Conclusions

Endoscopic rhinoplasty is performed under constant visual control. This fact which is principally differs from close rhinoplasty. In close rhinoplasty some stages of the operation are carried out «blindly» and a surgeon can rely on the palpation only.

With endoscopic rhinoplasty the tissue separation is made above bone –cartilages structures which do not touch the ligament apparatus and muscle-facial complex of the nose.

Besides, nasal tissue do not contact with the environment and suffer from the oxygen starvation. It is better in comparison with open rhinoplasty. That is why, the use of endoscopic technologies help to improve the operation results, diminish rehabilitation period and reduce complications.

1. Aesthetic rhinoseptoplasty / B. Chakyr; per. from English ed. A.V. Glushko.- M.: GEOTAR-Media, 2019, p. 191-195
2. Cerkes N. Concurrent elevation of the upperlateral cartilage perichondrium and nasal boneperiosteum for management of dorsum: the perichondro-periosteal flap.// Aesthet SurgJ. -2013.Aug 1,-33.-6. P.899-914.).
3. H. Behrbohm, J. May. Endoscopic Guided Rhinoplasty. Dpartment or Otorhinolaryngology and Facial Plastic Surgery, Facial Plast Surg 2013;29: 133-139).
4. Palhazi P, Daniel RK, Kosins AM. The osseocartilaginous vault of the nose: anatomy and surgical observations. Aesthet Surg J. 2015; 35(3):242-251.
5. V.V. Zholtikov et al., Rhinoplasty: A Sequential Approach to the Nasal Bone Pyramid. Plastic surgery and aesthetic medicine. 2020; 3: 25-37.
6. Comlications of Rhinoplasty.Joshua B. Surowitz,MD, Sam P. Most, MD. Facial Plast Surg Clin N Am 21(2013) 639-651

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Expression of cytokines and osteocalcin in the oral fluid in early postimplantation period

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It is considered that the activity of inflammatory processes, the feature and extent of periodontal tissue damage affects the balance of cytokines and their imbalance can create conditions for the destruction of soft and bone structures of the peri-implantation zone, weakening osseointegration which may lead to implant rejection in the future [1].

It is considered that osteocalcin one of the important markers of bone metabolism, which is a non-covalent calcium-ion binding protein also known as γ -carboxyglutamic acid protein produced by both osteoblast and odontoblast. The available literature data presents the results of the content of osteocalcin mainly in the blood and there are recommendations concerning investigations of its local level. It was reported that TNF- α and IL-1 β inhibits osteocalcin production by osteoblasts [2].

Thus, the assessment of the state of bone tissues and soft tissues of the oral cavity around the implant is necessary to obtain the appropriate information for planning further treatment tactics.

Objective. Comparative assessment of the balance of cytokines and osteocalcin in the OF in patients with uncomplicated course and with an expressed inflammatory processes in the post-implantation period.

Material and methods. Dental intraosseous implantation was performed in 164 patients in the age of 45-60 years (the average age is 54.6 ± 4.17 years). Among examined patients there were 78 (47.6%) men and 86 (52.4%) women. Patients with a loss of more than 3 teeth are prevailed – 124 (75.6%) patients. The causes of teeth losses were complicated caries, periodontitis. There were different GIT pathology in 83 (50.6%) patients, in 59 (36.0%) patients diseases of the upper respiratory tract and allergic diseases were noted and in 22 (13.4%) patients no associated diseases were found. Patients with severe somatic diseases

in acute phase, myocardial infarction, ulcerative-erosive disorders of GIT, who took care with anticoagulants and corticosteroid therapy did not included to this research.

20 volunteers of comparable age with healthy periodontium and without dental implants are made up the control group. There were 9 (45.0%) men and 11 (55.0%) women. The research carried out in accordance with the Helsinki Declaration of the World Medical Association. Written informed consent was obtained from patients. All participants signed informed consent before the research.

641 screw intraosseous implants of the MIS (Medical Implant System, Israel) were installed altogether. Dental implantation was performed according to the standard protocol, the recommendations of the manufacturer and the patients' desire. 403 dental implants were installed on the upper jaw, 238 – on the lower jaw. 230 implants were installed by one-step and 411 – by two-step technique. Oral cavity was treated with antiseptic agents containing chlorhexidine just before implantation. After the implant installation patients were prescribed a rinse with 0.2% chlorhexidine solution, amoxicillin 500 mg 4 times a day for seven days, and analgesics, if necessary. The hygienic condition of the oral cavity was evaluated according to the Green-Vermillion (1964) before and after implantation; dental plaque occurrence and gingival bleeding were evaluated visually (Muhleman H.R., Cowell I., 1975). Oral fluid was collected on an empty stomach between 8.00- 9.30 AM. Before the investigation patients twice rinsed their mouths with drinking water, but the remaining water was removed with a clean cloth; after which they collected the OF into the sterile tubes that were frozen immediately and stored at -20°C temperature till the examination. We performed investigations before and 6-7 days after implantation. IL-1 β , TNF- α , IL-6, IL-10 cytokines and osteocalcin were determined in the OF. The concentration of cytokines was determined by solid enzyme immunoassay method using enzyme immunoassay test systems manufactured by CJS Company "Vector-Best" and "Pro Con" (Russia). The osteocalcin level was evaluated by luminescent analyzer "Elecsys 2010" (Roche Diagnostics, Switzerland) based on immune-enzyme assay with the help of Hoffman La Roche (Switzerland) diagnostic test kits.

Results of the research and there discussion. Before implantation patients complained gums bleeding with its progressive worsening, discharge from the interdental spaces, impairment of the statics of the teeth. It was revealed an insufficient hygienic care of the oral cavity which was manifested supra- and subgingival dental plaques. The average simplified oral hygiene index (OHI-S) was 2.64 ± 0.53 conventional units (control $\square 0.40 \pm 0.06$ CU, $p < 0.001$), bleeding index $\square 2.44 \pm 0.27$ CU (control $\square 0$, $p < 0.001$). Patients were held professional hygiene measures and traditional antimicrobial therapy and after that, i.e. immediately before dental implantation the average level of OHI-S and Mülleman-Cowell index was 0.62 ± 0.06 CU and 0.43 ± 0.04 CU accordingly. Just after implantation (1st and 2nd days) all patients complained pain, swelling and hyperemia that regressed among 119 (72.6%) patients on the 3rd day, but in 45 (27.4%) patients acute inflammatory process with intense swelling and hyperemia of soft tissues in the implant zone were detected; all implanted patients were divided into 2 groups respectively: I group – 119 patients without inflammation on the 6-7 days after implantation and II group – 45 patients with inflammation.

The value of TNF- α increased 2.3 ($p < 0.01$) and 6.4 times ($p < 0.001$) in patients of I and II groups respectively on the 6-7th days after implant placement. The research revealed that the local level of TNF- α after implantation exceeded the control values by an average of 2.5 ($p < 0.01$) and 8.6 times ($p < 0.001$) respectively in I and II groups. At the same time in the post-implantation period the concentration of this cytokine in patients of II group was 3.4 times higher than in I group ($p < 0.01$).

The level of IL-1 β and IL-6 in patients with uncomplicated postimplantation period (I group) increased 1.1 and 1.4 times respectively compared with the baseline ($p < 0.05$). In patients with inflammation (II group) IL-1 β and IL-6 concentrations in OF increased 4.2

($p < 0.01$) and 13.3 times ($p < 0.001$) respectively. The concentration of IL-1 β on 6-7 days of the post-implantation period in patients of I group was slightly lower than the control indicator, whereas in patients of II group it exceeded the control value on average by 3.8 times ($p < 0.01$). Intergroup analysis revealed an increased level of this cytokine after implantation for 4 times ($p < 0.01$) in patients of II group compared with I group. Changes of IL-6 concentration after dental implantation was considerably similar to changes of TNF- α and IL-1 β . In patients of both groups the concentration of IL-6 before implantation not differ significantly from the control group. In the postimplantation period the local level of IL-6 in patients with uncomplicated course was on average 1.6 times higher than the control group ($p < 0.05$) while in patients with inflammation it was 16.0 times higher ($p < 0.001$) and 9.7 times higher in I group ($p < 0.001$).

Before implantation the concentration of IL-10 among patients and control group was almost the same. In patients of I group on the first 6-7 days after implantation the level of IL-10 decreased slightly in comparison with baseline; in II group the concentration of IL-10 was 1.3 times lower in comparison with baseline ($p < 0.05$). In contrast to the control values there was a decrease in production of IL-10 but a significant difference was found in patients with complicated post-implantation course (1.4 times, $p < 0.05$). Intergroup analysis revealed that during inflammation as distinct from the uncomplicated post-implantation period the concentration of IL-10 was lower for 19.6%.

Calculation of the correlation ratio of proinflammatory and anti-inflammatory cytokines showed the prevalence of hyperproduction of proinflammatory cytokines in patients of II group. Among patients of II group the correlation ratio of TNF- α /IL-10 before implantation exceeded the control values by 1.5 times ($p < 0.05$). In early post-implantation period the value of TNF- α /IL-10 increased in both groups exceeding the control by 2.9 ($p < 0.01$) and 12.9 times ($p < 0.001$) in I and II group respectively. Also significant differences were determined between groups. So it was 4.5 times higher ($p < 0.01$) in I group in comparison with II group.

In the II group on 6-7th days after implantation correlation ratio of IL-1 β /IL-10 was 5.4 ($p < 0.01$) times higher than baseline and 5.3 ($p < 0.01$) times higher for the control values; in the I group the differences in values made up 1.1 times respectively. A statistically significant increases of IL-6/IL-10 was observed between the baseline values and after implantation. In I group these differences revealed 1.5 ($p < 0.05$) times and in II group – 18.9 times ($p < 0.001$). When comparison with the control values the ratio of IL-6/IL-10 in the early post-implantation period in I group was 1.8 ($p < 0.05$) times higher and in II group – 22,7 ($p < 0.001$) times higher. The differences between the patients' groups was 12.3 times ($p < 0.001$).

It was paid attention to the fact that the highest rates of pro-inflammatory cytokines and the lowest values of anti-inflammatory cytokine were observed in 41 patients with 5 implants. The number of osteocalcin in OF after implantation increased in patients of both groups. However, if in I group the concentration of osteocalcin increased slightly, then in patients of II group it was relatively expressed. Before implantation the osteocalcin level in the OF of both groups was slightly higher in comparison with the control group – on average by 4.0%. After implantation, on day 7, patients of I group showed a slight increase in the level of this protein (by 3.9% compared with baseline and by 8.1% compared with control), in II group patients concentration of this protein increased by 17.9% compared with baseline and 24.3% ($p < 0.05$) compared with the control.

A correlation analysis between the levels of osteocalcin and local immunity indicators revealed a positive mean correlation between osteocalcin and TNF- α ($r = 0.402$ and $r = 0.463$, respectively in I and II groups) and also with IL-1 β ($r = 0.388$ and $r = 0.416$ respectively in I and II groups). A positive mean correlation was detected between osteocalcin and IL-6 in patients with a complicated course (II group) – $r = 0.377$. There were weak positive relations between other indicators. So, during dental implantation especially complicated by acute inflammatory

process an increase in the production of pro-inflammatory cytokines as TNF- α , IL-1 β and IL-6 correlated with the level of osteocalcin and influenced to the process of osseointegration. In terms of the fact that the diagnostic significance of determining cytokines increases when they are studied directly in the focus of a specific inflammatory process we investigated the cytokine concentration in the OF. Statistically significant changes of the concentration of TNF- α , IL-1 β and IL-6 were obtained. It should be noted that cytokines along with endothelial cells, blood cells, connective tissue coordinate the development of a local defense response that is manifested by typical inflammatory response.

It has been determined that IL-6 during acute inflammation reveal immunoregulatory properties which allow it to convert inflammation from the acute to the chronic phase resulting in the formation of mononuclear granulomas [3]. Hence, IL-6 is able to switch the development of protective reactions from the initially developing inflammation and innate immunity reactions to the reactions of acquired immunity. Elevated levels of this cytokine indicate to the activity of inflammation.

The results we obtained regarding the level of IL-6 and TNF- α denote the activity of inflammation. Increasing of osteocalcin concentration in OF obtained by us in the study indicates on an increased bone resorption 6-7th days after implantation, especially in patients with severe inflammatory processes.

According to our results the level of osteocalcin in the OF in the presence of implants increased, indicating a decrease in mineralization. The results of our research showed an increase of osteocalcin level in the OF in patients of both groups and especially in patients with acute inflammation. Inflammation of the soft tissues around the dental implants promote to increase of osteocalcin levels.

Thus, elevated levels of pro-inflammatory cytokines (IL-1 β , TNF- α , IL-6) in the OF are the result of their activation in the inflammatory processes of the peri-implantation gum tissue, and this activation may promote to the transition of acute inflammation to chronic.

A comparative study of oral homeostasis in patients with uncomplicated early postimplantation course and during inflammatory process showed a unidirectional change in pro- and anti-inflammatory cytokines and osteocalcin but in acute inflammation these changes were more expressed.

Conclusion. The concentration of cytokines in the OF before and after dental implantation indicates a change in the balance of pro- and anti-inflammatory cytokines. An increase in osteocalcin and pro-inflammatory cytokine production in the OF indicates the development of inflammatory and destructive processes. Elevated levels of IL-1 β , TNF- α and IL-6 correlated with an increase in osteocalcin quantity in the presence of dental implants.

Determining the cytokine status and level of osteocalcin in the OF allows to judge the intensity of inflammatory, infectious, immunopathological processes and is alert in terms of the development of chronic inflammation which has an important prognostic value.

1. Al Duboni G., Osman M.T., Taha B.I., Muhamed L.A. The Potential Role of Inflammatory Cytokines as Useful Diagnostic Indicators in Osseointegrated Dental Implants. *World Applied Sciences Journal*. 2012; 20 (5): 649-655. DOI: 10.5829/idosi.wasj.2012.20.05.801
2. Ding J, Ghali O, Lencel P, Broux O, Chauveau C, Devedjian JC, et al. TNF-alpha and IL-1beta inhibit RUNX2 and collagen expression but increase alkaline phosphatase activity and mineralization in human mesenchymal stem cells. *Life Sci*. 2009;84(15-16):499-504. doi: 10.1016/j.lfs.2009.01.013.
3. Robati M., Yousefimanesh H., Maleki R., Ghafourian MB. Salivary tumor necrosis factor alpha and interleukin 6 levels in oral lichen planus patients. *Indian J Oral Sci*. 2016; 7: 79-82. DOI: 10.4103/0976-6944.194206
4. Maheswari K., Jia Hao, Lin Z., Nakata H., Kasugal S., Kuroda S. Cytokines Levels in Peri-Implant Crevicular Fluid in the Intial Stages of Dental Implant Treatments - A Preliminary Clinical Study. *J Oral Tissue Engin*. 2016;14(1):2-8. DOI: 10.11223/jarde.14.2