

# CYTOKINE PROFILE OF PERIODONTAL POCKET CONTENTS IN ESTIMATING THE SEVERITY AND EFFICIENCY OF TREATMENT OFFERED TO PATIENTS WITH REFRACTORY PERIODONTITIS

*Article history:*  
Submitted 11 April 2019  
Accepted 17 June 2019

**Natalia Bulkina<sup>1</sup>, Victoria Morgunova<sup>1\*</sup>, Yulia Osipova<sup>1</sup>,  
Nadezhda Pronina<sup>1</sup>, Elena Polosukhina<sup>1</sup>, Olga Guseva<sup>1</sup>,  
Anna Kropotina<sup>2</sup>, Valeriy Konnov<sup>3</sup>**

<sup>1</sup> Department of Therapeutic Dentistry; Saratov State Medical University, Saratov, Russia

<sup>2</sup> Department of Clinical Dentistry, St. Petersburg Medical and Social Institute, St. Petersburg Russia

<sup>3</sup> Department of Orthopedic Dentistry; Saratov State Medical University, Saratov, Russia

\*Corresponding Author: [victoriamorg@yandex.ru](mailto:victoriamorg@yandex.ru)

**ABSTRACT** — Recent years have witnessed an increase in periodontitis prevalence, which is hard to cure while the treatment is administered properly, and has a persistently relapsing course. In this article, the enzyme-linked immunoassay with identification of the periodontal pockets exudate cytokine profile, allows us to carry out a better evaluation of the severity and effectiveness of treatment for patients with refractory periodontitis.

**KEYWORDS** — periodontal issues; refractory periodontitis

## INTRODUCTION

Refractory (resistant) periodontitis develops despite treatment, has a complex course and reveals a huge number of complications [3, 6]. At the same time, the loss of supporting tissues goes on in several areas of periodontium [4, 7, 9, 11, 12]. The affected areas are infected with periodontal pathogens [8]. During that, the pathological process is accompanied by the development of dysbiosis and an imbalance of pro-inflammatory and anti-inflammatory cytokines in the periodontal pockets exudate, the severity of which features a direct dependence on the severity of inflammatory & destructive processes that are underway in periodontal tissues [5, 10]. This pathological process may get enhanced in case of comorbid conditions [13–22].

*Aim of study:*

to identify the clinical efficiency of the cytokine profile in the pro-inflammatory cytokines IL-1 $\beta$ , TNF- $\alpha$  and the anti-inflammatory cytokine IL-10 in order to

evaluate the severity and effectiveness of the treatment for refractory periodontitis.

## MATERIAL AND METHODS

The examination involved 100 patients (53 females and 47 males). Group 1 included 40 patients with chronic generalized periodontitis, Group 2 — 40 patients with refractory periodontitis. The control group included 20 volunteers with intact periodontium. Refractory periodontitis was verified subject to the classification by G.F. Beloklitskaya (2007) [1, 2].

The criteria for setting the diagnosis of refractory periodontitis include a persistently relapsing course; loss of supporting tissues in several areas of the periodontium; massive loss of supporting tissues followed by teeth loss; a large number of exacerbations and complications.

All the patients underwent a comprehensive examination using standard clinical, laboratory and radiological methods. The immunological checkups included an assessment of the content of interleukin 1 $\beta$ , tumor necrosis factor  $\alpha$ , and interleukin 10 in the gingival fluid, which was done through enzyme-linked immunoassay. The dynamics study for the immunological parameters of periodontal pockets exudate was performed both in the main group and in the comparison group. In order to obtain control values, a study of gingival fluid immunological parameters was performed in 20 healthy individuals with intact periodontium.

## RESULTS AND DISCUSSION

Immunological studies showed a significant increase in the proinflammatory interleukin 1 $\beta$  concentration in the periodontal pockets fluid in both groups, while the patients with refractory periodontitis had an increase in IL-1 $\beta$  that was more prominent and reached  $320.3 \pm 20.6$  pg/ml against  $205.5 \pm 19.5$  pg/ml in the group with chronic periodontitis, whereas the control values were  $110.2 \pm 12.5$  pg/ml. The increase in IL-1 $\beta$  is responsible for massive destruction of periodontal tissues due to stimulation of fibroblasts to the collagenase synthesis, and osteoblasts — to transformation into osteoclasts.

In the contents of periodontal pockets, the TNF- $\alpha$  indices in patients with refractory periodontitis exceeded significantly those in patients with chronic periodontitis ( $765.2 \pm 34.2$  pg/ml and  $396.6 \pm 47.5$  pg/ml, respectively; control —  $70.5 \pm 10.7$  pg/ml). Therefore, the higher the concentration of IL-1 $\beta$  and TNF- $\alpha$ , the more prominent the clinical image of the disease, since IL-1 $\beta$  and TNF- $\alpha$  are involved in the connective tissue destruction and bone resorption during periodontitis.

However, in patients with chronic generalized periodontitis, the content of IL-10 was reduced down to  $5.3 \pm 1.4$  pg/ml, and in cases with refractory periodontitis — to  $3.3 \pm 2.1$  pg/ml, at  $14.1 \pm 1.1$  in control.

A comparison of the concentrations of pro- and anti-inflammatory cytokines revealed an imbalance in their ratio compared with the control values ratios. So, if in healthy donors the ratio of the IL-1 $\beta$  / IL-10 content in the gingival fluid was 7.9, then in chronic periodontitis this ratio enhanced due to an increase in IL-1 $\beta$  up to 47.7, and with refractory periodontitis — to 97.1

The content of the examined cytokine profile parameters (IL-1 $\beta$ , TNF- $\alpha$ , IL-10) in periodontal pockets varied depending on the periodontal tissues damage severity. We detected a direct correlation between the IL-1 $\beta$  and TNF- $\alpha$  concentration, and the values of the index describing the degree of inflammation in periodontal tissues (PMA), in case of chronic generalized periodontitis ( $r = 0.61$ ,  $r = 0.59$ , respectively, with  $p < 0.05$ ). In case of refractory periodontitis, a negative correlation was observed between the concentration of the anti-inflammatory cytokine IL-10 and the PMA values ( $r = -0.54$ ,  $p < 0.05$ ).

## CONCLUSION

The immunological studies indicate that these processes in the oral cavity are accompanied by greater changes in local immunity in patients with refractory periodontitis, while secondary immune deficiency is developing, and these indicators (IL-1 $\beta$ , TNF- $\alpha$  and IL-10) can be used as reliable criteria for evaluating the severity of inflammatory periodontal diseases as well as the nature of their course.

## REFERENCES

1. **BELOKLITSKAYA, G.F.** Modern view on the classification of periodontal diseases / G.F. Beloklitskaya // *Modern Dentistry*. – 2007. – №3 (39). – P. 59–64. (In Russ.).
2. **BELOKLITSKAYA, G.F.** Clinical and immunological features of generalized periodontitis associated with various forms of rheumatoid arthritis / G.F. Beloklitskaya, N.V. Tsetsura, A.M. Vorobyov // *Periodontology*. – 2010. – №4 (57) – P. 3–6. (In Russ.).
3. **GRUDYANOV, A.I.** Rapidly progressive periodontitis. Features of the clinical course / A.I. Grudyanov, I.V. Bezrukova // *Dentistry*. – 2000. – T. 79., №5. – P. 24–27. (In Russ.).
4. The rationale for the differential approach to antibiotic therapy for acute exacerbation of chronic generalized periodontitis / O.Yu. Guseva, N.V. Bulkina, Yu.L. Osipova, A.Yu. Kropotin, Yu.N. Albitskaya // *Saratov Journal of Medical Scientific Research*. – 2011. – T.7, №1. (attachment). – P. 287–288. (In Russ.).
5. Study of molecular mechanisms of reparative-regenerative processes in a wound during stimulation with chitosan / A.P. Vedyeva, N.V. Bulkina, P.V. Ivanov and others. // *Periodontology*. – 2017. – Vol. 22., No. 4. (85). – P. 35–39. (In Russ.).
6. **MODINA, T.N.** Pathogenetic criteria for the diagnosis and treatment of various forms of rapidly progressive periodontitis / T.N. Modina: Author. dis. ... dr. med sciences. – M., 2002. – 43 p.
7. **MORGUNOVA, V.M.** Clinical, immunological and molecular genetic criteria for the diagnosis and treatment of patients with refractory periodontitis: Author. dis. ... cand. med sciences / V.M. Morgunova. – Saratov, 2013. – 26 p.
8. **MORGUNOVA, V.M.** Microbiological characteristics of the contents of periodontal pockets of patients with periodontitis / V.M. Morgunova // *Saratov Journal of Medical Scientific Research*. – 2011. – T.7., №1. – P. 312–314. (In Russ.).
9. Rationale for a differentiated approach to antibiotic therapy for acute exacerbation of chronic generalized periodontitis / O.Yu. Guseva, N.V. Bulkina, Yu.L. Osipova et al. // *Saratov Scientific Medical Journal*. – 2011 – T.7., №1. – P. 287–288. (In Russ.).
10. The use of the immunomodulator Gepon in the complex therapy of patients with chronic generalized periodontitis / N.V. Bulkina, L.V. Lukin, A.P. Glybochko et al. // *Russian Dental Journal*. – 2008. – №6. – P. 20–21. (In Russ.).
11. **OSTROVSKAYA, L.YU.** Periodontal tissue condition in patients with post-gastro-resection disorders / L.Yu. Ostrovskaya, N.V. Bulkina // *Experimental and clinical gastroenterology*. – 2017. – №8. (144). – P. 12–16. (In Russ.).
12. Indicators of cell renewal and gum apoptosis in patients with rapidly progressive periodontitis. / Yu.L. Osipova, S.A. Akimova // *Morphology*. – 2018. – T.153., №3. – P. 209–210. (In Russ.).
13. Clinical manifestations of temporomandibular joint dysfunction in patients with free-end edentulous space / E.N. Pichugina, V.V. Konnov, N.V. Bulkina, T.V. Matytsina, M.V. Vorobeva, S.N. Salnikov, R.N. Mukhamedov, V.A. Mikailova, I.V. Matysina // *Archiv EuroMedica*. – 2019. – Vol. 9, № 1. – P. 175–176. <https://doi.org/10.35630/2199-885X/2019/9/1/175>
14. Causes behind distal occlusion / M.V. Vorobieva, V.V. Konnov, N.V. Bulkina, A.A. Bizyaev, D.N. Maslennikov, A.S. Khodorich, E.S. Popko, S.V. Konnov, I.V.

- Matytsina // *Archiv EuroMedica*. – 2019. – Vol. 9, № 1. – P. 191–193. <https://doi.org/10.35630/2199-885X/2019/9/1/191>
15. Morphofunctional changes in temporomandibular joint correlating with its morphological variations in patients with dentition defects complicated by distal occlusion / V.V. Konnov, A.P. Vedyeva, D.Kh. Razakov, E.N. Pichugina, T.V. Matytsina, S.N. Salnikova, M.V. Vorobeva, R.N. Mukhamedov, I.V. Matysina // *Archiv EuroMedica*. – 2019. – Vol. 9, № 1. – P. 52–58. <https://doi.org/10.35630/2199-885X/2019/9/1/52>
  16. Temporomandibular joint morphology at orthognatic bite / A.R. Arushanyan, V.V. Konnov, A.P. Vedyeva, D.Kh. Razakov, T.V. Matytsina, D.N. Maslennikov, R.N. Mukhamedov, A.S. Khodorich, I.V. Matysina // *Archiv EuroMedica*. – 2019. – Vol. 9, № 1. – P. 18–19. <https://doi.org/10.35630/2199-885X/2019/9/1/18>
  17. DOMENYUK D.A., PORFYRIADIS M.P., BUDAYCHIEV G. M-A. Contemporary methodological approaches to diagnosing bone tissue disturbances in children with type 1 diabetes. *Archiv EuroMedica*, 2018; 8(2): 71–81.
  18. BASOV A.A., IVCHENKO L.G., DOMENYUK D.A., DMITRIENKO T.D., NUZHAYAYA C.V. The role of oxidative stress in the pathogenesis of vascular complications in children with insulinable sugar diabetes. *Archiv EuroMedica*, 2019; 9(1): 136–145. <https://doi.org/10.35630/2199-885X/2019/9/1/136>
  19. DAVYDOV B.N., DOMENYUK D.A., DMITRIENKO S.V. Peculiarities of microcirculation in periodont tissues in children of key age groups sufficient type 1 diabetes. Part I. *Periodontology*, 2019; Vol. 24; 1–24(90): 4–10. DOI: 10.25636/PMP.1.2019.1.1
  20. DAVYDOV B.N., DOMENYUK D.A., DMITRIENKO S.V. Peculiarities of microcirculation in periodont tissues in children of key age groups sufficient type 1 diabetes. Part II. *Periodontology*, 2019; Vol. 24; 2–24(91): 108–119. DOI: 10.33925/1683-3759-2019-24-2-108-119
  21. DAVYDOV B.N., DOMENYUK D.A., BYKOV I.M., IVCHENKO L.G., DMITRIENKO S.V. Modern possibilities of clinical-laboratory and x-ray research in pre-clinical diagnostics and prediction of the risk of development of periodontal in children with sugar diabetes of the first type. Part I. *Periodontology*, 2018; Vol. 23; 3–23(88): 4–11. DOI:10.25636/PMP.1.2018.3.1
  22. DOMENYUK D.A., DAVYDOV B.N., DMITRIENKO S.V., SUMKINA O.B., BUDAYCHIEV G. M-A. Changes of the morphological state of tissue of the paradontal complex in the dynamics of orthodontic transfer of teeth (experimental study). *Periodontology*, 2018; Vol. 23; 1–23(86): 69–78. DOI:10.25636/PMP.1.2018.1.15