



ASSESSMENT OF THE PATHOGENICITY OF ODONTOGENIC FOCI OF CHRONIC INFECTION IN PATIENTS WITH CARDIOVASCULAR DISEASES

¹D. B. Rajabova, ²N. N. Khabibova, ³A. A. Khadzhimetov

Cafedra's assistant Public health and health care organization of Bukhara State Medical Institute¹, Associate Professor, Head of the Department of Therapeutic Dentistry BGMI², Professor of the Department of Medical and biological chemistry Tashkent State Dental Institute, Tashkent. 700100, Yakkasaray district, st. Bakht 17³

SUMMARY

The aim of this study is to assess the role of the pathogenicity of odontogenic infection in the development of CVD. The objects of the study were 64 patients, of which group I included 31 patients at the stages of treatment for CVD in whom microbiological examination revealed the causative agent "(Porphyromonas gingivalis". Group 2 - (34) patients consisted of a CVD patient without periodontal pathology. microbiological, immunological and enzyme-linked immunosorbent assay. It was revealed that a high prevalence of gingivitis, respectively, in patients with CVD. A decrease in the synthesis of chemotactic factor in patients with CVD is accompanied by a significant decrease in the content of IL-8 in mixed saliva, which leads to a reduction in the life span of neutrophils

Key words: *gingivitis, CVD, phagocytosis, chemotaxis, IL-8.*

INTRODUCTION

The problem of the relationship between dental status and the general condition of a person is relevant at all times. Particularly acute is the question of the influence of the state of the oral cavity on the development of general somatic pathology of the body, in particular, diseases of the cardiovascular system (6,9,12). Analysis of literary sources submitted to the problem, it is necessary to point out the relevance of studying the relationship between diseases of the oral cavity and general somatic pathology.

As you know, the oral cavity is a specific, special, complex and independent microbiocenosis, with stable conditions for the existence and maintenance of the vital activity of bacteria. As a result, the species and quantitative composition of microorganisms in the oral cavity is very diverse. In the oral cavity, populations of microorganisms are constantly changing both in morphological and physiological terms, self-regulating "living" systems, which under certain conditions, such as a decrease in the level of resistance, stress effects, can change, and lead to a predisposition to the occurrence of various acute and chronic inflammatory diseases of the oral cavity. The most common cause of inflammatory processes in the oral cavity is due to the pathological effects of obligate anaerobes and facultative anaerobic cocci (1,3,4,7,8,9,11,12,15). According to numerous researchers, in the etiopathogenesis of inflammatory periodontal diseases, the main place is occupied by periodontal pathogenic microflora - Treponema denticola, Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Streptococcus mutans, Peptostreptococcus anaerobius, Neisbacteria sp., Corineis oralis sp., Corineis oralis sp., Corineis oralis sp. , S. salivarius and S. macacae, etc. Moreover, the severity and severity of inflammation depend on the type and pathogenicity of these microorganisms (2,5,10,13,16,18,20,22,24). In turn, the relationship of the oral microflora with diseases of various organs and systems of the body, characterizes the polymorbidity of pathologies. At the same time,

dysbiosis of the oral cavity aggravates the severity and prognosis of concomitant diseases, and an effective fight against dysbiotic disorders in the oral cavity gives better results in the treatment of the main concomitant pathology. The comorbidity of cardiovascular diseases and periodontal pathology has been noted by many authors (14,17,19,21,23,25), however, the microbiological and immunological components of this state of the oral cavity have not been fully studied, which, in our opinion, is one of the main links in the development of cardiovascular pathology. In this regard, the necessity and timeliness of this study is beyond doubt. The aim of this study was to study the role of the pathogenicity of odontogenic chronic infection during diseases of the cardiovascular system of the body.

MATERIAL AND RESEARCH METHODS

To achieve the goal and implement the set tasks, we carried out a comparative study of the features of microbiocenosis and the severity of general and local immunity of the oral cavity in patients with gingivitis with concomitant cardiovascular disease (CVD). This study was carried out at the clinical bases of the Department of Dentistry, BukhMI. The objects of the study were 64 patients who were divided into the main study group and the control group. Of them in

Group I included 31 patients (22 men and 9 women) aged 18 to 65 years (mean age 47.6 years) who were at the stages of treatment for CVD in whom microbiological examination revealed the causative agent "(Porphyromonas gingivalis". 2 group (34) patients consisted of a CVD patient without periodontal pathology. The control group consisted of 14 people, aged 18 to 65 years (9 men and 5 women), who applied for dental care at the Department of Dentistry, BukhGMI. The diagnosis was "healthy" on the basis of the clinical and radiological picture and the conclusions of the therapist. Comprehensive dental examination and laboratory study of patients of 3 groups were carried out at the clinical bases of the BukhGMI. mouth IGR-U, papillary-marginal-alveolar index, assessment of gingival bleeding groove according to M.R. Muhlemann method, periodontal index (PI) according to A. Russel, gingivitis index GI. In addition, the dental chart noted the presence of non-cariou lesions of the teeth and diseases of the oral mucosa (OOM). The study of the characteristics of the composition of the microflora of the oral cavity for the presence of pathogenic and opportunistic microflora in the examined persons was carried out in the microbiological laboratory of the BukhGMI. For microbiological examination, all patients were taken with a sterile cotton swab, which was then placed in a tightly closed sterile tube. The material was taken on an empty stomach, before brushing the teeth. With the help of the cultural method of bacteriological research, identification and counting of pure cultures of certain microorganisms is carried out, which makes it possible to most accurately judge the etiological affiliation of the obtained microorganisms. The number of colonies of microorganisms was expressed in terms of CFU / ml. The identification of the obtained cultures of microorganisms was carried out in accordance with the Bergey's determinant of bacteria (1997) and manuals on microbiology. Immunological research was carried out on the basis of the clinical laboratory of BukhGMI. To assess local and general immunity, blood was taken in the morning, on an empty stomach, as well as oral fluid. Evaluation of indicators of both cellular and humoral immunity was carried out using the enzyme immunoassay method. The concentration of interleukin 8 was determined by the enzyme immunoassay on a Mindray analyzer using Human reagents. Determination of the phagocytic function of neutrophils in the free oral cavity

liquids were evaluated for their ability to absorb latex particles by the method
Freidlin. To study the ability of neutrophils to free the oral cavity

liquid to phagocytosis 0.2 ml of oral secretion suspension was mixed with 0.02 ml of latex suspension 1.7 μm in diameter (10 particles / ml) obtained from

All-Union Research Institute of Synthetic Rubber named after Academician S. V. Lebedev (St. Petersburg). After a half-hour incubation at 37 ° C, smears were prepared, which were dried, fixed with 96% ethanol and stained with

Romanovsky-Giemsa. When analyzing phagocytosis, the activity, intensity of phagocytosis and phagocytic number were calculated. Phagocytosis activity was calculated as the number of neutrophils containing latex particles per 100 cells counted. The intensity of phagocytosis was determined by the number of latex particles per 100 cells per 1 cell. The results are presented as the arithmetic mean with the indication of the value of the standard deviation. The significance of differences was assessed using the STATISTICA software package using the Student's t-test

MATERIAL AND RESEARCH METHODS

To achieve the goal and implement the set tasks, we carried out a comparative study of the features of microbiocenosis and the severity of general and local immunity of the oral cavity in patients with gingivitis with concomitant cardiovascular disease (CVD). This study was carried out at the clinical bases of the Department of Dentistry, BukhMI. The objects of the study were 64 patients who were divided into the main study group and the control group. Of them in

Group I included 31 patients (22 men and 9 women) aged 18 to 65 years (mean age 47.6 years) who were at the stages of treatment for CVD in whom microbiological examination revealed the causative agent "(Porphyromonas gingivalis". 2 group (34) patients consisted of a CVD patient without periodontal pathology. The control group consisted of 14 people, aged 18 to 65 years (9 men and 5 women), who applied for dental care at the Department of Dentistry, BukhGMI. The diagnosis was "healthy "on the basis of the clinical and radiological picture and the conclusions of the therapist. Comprehensive dental examination and laboratory study of patients of 3 groups were carried out at the clinical bases of the BuhGMI. mouth IGR-U, papillary-marginal-alveolar index , assessment of gingival bleeding groove according to MR Muhlemann method, periodontal index (PI) according to A. Russel, gingivitis index GI. In addition, the dental chart noted the presence of non-carious lesions of the teeth and diseases of the oral mucosa (OOM). The study of the characteristics of the composition of the microflora of the oral cavity for the presence of pathogenic and opportunistic microflora in the examined persons was carried out in the microbiological laboratory of the BukhGMI. For microbiological examination, all patients were taken with a sterile cotton swab, which was then placed in a tightly closed sterile tube. The material was taken on an empty stomach, before brushing the teeth. With the help of the cultural method of bacteriological research, identification and counting of pure cultures of certain microorganisms is carried out, which makes it possible to most accurately judge the etiological affiliation of the obtained microorganisms. The number of colonies of microorganisms was expressed in terms of CFU / ml. The identification of the obtained cultures of microorganisms was carried out in accordance with the Bergey's determinant of bacteria (1997) and manuals on microbiology. Immunological research was carried out on the basis of the clinical laboratory of BukhGMI. To assess local and general immunity, blood was taken in the morning, on an empty stomach, as well as oral fluid. Evaluation of indicators of both cellular and humoral immunity was carried out using the enzyme immunoassay method. The concentration of interleukin 8 was

determined by the enzyme immunoassay on a Mindray analyzer using Human reagents. Determination of the phagocytic function of neutrophils in the free oral cavity

liquids were evaluated for their ability to absorb latex particles by the method

Freidlin. To study the ability of neutrophils to free the oral cavity

liquid to phagocytosis 0.2 ml of oral secretion suspension was mixed with 0.02 ml of latex suspension 1.7 μm in diameter (10 particles / ml) obtained from

All-Union Research Institute of Synthetic Rubber named after Academician S. V. Lebeden

(St. Petersburg). After a half-hour incubation at 37 ° C, smears were prepared, which were dried, fixed with 96% ethanol and stained with

Romanovsky-Giemsa. When analyzing phagocytosis, the activity, intensity of phagocytosis and phagocytic number were calculated. Phagocytosis activity was calculated as the number of neutrophils containing latex particles per 100 cells counted. The intensity of phagocytosis was determined by the number of latex particles per 100 cells per 1 cell. The results are presented as the arithmetic mean with the indication of the value of the standard deviation. The significance of differences was assessed using the STATISTICA software package using the Student's t-test

Periodontal disease	1 –group (n=31)	2 group (n=33)	Control group (n=14)
PMA,%	62,3±4,6%	27,3±2,1%	19,8±2,1%
Assessment of bleeding by	1,5±0,67	0,7±0,62	0,4±0,12
M.R. Muhlemann method	3,6±0,51	1,8±0,24	1,4±0,37
PI by A. Russel	3,1±0,44	1,9±0,13	1,3±0,95
CPITN	1,9±0,14	0,9±0,08	0,3±0,04

Various microorganisms, including *Porphyromonas gingivalis*, colonize the glycoprotein-containing layer (plaque) above and below the gingival margin to form above and subgingival plaque layers. Further, bacterial-endothelial cell interactions occur in periodontal pockets, creating and exchanging signals between microorganisms and neighboring cells of the immune system. *Porphyromonas gingivalis* is attracted and absorbed through receptor-mediated endocytosis in the epithelial cells lining the sulcus. Thus, endotoxin (e.g. lipopolysaccharide) -producing *Porphyromonas gingivalis* are protected from the immune system and can

multiply within cells and possibly spread systemically through the circulation, causing a generalized immune response

Analysis of the structure of periodontal diseases in the examined patients with CVD are presented in the table.

Table

Structure of periodontal diseases in patients with CVD (absolute number and%)

Diseases periodontium	1 –группа (n=31)		2 группа (n=34)		Контрольная группа (n=14)	
	Clean absolute	%	Absolute clean	%	Absolute clean	%
	-	-	4	11,8	9	64,3
Healthy periodontium	22	71,9	-	-	-	-
Catarrhal marginal gingivitis	6	18,8	-	-	-	-
Hypertrophic gingivitis	-	-	-	-	-	-
	3	9,3	30	88,2	5	35,7
Acute periodontitis	-	-	-	-	-	-

The anti-infectious protection of the mucous membranes, along with the epithelial barrier, includes the cellular link of anti-infectious protection, humoral immunity factors and the normal microflora of the oral cavity, existing in the form of biofilms on the surface of the epithelium or in planktonic form in free oral fluid. To assess the functional activity of neutrophils in the free oral fluid, the spontaneous and latex-induced reduction of NBT to diformazan was studied, and the ability of neutrophils to phagocytosis of latex particles was determined. As can be seen from the presented research results, the indicators of the NBT test of oral fluid neutrophils in patients with CVD had a peculiar dynamics when compared with the indicators of healthy individuals. Thus, with a spontaneous test, the activity of neutrophils in patients with CVD decreased on average by 1.75 times, while with an induced decrease in NBT, the activity of neutrophils was more pronounced and, on average, decreased when compared with indicators of healthy individuals by 3.5 times, thereby indicating very low phagocytic activity of neutrophils. Indicators of the intensity of phagocytosis in the examined individuals had a similar dynamics. As you know, porphyromonas (*Porphyromonas gingivalis*) are bacteria that actively contribute to the onset of inflammation. Typically, these bacteria are located in the areas of the gums that are directly adjacent to the tooth. They are obligate anaerobic and often form protective biofilms based on resistant tooth tissues.

Table 4.1

Indices of NBT-test of oral fluid neutrophils in patients with CVD

Indexing		1 –group (n=31)	2 group (n=34)	Control (n=14)
NST spontaneous	Activity,%	12,01±0,76	15,01±1,04	21,04±0,98
	Intensity	0,13±0,01	0,18±0,01	0,28±0,01
	conventional units	7,46±0,57	16,23±1,12	26,27±1,23
	Activity,%	0,068±0,01	0,14±0,01	0,22±0,01

Note: * - differences regarding group data comparisons are significant ($P < 0.05$)

This is how plaque builds up. Therefore, as the disease progresses, acute inflammation becomes chronic. The reason for this is *P. gingivalis*, which disrupts the synthesis of the chemotactic factor IL-8 and the adhesion molecule E-selectin in gum cells in order to feed normally, activated by neutrophils. As can be seen from the presented research results (table), a decrease in the synthesis of chemotactic factor in patients with CVD is accompanied by a significant decrease in the content of IL-8 in mixed saliva, which leads to a reduction in the neutrophil life span. As a result, neutrophils become the main mediators involved in damage to the gums and alveolar bone during the development of periodontitis.

One of the important indicators of the course of the inflammatory process is the intensity of mobility of phagocytes (chemotaxis). It is the mobility of macrophages that is one of the mechanisms that determine the number of cells - phagocytes in the focus of inflammation and ultimately determines the effectiveness of the phagocytic process. Analysis of the presented research results indicates a decrease in the intensity of macrophage chemotaxis. One of the reasons for the decrease in the intensity of neutrophil chemotaxis and the decrease in the level of IL-8 is the high requirement of neutrophils for pathogens. This is probably why the blockage of chemotaxis has a short duration in time, which leads to excessive accumulation of neutrophils in the focus of inflammation.

Table 4.3

The intensity of phagocytosis, chemotaxis of macrophages in the dynamics of periodontal inflammation caused by (*Porphyromonas gingivalis*)

Indicators	Control (n=14)	1 -group (n=31)	2 group (n=34)
Interleukin-8 (IL-8) pg / ml	167,31±12,04	90,54±8,16*	124,32±9,73
in mixed saliva	0.08±0.001	0.05±0.001*	0.07±0.001*

Note: * - data differences control group significant (- P <0.05)

Thus, in patients with periodontitis, pronounced absolute leukocytosis was found in the periodontal tissues and in the oral fluid, which indicates the persistence of signs of local inflammation. Thus, the primary damage to the periodontal tissues caused by (*Porphyromonas gingivalis* over time, the area of damage begins to gradually increase. In this case, the subsequent inflammatory process spreads from the gums to the alveolar bone along the periodontium, neurovascular bundles. In the places where the vessels exit from the alveolar bone, the inflammatory process of the bone begins fabrics.

CONCLUSION

1. Note: * - data differences
2. Control group significant (- P <0.05)
3. Thus, in patients with periodontitis, pronounced absolute leukocytosis was found in the periodontal tissues and in the oral fluid, which indicates the persistence of signs of local inflammation. Thus, the primary damage to the periodontal tissues caused by (*Porphyromonas gingivalis* over time, the area of damage begins to gradually increase. In this case, the subsequent inflammatory process spreads from the gums to the alveolar bone along the periodontium, neurovascular bundles . In the places where the vessels exit from the alveolar bone, the inflammatory process of the bone begins fabrics..

REFERENCES

1. Bulannikov AS Periodontal disease. Clinic, diagnosis and treatment // Medical assistance. - 2005. - No. 4. - S. 21-24.
2. Vertieva, E.Yu. Characteristics of toxins and adhesins *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* - causative agents of aggressive forms of human periodontitis: author. dis. ... Cand. honey. sciences. - M., 2013. -- 22 p.
3. Grudyanov A.I., Zorina O.A. Methods for the diagnosis of inflammatory periodontal diseases: A guide for physicians. - M.: Medical Information Agency, 2009. - 112 p.
4. Money OV Clinical and laboratory assessment of the effectiveness of a complex of adaptogens and physical factors on the biochemical parameters of the oral cavity in patients with chronic catarrhal gingivitis / O.V. Denga, D.D. Zhuk, O. A. Makarenko // Vyunik dentists. - 2004. - No. 4. - S. 3-8.

5. Zhavoronkova, T.N. Suborova // Periodontology. - 2013. - T. 18, No. 2. - S. 9-13.
6. Kirsanov A.I. Mechanisms of interrelation of pathology of internal organs and periodontium / A.I. Kirsanov, I.A. Gorbachev // Periodontology. - 1999. - No. 1. - S. 35-36.
7. Kosenko K.N. et al. Microbial associations of periodontal pocket in patients with generalized periodontitis // Vyunik stomatologists. - 2000. - No. 3. - S. 10-13.
8. Krechina E.K., Kozlov V.I., Maslova V.V. // Microcirculation in the tissues of the periodontal gums: manual / M.: Geotar Media, 2007. - 75 p.
9. Krechina E.K., Rakhimova E.N. Assessment of hemodynamic disturbances of tissue blood flow in the gum tissues in normal conditions and in periodontal diseases according to Doppler ultrasound data // Dentistry. - 2005. - T. 84, No. 5. - S. 24-27.
10. Orekhova, L.Yu. Modern technologies of bacteriological research of periodontal spaces / L.Yu. Orekhova, M.D.
11. Papapanou P.N. The relationship between periodontitis and vascular atherosclerosis: actual data and significance for specialists and society. Attending doctor. - 2013. - No. 7. - P. 17.
12. Reshetnikov O.V., Kurilovich S.A., Nikitin Yu.P. Periodontal infection and their possible influence on the development of atherosclerosis and its complications // Atherosclerosis. T.11, No. 1 2015 S 56-68;
13. Accarini R. Periodontal disease as a potential risk factor for acute coronary syndromes / R. Accarini, M.F. de Godoy // Arq. Brasil. Cardiol. - 2006. - Vol. 87, № 5. - P. 592-6.
14. Bascones-Martinez P., Matesanz-Perez M., Escribano-Bermejo M.A., Gonzalez- Moles J., Bascones-Ilundain J.H., Meurman A. Periodontal disease and diabetes-Review of the Literature // Med Oral Patol Oral Cir Bucal. - 2011. - Jan 3. - P. 18-24.
15. Birkedal Hansen H. Role of cytokines and inflammatory mediators in tissue destruction / H. Birkedal Hansen // J. Periodont. Res. - 1993. - Vol. 28. - P. 500-510.
16. Blake G.J., Ridker PM. // Inflammatory bio-markers and cardiovascular risk prediction. - J Intern Med. 2002 Oct; 252(4):283-94. Review.
17. Bostanci, N. Porphyromonas gingivalis: an invasive and evasive opportunistic oral pathogen / N. Bostanci, G.N. Belibasakis // FEMS Microbiol. Lett. - 2014. - Vol. 333, №2 1. - P. 1-9.
18. Danger signal adenosine via adenosine 2a receptor stimulates growth of Porphyromonas gingivalis in primary gingival epithelial cells / R. Spooner [et al.] // Mol. Oral Microbiol. - 2014. - Vol. 29, № 2. - P. 67-78.
19. Elevated antibody levels to P. gingivalis detected in rheumatoid arthritis patients with a specific anti-citrullinated protein/peptide antibody profile / N. Kharlamova [et al.] // Annal. Rheum. Dis. - 2014. - Vol. 73, suppl. 1. - P. A73-A74.
20. Importance of biofilm formation and dipeptidyl peptidase IV for the pathogenicity of clinical Porphyromonas gingivalis isolates / S. Clais [et al.] // Pathog. Dis. - 2014. - Vol. 70, № 3. - P. 408-13.
21. Salivary biomarkers of bacterial burden, inflammatory response, and tissue destruction in periodontitis / A. Salminen [et al.] // J. Clin. Periodontol. - 2014. - Vol. 41, № 5. - P. 442-50.
22. Porphyromonas gingivalis LPS inhibits osteoblastic differentiation and promotes pro-inflammatory cytokine production in human periodontal ligament stem cells / H. Kato [et al.] // Arch. Oral Biol. - 2014. - Vol. 59, №2 2. - P. 167-175.
23. Hajishengallis G. Complement and dysbiosis in periodontal disease / G. Hajishengallis, J.D. Lambris //

Immunobiology. - 2013. - Vol. 217, № 11. - P. 1111-1116.

24. Porphyromonas gingivalis regulates TREM-1 in human polymorphonuclear neutrophils via its gingipains / N. Bostanci [et al.] // PLoS ONE. - 2013. - Vol. 8, № 10. - P. e75784.

