavity, systemic inflammatory or autoimmune disorders, severe decompensated chronic conditions, those undergoing exposure to occupational hazards, suffering from decompensated occupational diseases, severe metabolic disorders (diabetes mellitus, obesity, gout, etc.), acute inflammation (acute respiratory infection, pneumonia, bronchitis, etc.), menopausal disorders, smoking, alcohol/drug abuse, as well as pregnant patients and those unwilling to comply with the study rules.

The study group received standard therapy against moderate GCP recommended by RDA: the oral cavity was rinsed with chlorhexidine, miramistin or triclosan; full mouth debridement was performed (plaques and calculus were removed) and metronidazole was applied locally. On average, the course of treatment lasted 10 to 14 days.

SIgA concentrations were measured in the samples of oral fluid and peripheral blood serum before and after the treatment using ELISA. For the analysis, we used monoclonal antibodies specific to the secretory immunoglobulin component (Seramun Diagnostica GmbH; Germany). Saliva samples were either fasting or collected no sooner than one hour after meals.

The obtained data was analyzed using Student's t-test for normal distribution. Normality of data distribution was assessed with the Shapiro-Wilk test: if the yielded value was over 0.05, distribution was considered normal. Sample variance was calculated before and after the treatment. If the obtained values were equal, means (M) and the standard deviation (σ) were computed and compared to the reference values, considering that differences were significant at $p < 0.05$. The results were presented as $M \pm \sigma$.

Statistical analysis was performed in *Statistica* v10.0 (*StatSoft*; USA).

RESULTS

Secretory immunoglobulin A is produced by plasma cells arising from the differentiation of B lymphocytes associated with major and minor salivary glands or present in the *lamina propria* of the oral mucosa. The immunoglobulin is released into the cavities lined with mucosa and is not expected to be found in the peripheral blood. So, we hypothesized that damage to the oral mucosa would result in the "leakage" of sIgA into the blood serum.

We found that sIgA was present in the serum and oral fluid of patients with GCP. SIgA concentrations in the oral fluid were significantly lower in the diseased individuals than in the healthy volunteers both before and after the treatment. Before the treatment, sIgA levels in the blood serum of the patients were 0.21 ± 0.28 μg/ml, exceeding the values demonstrated by the healthy participants (0.11 ± 0.06 μg/ml).

Before the treatment, sIgA concentrations measured in the oral fluid of the patients were 36.5 ± 28.6 μg/ml, whereas after the treatment the figures changed to 54.6 ± 30.5 μg/ml, which was significantly lower ($p < 0.05$) than in the healthy volunteers (151.2 ± 105.2 μg/ml). SIgA was present in the serum of patients with GCP both before and after the treatment. Upon completing the treatment course, SIgA concentrations were found to have increased from 0.21 ± 0.28 to 0.35 ± 0.47 μg/ml. This is not typical, but considering that sIgA levels in the oral fluid and in the serum had risen by 52% and 50%, respectively, by the end of the treatment course, we can assume that the mucosal barrier did not recover and its permeability remained high. Therefore, the rise in sIgA concentrations both in the oral fluid and blood serum was almost identical (Fig. 1 and 2).

DISCUSSION

By the end of the treatment course, sIgA had increased by 51% relative to its initial concentrations, but the increase amounted to only 35% of the reference values, which is apparently not enough to ensure effective protection, regeneration and stability of periodontal tissue in the presence of other factors promoting susceptibility to periodontitis. Under such

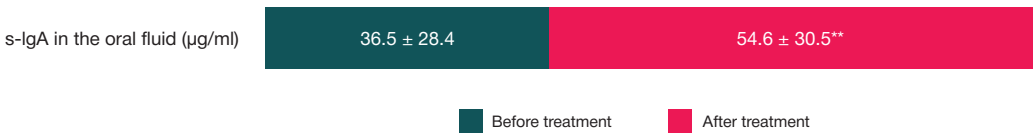

Fig. 1. SIgA concentrations in the oral fluid of patients with GCP before and after the standard treatment (** $p < 0.05$)

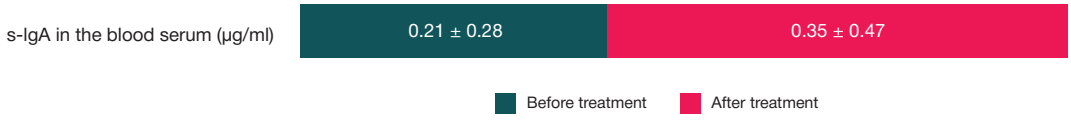

Fig. 2. SIgA concentrations in the blood serum of patients with GCP before and after the standard treatment

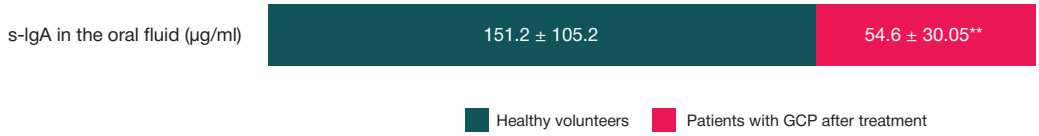

Fig. 3. Comparison of SIgA concentrations in the oral fluid of patients with GCP after the standard treatment and in healthy volunteers (** $p < 0.05$)

Fig. 4. Comparison of SIgA concentrations in the blood serum of patients with GCP after the standard treatment and in healthy volunteers (** $p < 0.05$)

conditions, microorganisms thrive, continuing to colonize the periodontium of the patients with compromised innate and acquired (lysozyme, interferons, lactoferrin, etc.) immunities (Fig. 3) [8].

Our hypothesis about damage to the mucosal barrier in patients with GCP is supported by the results of sIgA measurements in the blood serum of such patients. After the treatment, sIgA was elevated. Increased sIgA in the oral fluid can be explained by the fact that standard therapies rely on the use of antimicrobial drugs and professional dental cleaning, which reduces bacterial burden in periodontal tissue. As the bacterial population shrinks, sIgA concentrations grow since sIgA is utilized by the organism less intensively; however, its synthesis does not increase (Fig. 4).

In addition, our study demonstrates that conventional therapy causes only temporary improvement in the periodontal tissue state, ensuing from the use of antimicrobial agents and professional dental cleaning procedures. Recovery of the mucosal barrier does not occur because its permeability remains abnormally high even after the treatment. We observed an increase in sIgA levels both in the oral fluid and blood serum of the patients who underwent the full treatment course. Therefore, in spite of positive dynamics of periodontal indices and mitigated symptoms of inflammation (reduced swelling and bleeding, alleviated pain, partial or full resolution of discomfort in the mouth), the efficacy of treatment for chronic periodontal inflammation should be improved further. The applied therapies should account for all known mechanisms of pathology, including damage to the mucosal barrier.

CONCLUSIONS

The standard treatment regimen for GCP includes professional dental cleaning procedures, antimicrobial and anti-inflammatory drugs. It does not have a healing effect on the mucosal barrier, which largely determines the ability of periodontal tissue to regenerate. This conclusion was drawn from the increased sIgA concentrations in the blood serum of patients with GCP after completing the full therapy course. When the integrity of the mucosal barrier breaks, pathogenicity factors damage periodontal tissue, leaving it remodeled and unresponsive to treatment. In patients with periodontal inflammation, treatment outcomes can be improved by using a comprehensive approach that accounts for all known mechanisms of this pathology.

References

1. Sashkina TI, Volozhin AI, Atakanova ZA, Shevchenko TV. Povyshenie mestnogo immuniteta v polosti rta s pomoshh'ju zhevatel'nyh tabletok Kolostrum (molozivo novozelandskih korov). Cathedra. Stomatologicheskoe obrazovanie. 2007; 6 (3): 30–3. Russian.
2. Horuzhaya RE, Horuzhij ME, Isakov SV. Sostojanie slizistoj obolochki polosti rta i tkanej parodontal'nogo kompleksa u pacientov kardiologicheskogo profilja. Vestnik neotlozhnoj i vosstanovitel'noj mediciny. 2011; 12 (2): 287–90. Russian.
3. Kim MI. Vospalitel'nye zabolevanija parodonta kak projavlenie sistemnoj disfunkcii jendotelija. Krims'kij terapevtichnij zhurnal. 2012; (2): 38–40. Russian.
4. Dmitrieva LA, redaktor. Parodontit. Uchebnoe posobie. M.: MEDpresInform, 2007; 25 s. Russian.
5. Shatohin AI. Parodontopatii pri VICh-infekcii kak prognosticheskij pokazatel' immunosupressii. Parodontologija. 2012; 17 (3): 3–6. Russian.
6. Strobel S. Oral tolerance, systemic immunoregulation and autoimmunity. Ann N Y Acad Sci. 2002; (958): 47–58.
7. Sugawara S, Uehara A, Tamai R, Takada H. Innate immune responses in oral mucosa. J Endotoxin Res. 2002; 8 (6): 465–8.
8. Churilov LP, Vasilyev AG. Patofiziologija immunnoj sistemy. SPb.: Foliant, 2014; 664 s. Russian.

Литература

1. Сашкина Т. И., Воложин А. И., Атаканова З. А., Шевченко Т. В. Повышение местного иммунитета в полости рта с помощью жевательных таблеток Колострум (молозиво новозеландских коров). Cathedra. Стоматологическое образование. 2007; 6 (3): 30–3.
2. Хоружая Р. Е., Хоружий М. Е., Исаков С. В. Состояние слизистой оболочки полости рта и тканей пародонтального комплекса у пациентов кардиологического профиля. Вестник неотложной и восстановительной медицины. 2011; 12 (2): 287–90.
3. Ким М. И. Воспалительные заболевания пародонта как проявление системной дисфункции эндотелия. Кримський терапевтичний журнал. 2012; (2): 38–40.
4. Дмитриева Л. А., редактор. Пародонтит. Учебное пособие. М.: МЕДпресИнформ, 2007; 25 с.
5. Шатохин А. И. Пародонтопатии при ВИЧ-инфекции как прогностический показатель иммуносупрессии. Пародонтология. 2012; 17 (3): 3–6.
6. Strobel S. Oral tolerance, systemic immunoregulation and autoimmunity. Ann N Y Acad Sci. 2002; (958): 47–58.
7. Sugawara S, Uehara A, Tamai R, Takada H. Innate immune responses in oral mucosa. J Endotoxin Res. 2002; 8 (6): 465–8.
8. Чурилов Л. П., Васильев А. Г. Патофизиология иммунной системы. СПб.: Фолиант, 2014; 664 с.