

DIAGNOSTIC AND THERAPEUTIC APPROACHES FOR THE IDENTIFICATION OF INFLAMMATORY AND DESTRUCTIVE PROCESSES OCCURRING IN THE PERI-IMPLANT ZONE IN PATIENTS WITH COMBINED PERIODONTAL PATHOLOGY

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Abstract: *Diagnostic and treatment approaches aimed at identifying risk factors for the development and formation of recurrent dental per implants has been developed. Complex therapy of destructive processes in periodontitis was carried out in 74 patients with chronic generalized periodontitis of combined cardiovascular system and with partial secondary adentia before dental implantation. It was found out that the key risk factors of early inflammatory complications and dental mucositis development in the delayed period of implant functioning are the pathogenic flora increase in the peri-implant zone.*

Keywords: *dental per implants, peri-implant, dental implantation, perimplantitis*

Introduction

At present, the problem of reducing the number of complications after implant placement and increasing the service life of implants remains relevant, because inflammatory and destructive processes occurring in the peri-implant zone serve as a serious aggravating factor affecting the stability and safety of the implant. The most frequent complications accompanying dental implantation are characterized by the development of a chronic inflammatory process in peri-implant tissue with predominant destructive changes in the surrounding bone tissue. The analysis of literature sources and the research carried out in different periods on this problem [2,5,7] showed that the inflammatory process in the peri-implant zone is the basis for the destruction and resorption of bone structures in the implant area. The peculiarity of dental peri-implant, as the authors point out, is its progressive nature, resistance to treatment measures and tendency to relapse. According to the authors, the researches carried out in this direction force to develop not only hygienic and etiotropic therapy of pathological conditions in the peri-implant zone, but also comprehensively study the causes of recurrent peri-implants and develop a comprehensive pathogenetic therapy based on it. It is not excluded that the degree of decrease of local mineral density of bone tissue and disturbance of its metabolism, as well as of its protective system, can probably be caused by a long-term inflammatory and destructive process that occurred in the peri-implant zone. An aggravating factor in this situation may be associated diseases, in particular, cardiovascular system. From these positions, the relevance of this study is to improve diagnostic approaches and therapeutic measures aimed at identifying risk factors for the development and formation of recurrent

dental peri-implants. This study is aimed at solving this problem.

Research material and methods

Clinical and laboratory tests were conducted in 74 patients, including 74 patients: I - group (14 patients) with chronic generalized periodontitis of medium severity, II - group (26 patients) with chronic generalized periodontitis of the cardiovascular system combined with cardiovascular system disease and III - group (34 patients) with chronic generalized periodontitis of the cardiovascular system combined with cardiovascular system disease with partial secondary adenitis with (absence of 1-2 teeth, duration of the defect in the tooth rows up to 1 year), to dental implantation. Besides, II- group of patients received the traditional medical-prophylactic complex before dental implantation; III- group of patients received the medical-prophylactic complex developed by us for prophylaxis and treatment of chronic inflammatory-destructive processes in periodontium and prevention of cardiovascular pathology. This decision was made jointly with cardiologists. To reduce the risk of cardiovascular disasters, a hypolipidemic drug Atorvastatin (KRKA, Slovenia), anaerobocidal metronidazole in combination with chlorhexidine in the form of a gel, probiotics latobacterim and bifidobactrim were used. To prevent the processes of destruction and resorption of bone structures in the implant area, an additional course of glucosamine sulfate and sodium chondroitin sulfate (Theraflex®, Sagemel, Inc., USA) was administered. The preparation was administered orally according to the following scheme: 2 capsules per day containing 1500 mg of glucosamine sulfate and 1200 mg of chondroitin sulfate, regardless of the meal, with a small amount of water. The recommended duration of treatment was up to 3 months, but patients were examined before dental implantation, at 14 after traditional and complex therapy.

This comprehensive treatment approach for patients with combined pathology was carried out 14 days before dental implantation in order to eliminate chronic inflammation foci in the peri-implantation tissues and to prevent both recurrence and development of destructive processes in the alveolar bone in the peri-implantation area. To ensure the medicinal effect on all components of pain response (sensory, psycho-emotional, vegetative and motor) we used combined pain relief, which included local anesthesia and sedative premedication by oral application of relaxium solution at the rate of 0.03 mg / 1 kg of patient's body weight. All patients were sent for a consultation with a cardiologist to get a conclusion about the possibility of surgical stage of dental implantation. General clinical, radiological, functional and laboratory methods of examination were used for examination of patients at the preoperative stage. Also in this work we used a computer tomography located in the X-ray department of private medical firm "DIOR", "HiSpeed DX-I Plus" produced by General Electric with the software "Dento Scan" and the following technical parameters. Together with the cardiologists and the conclusion of the radiation diagnostics physician, the decision was made on the possibility of performing intraosseous dental implantation in patients with cardiovascular pathology. The examination was preceded by a five-minute rest of the patient in a lying position and in a quiet room. Blood pressure was measured on both hands. Each arm was measured 2-3 times. If the readings differed, the highest value was recorded in the examination report. To detect possible atherosclerotic lesions of blood vessels and disorders of the blood coagulation system, at the planning stage of intraosseous dental implantation surgery, we conducted a study of the hemostasis system.

To determine the intensity of pathological processes the resorption was determined by the level of osteomatrix destruction products - collagen type 1 decomposition fragments (P-Cross-Laps) in oral fluid, the state of bone formation was judged by the blood content of osteocalcin (OC) synthesized by osteoblasts, alkaline phosphatase and homocysteine by immunoenzyme method using BioChemMac reagent kits (Russia). Oral fluid was taken

between 8-9 a.m., strictly on an empty stomach, until teeth were cleaned by spitting in sterile measuring tubes. Samples containing oral fluid were centrifuged for 10 minutes before use to determine elastase activity. Determination of elastase activity in oral fluid was carried out according to the method proposed by Gun-Hwan and Kim-Hyun and modified by the Department of Clinical Microbiology of EE "VGMU" (K. Morihara., H Tsuzuki, 1977). The result was expressed in optical units (Eo) calculated as the difference between the optical densities of the prototype samples and their corresponding countermeasures. The statistical processing of the obtained data was carried out with the use of variation statistics, calculation of the arithmetic mean, degree of freedom of the arithmetic mean The reliability of differences between the mean values of the groups under study and control groups was determined by the Student's t-criterion.

Research results and discussion

Our previous studies have shown that chronic inflammatory-destructive changes in the peri-implant zone in patients with chronic generalized periodontitis of the cardiovascular system combined with cardiovascular disease are caused by periodontal infection consisting of 6-7 periodontopathogenic bacteria. To them we have included *A. actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Fusobacterium necrophorum*, *Treponema denticola* and *Eikenella corrodens*, which according to our data have their own pathogenic effect on periodontal tissue in this contingent of patients. Our microbiological studies using PCR method showed the presence of higher values of *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* on the developed around the inflammatory periodontal focus, especially in patients with the combined form of periodontal disease and cardiovascular system. Thus, DNA of *Porphyromonas gingivalis* (Pg) was found in 76% of patients in the first group, while in the second group it was equal to 89% and in the third group - to 92%. *Aggregatibacter actinomycetemcomitans* (Aa) was found in 71% of patients in the first group, in the second group - 80%, and in the third group - 89%. Also in the patients of the second group it was revealed DNA of *Tannerella forsythensis* (Tf) in 66% of cases, DNA of *Tannerella intermedia* in 62% of observations and DNA of *Treponema denticola* in 71% of cases. At the same time, the aggressive properties of the bacteria are caused by exposure to not only inflammatory but also destructive process in periodontal tissues. As it is known, these groups of microorganisms trigger a whole complex of mechanisms - invasion, adhesion, colonization of endotoxins, enzymes and other antigenic complexes that initiate both inflammatory and destructive process. Studies [1,6] show that toxins from the above pathogens may persist for a long time in the body and cause systemic or local inflammatory reactions in the cardiovascular system. In addition, the chronization of this process may adversely affect the functioning of orthopedic superstructures on implants and eventually lead to the loss of the supports (implants) themselves. Preventing this complication is possible by using not only anti-inflammatory drugs, but also taking into account the combination of periodontal pathology with the cardiovascular system to use comprehensive therapy in the preparation of patients for dental implantation.

As can be seen from the presented research results (Table 1), in patients with chronic periodontal disease without concomitant pathology, oral fluid elastase activity was 0.017 ± 0.02 O.P. units. This index in patients with chronic generalized periodontitis of average severity of the combined disease of cardiovascular system was $0,043 \pm 0,005$ units of O.P.L. In patients with CGP of the combined disease of cardiovascular system with partial secondary adentia with (absence of 1-2 teeth, duration of the defect in the dental rows up to 1 year), before dental implantation was equal to $0,046 \pm 0,006$ SRP. Therefore, in patients with chronic generalized periodontitis combined with the pathology of the cardiovascular system, especially with adhesion, the activity of neutrophil elastase of oral fluid is statistically

significantly increased.

It is known that in the process of destruction of the components of the extracellular matrix, in addition to neutrophil elastase, other groups of proteases are involved, primarily matrix metalloproteinases, which are the product of neutrophils (MMP-8, MMP-9) and macrophages (MMP-1). However, unlike serine proteases, matrix metalloproteinases are isolated into intercellular space in an inactive form. In order to realize their lithium potential, the protease parameters must be increased and their activity is induced by neutrophil elastase. Therefore, in addition to the direct elastolytic effect, neutrophil elastase in this situation indirectly affects the destruction of other components of the extracellular matrix (collagen, gelatin) by metalloproteinases. Based on the above, one of the tasks of our study was to study the nature of bone remodeling processes and assess the activity of destructive process in bone tissue in the peri-implant zone in preparation for dental implantation.

The analysis of the study of bone metabolism showed that the average value of osteocalcine in the blood of patients with CGP combined cardiovascular pathology decreased by 18% relative to the group of patients with periodontal pathology. More pronounced changes were observed in patients with CGP combined cardiovascular pathology in the background of adentia. Different dynamics was noted for the products of destruction of osteomatrix in oral fluid, where its concentration exceeded the initial indexes in 1.5 times. The recorded increase in the average concentration of osteocalcine in saliva indicates an increase in the functional ability of the osteotopic series, which seems to indicate compensatory stress of the inflammatory process in bone tissue and activation of the resorption process in the peri-implant zone. Violation of bone remodeling was especially pronounced in patients with CGP combined with the pathology of the cardiovascular system in the background of adentia. Thus, this contingent of patients has the content of osteomatrix proteins in oral fluid.

was 0.0195 ± 0.001 pg/ml, which indicated the disintegration of collagen of the first type. From our point of view, the revealed changes in bone metabolism in the examined patients with combined pathology, where we observed changes in osteocalcin and P-Cross-Laps indices in the oral fluid, indicate the dominance of the resorption process in the alveolar bone over the process of its construction. The accumulation of P-Cross Laps in the oral fluid is undoubtedly associated with destructive changes in bone tissue in the peri-implant area. The revealed regularity gives all grounds to consider the increased concentration of P-Cross-Laps in the oral fluid as one of the risk factors for the development of inflammatory and destructive process in the area of osseointegrated implants and the emergence of dental peri-implant.

In studies [3,10] it is proved that the enzyme alkaline phosphatase is a marker of bone mineralization. This enzyme is expressed from osteoblasts in large quantities and is distributed mainly in cytoplasmic processes that are interwoven into the osteoid layer. The high activity of alkaline phosphatase is determined in young osteoblasts and the forming organic matrix and is considered as a system indicator of osteo formation. As osteoid is accumulated and mineralized, the activity of alkaline phosphatase decreases and then disappears, which makes it possible to judge the rate of mineralization of bone regenerate from the activity of alkaline phosphatase

Table 1: Rates of elastase and bone metabolism markers in patients with chronic generalized periodontitis with combined cardiovascular disease before and after therapy

Indicators	I – group n=14	II – group n=26	III – group n=34
Before therapy			

Neutrophilic Elastase Unit of op. cit.	0,017±0,002	0,043±0,005*	0,046±0,006*
Blood osteocalcine (OK) pg/ml	1,15±0,09	0,94±0,06	0,92±0,07*
Osteomatrix in oral fluid (P-Cross-Laps) pg/ml	0,0126±0,001	0,0189±0,003*	0,0195±0,001*
Alkaline blood phosphatase Power unit/l	24,34±1,67	19,12±1,08*	17,49±1,24*
Homocysteine content in saliva µM/l	0,76±0,05	1,64±0,12*	1,96±0,14*
In 14 days			
Neutrophilic Elastase Unit of op. cit.	0,016±0,002	0,039±0,005	0,021±0,006**
Blood osteocalcine (OK) pg/ml	1,12±0,08	0,98±0,07	1,09±0,05**
Osteomatrix in oral fluid (P-Cross-Laps) pg/ml	0,0123±0,001	0,0168±0,003	0,0132±0,003**
Alkaline blood phosphatase Power unit/l	23,27±1,13	22,31±1,53	26,03±1,33**
Homocysteine content in saliva µM/l	0,73±0,04	1,23±0,08	0,68±0,05**

Note: * - reliability of differences with indicators of comparison group $P < 0,05$; ** - with indicators before and after therapy

In the study of blood of patients with Cerebral Cordovascular System combined with the disease of cardiovascular system a decrease in the average indexes of total alkaline phosphatase was revealed and on average it was equal to 19.12 ± 1.08 U/L vs. 24.34 ± 1.67 U/L in the comparison group. A decrease of alkaline phosphatase index in blood in patients of Group III was noted, where it was 28% lower than the initial values, which in [4] opinion leads to slowdown of reparative regeneration.

As it was mentioned above, we performed the generally accepted therapy and Complex treatment in the preoperative preparation of the examined patients before the dental implantation within 14 days allowed to estimate the character of changes in inflammatory and destructive processes in the field of implants. Thus, against the background of anti-inflammatory therapy there were significant changes in neutrophilic elastase indices in blood in patients of Group III as compared to the comparison group. Similar dynamics was noted in relation to the indices of osteocalcine in blood and oral fluid of P-Cross Laps. The revealed regularity in the obtained research results after the corresponding therapy of patients with CGP combined with the disease of cardiovascular system gives all grounds to consider the decrease of osteocalcine concentration in the blood and P-Cross-Laps in the oral liquid as one of the preventive measures for the development of inflammatory and destructive process in the field of osteointegrated implants and cuppylation of dental peri-implant. Уровень щелочной фосфатазы в крови у обследуемых лиц II и III- групп на 14 день после традиционной и комплексной терапии повысилось, соответственно на 14% и 33% при сравнение исходными показателями, что указывало на формирующемся органическом матриксе и остеообразования.

It is known that microcirculation disorder in the dental system develops against the

background of chronic ischemia, which leads to trophic changes in periodontal tissues. One of the causes of blood flow disorders is hypercoagulability, which is created by activated clotting factors available not only in blood but also in saliva [8,9]. As the authors note, the procoagulants include homocysteine. The next task of our study was to study the nature of changes in the homocysteine content in mixed saliva in patients with cerebral palsy combined with the pathology of the cardiovascular system.

The analysis of the obtained results, presented in the table, showed that the concentration of homocysteine in mixed saliva in patients with cerebral palsy combined with the pathology of cardiovascular system (II-group) reliably exceeded the indicators obtained in patients with cerebral palsy without associated pathology in average 2.2 times. In patients of III-group the studied index exceeded the initial level in 2.6 times. A different dynamics was observed after the corresponding therapy of the patients under study, where the homocysteine level in saliva had a decreasing dynamics, in particular, in the II group of patients against the background of traditional therapy by 25% against patients before the therapy, and in the III group of patients by 35% against this group of patients before the therapy. Thus, the results of the study indicate that patients with CGP of combined pathology of the cardiovascular system have a process of root resorption accompanied by trophic changes in periodontal tissues, which are manifested by an increase in homocysteine content in saliva.

Conclusion

Our studies in patients with CGP of the combined pathology of the cardiovascular system, especially in adentia, indicate that the key risk factors for the development of early inflammatory complications and dental mucositis in the delayed period of implant operation are: an increase in the pathogenic flora in the peri-implant area, *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*. In this case, the aggressive properties of the bacteria are carried out by exposure causing not only inflammatory but also destructive process in periodontal tissues. In patients with chronic generalized periodontitis combined with the pathology of the cardiovascular system, especially with adentia, the activity of neutrophil elastase of oral fluid is statistically significantly increased, indicating the destruction of components of the extracellular matrix (collagen, gelatin) by metalloproteinases. The increased content of osteomatrix proteins in oral fluid noted by us in this contingent of patients indicated the disintegration of collagen of the first type. The accumulation of P-Cross Laps in oral fluid is undoubtedly associated with destructive changes in bone tissue in the peri-implant area, which is one of the risk factors for the development of inflammatory and destructive process in the osteointegrated implants and the emergence of dental peri-implantitis. The marked decrease of alkaline phosphatase index in the blood of Group III patients is one of the reasons for the slowdown of reparative regeneration. Our 14-day therapy during the preoperative preparation of the examined patients before the dental implantation allowed us to estimate the character of changes in inflammatory and destructive processes in the implant area.

The obtained results of the research on the background of complex therapy of patients with combined pathology within 14 days prior to dental implantation give all grounds to consider the decrease of osteocalcine concentration in blood and P-Cross-Laps in oral fluid, as well as changes in the activity of elastase, alkaline phosphatase and homocysteine content as one of the preventive measures for the development of inflammatory and destructive processes in the field of osteo-integrated implants and to stop the occurrence of dental perimplantitis.

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