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INCREASING THE EFFICIENCY OF OSSEOINTEGRATION IN DENTAL IMPLANTATION IN PATIENTS WITH DIABETIC OSTEOPATHY BY REMODELING BONE TISSUE AND INTENSIFYING ITS DENSITY

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Ключові слова: *пародонтит, патологія пародонта, швидкопрогресуючий генералізований пародонтит, цукровий діабет, маркери кісткового метаболізму, дентальна імплантація, рекомбінантний морфогенетичний білок BMP-2, осеїн-гідроксіапатитний комплекс*

Abstract. Increasing the efficiency of osseointegration in dental implantation in patients with diabetic osteopathy by remodeling bone tissue and intensifying its density. Gudarian O.O., Cherednyk D.O. *The purpose of the study was to increase the effectiveness of osseointegration of implants in dental implantation in patients with rapidly progressing generalized periodontitis combined with diabetic osteopathy by restoring normal remodeling of bone tissue and intensifying its density. The study included 84 patients aged 30 to 50 years (average 41.9±2.36 years) with type 2 diabetes mellitus associated with generalized periodontitis, among them 56 women and 28 men and 19 volunteer donors without periodontal and detected somatic pathology, identical by gender and age. Surgical intervention for the installation of dental implants was performed in 3 groups of patients identical by gender and age: I, II and III groups. Groups I and II included 52 patients (26 patients in each) with rapidly progressing generalized periodontitis, with type 2 diabetes, complicated by systemic osteoporosis, who differed only in the prescribed treatment complex. Group III was formed by patients with a similar pathology of periodontal tissues, but without background diabetic osteopathy (32 patients), who received an identical treatment complex with patients in Group II. During the surgical intervention, 282 dental implants were installed: 92 implants in group I patients, 89 implants in group II, and 101 dental implants in group III. At the same time, we strove to ensure that the percentage of the performed operations was approximately the same. The analysis of the obtained data of laboratory studies showed that in patients with diabetic osteopathy with rapidly progressing periodontitis and rapidly progressing generalized periodontitis without background pathology, a deeper imbalance of the processes of bone remodeling with high level of both – bone resorption and osteogenesis is observed, which causes acceleration of the destruction of periodontal bone tissue and their loss. At the same time, it was found that with a complex and correct selection of antiresorptive therapy, the level of markers of bone metabolism approaches the norm, which is positively reflected in the dynamics and frequency of osseointegration of dental implants. Our research and received data from laboratory studies showed that in patients with rapidly progressing generalized periodontitis with and without diabetic osteopathy, there is an inhomogeneity and imbalance in the functioning of bone remodeling, which negatively affects the process of osseointegration of dental implants and requires a complex approach in the selection of antiresorptive therapy. Inclusion in the protocol of dental implantation of recombinant morphogenetic protein in patients with diabetes with osteopathology leads to completion of osseointegration of dental implants in the term up to 3 months, and monotherapy with ossein-hydroxyapatite complex in patients with rapidly progressing generalized periodontitis has a similar effect on the osseointegration process – it accelerates the recovery of bone tissue around dental implants.*

Реферат. Підвищення ефективності остеоінтеграції при дентальній імплантації у хворих на діабетичну остеопатію шляхом ремоделяції кісткової тканини та інтенсифікації її щільності. Гудар'ян О.О., Чередник Д.О. *Метою дослідження було підвищення ефективності остеоінтеграції імплантатів при дентальній імплантації у хворих на швидкопрогресуючий генералізований пародонтит, поєднаний з діабетичною остеопатією шляхом відновлення нормального ремоделювання кісткової тканини та інтенсифікації її*

щільності. Оперативні втручання зі встановлення дентальних імплантатів проведено в 3 ідентичних за статтю і віком групах хворих: I, II, III групи. У I і II групи були включені 52 пацієнти (по 26 пацієнтів) із швидкопрогресуючим генералізованим пародонтитом, з цукровим діабетом 2 типу, що ускладнювався системним остеопорозом, які відрізнялися тільки призначеним лікувальним комплексом. III групу формували пацієнти з аналогічною патологією тканин пародонта, але без фонової діабетичної остеопатії (32 пацієнти), які отримували ідентичний з II групою лікувальний комплекс. У ході оперативних втручанн було встановлено 282 дентальних імплантати: у хворих I групи – 92 імплантати, у II групі – 89 імплантатів і в III групі – 101 дентальний імплантат. При цьому ми прагнули до того, щоб у відсотковому співвідношенні кількість проведених операцій була приблизно однаковою. Аналіз отриманих даних лабораторних досліджень показав, що при діабетичній остеопатії у хворих на швидкопрогресуючий пародонтит і швидкопрогресуючий генералізований пародонтит без фонової патології чітко простежується більш глибоке розбалансування процесів кісткового ремоделювання з високим рівнем як остеорезорбції, так й остеогенезу, що зумовлює прискорення деструкції кісткової тканини пародонта і їх втрату. Одночасно виявлено, що при комплексному правильному підборі антирезорбтивної терапії рівень маркерів кісткового метаболізму приходить до норми, що позитивно відображається на динаміці та частоті остеоінтеграції дентальних імплантатів. Наші дослідження та отримані дані лабораторних досліджень свідчать про те, що в пацієнтів, хворих на швидкопрогресуючий генералізований пародонтит з діабетичною остепатією та без неї, відмічається неоднорідність та дисбаланс функціонування кісткового ремоделювання, що негативно впливає на процес остеоінтеграції дентальних імплантатів і потребує комплексного підходу в підборі антирезорбтивної терапії. Включення в протоколи дентальної імплантації рекомбінантного морфогенетичного білка у хворих на діабетичну остеопатологію сприяє завершенню остеоінтеграції дентальних імплантатів у термін до 3 місяців, а призначення монотерапії у вигляді остеогенону у хворих із швидкопрогресуючим генералізованим пародонтитом чинить аналогічний вплив на остеоінтеграційний процес – пришвидшує відновлення кісткової тканини навколо дентальних імплантатів.

A priority and promising area of reconstructive medicine is dental implantation, which is based on the installation of intraosseous implants. In recent years, the method of dental implantation has been constantly improved and has become one of the leading methods in the elimination of dental defects [1, 2, 3, 4].

Despite the success of dental implantation, there is still a fairly high percentage of rejection of dental implants, the frequency of which, according to various sources, ranges from 3 to 10% [5, 6, 7].

It is believed that the result of dental implantation can be negatively affected by the patient's somatic pathology, which is accompanied by various side effects, including metabolic changes. Such diseases include type 2 diabetes, in which systemic osteoporosis is often detected, occurring against the background of altered remodeling of bone tissue. Violation of the balance between resorption and the creation of new bone in patients with diabetic osteopathology may in the future hinder the regeneration of bone tissue around dental implants and contribute to rejection [8, 9, 10, 11].

In addition, the relationship between bone metabolism disorders in type 2 diabetes and the severity of the destructive process in the periodontium has been proven, with the greater the severity of metabolic disorders, the greater the loss of alveolar bone [2, 5, 12, 13, 14]. In turn, it can be assumed that in such a situation, the osseointegration of implants will slow down, and complications of dental implants will develop more often.

Taking into account the above, it can be assumed that inhibition of bone resorption, activation of mineralization and bone formation can optimize osseointegration of implants. In the implementation of the above, there should be a comprehensive approach aimed, first of all, at normalizing bone metabolism and increasing the density of bone tissue.

In the literature, there are little data on the positive effect of calcium preparations in the prevention and treatment of systemic and local osteopathology associated with type 2 diabetes, as well as generalized periodontitis [15, 16, 17]. High anti-resorptive and reparative effectiveness of the ossein-hydroxyapatite complex has been shown in clinical studies [18]. This drug was not used in dental practice. Recently, publications have appeared that the use of recombinant morphogenetic protein (rhBMP2) in the minimally effective dosage stimulates a pronounced inductive effect and osteogenesis [19, 20]. Until now, there is no experience of complex use of this drug with a unique combination of properties in combination with antiresorptive drugs in dentistry. Based on the above, we formed the aim of study, which was the increasing the efficiency of osseointegration of implants during dental implantation in patients with rapidly progressive generalized periodontitis combined with diabetic osteopathy by restoring normal remodeling of bone tissue and intensifying its density.

MATERIALS AND METHODS OF RESEARCH

The study included 84 patients with type 2 diabetes mellitus associated with generalized periodontitis aged 30 to 50 years (average 41.9±2.4 years), among them 56 women and 28 men and 19 volunteer donors without periodontal pathology and detected somatic pathology, identical by gender and age.

All patients signed written informed consent for all examinations and planned conservative and surgical interventions.

The examination of patients was carried out in accordance with generally accepted Ukrainian standards for the examination of patients and in accordance with the principles of bioethics set out in the WMA Declaration of Helsinki – "Ethical principles for medical research involving human subjects" and "Universal Declaration on Bioethics and Human Rights" (UNESCO).

According to the extract from the protocol of the meeting of the Committee on Biomedical Ethics of the Dnipropetrovsk Medical University of the Ministry of Health of Ukraine No. 7 dated 28.10.2020, the work complies with generally accepted standards of morality, the requirements to respect the rights, interests and personal dignity of research participants, the risk for research subjects is absent. Research participants are informed about all aspects related to the purpose, tasks, methods and expected benefits of the research.

The research was conducted on the base of the medical center of the Dnipro Medical University in the period from 2020 to 2023.

Dental implantation in all groups of patients was performed according to a single standard protocol, recommended by the manufacturer of dental implants.

The installation of dental implants was started after preliminary preparation of patients for surgical interventions, which included sanitation of the oral cavity, carrying out professional hygienic and medical measures aimed at eliminating the activity of inflammatory phenomena in the oral cavity. Dental implantation was started if there was no infectious-inflammatory process in the periodontal tissues or a significant decrease in its efficiency according to the criteria of the main gingival and periodontal indices.

Operative interventions for the installation of dental implants were performed in 3 groups of patients identical in gender and age, which were distributed in group I, II and III according to clinical and radiological status. Groups I and II included 52 patients (26 patients each, which were distributed by the sealed envelope method) with rapidly progressing generalized periodontitis, with type 2 diabetes, established by endocrinologists, in whom they were on dispensary registration complicated by systemic osteoporosis, but with different prescribed treatment complex. Group III included patients with a similar pathology of periodontal tissues, but without background diabetic osteopathy (32 patients) administered a similar treatment complex as in group II. In the course of surgical interventions, 282 dental implants were installed: in patients of group I: 92 implants, in group II – 89 implants and in group III – 101 dental implants. At the same time, we strove to ensure that the percentage of the performed operations was approximately the same.

Markers of bone metabolism were determined by the method of solid-phase isozyme analysis using the "Metre Bar ElA kit" reagents of Quidel Corporation, CrossLaps Elisa, and Natrdic Bioscience Diagnostic AIS, according to the instructions.

In order to optimize osseointegration after dental implantation, taking into account the disorders of bone metabolism processes detected by laboratory methods, patients were given the following pharmacotherapy: the patients of the first group received a medical complex that had a potentiated effect on the restoration of bone tissue and at the same time it suppressed increased resorption of bone structures: recombinant morphogenetic protein (rhBMP-2 at a concentration of 10 μg/ml), compatible with osteogenon, in a daily dosage of 830 mg for a course of 1.5 months. The choice of osteogenon was due to the double effect of the drug on bone tissue remodeling: activation of osteoblasts and inhibitory effect on the function of osteoclasts. Group II and III received only osteogenon in a daily dosage of 830 mg for a course of 1.5 months.

Statistical processing was carried out on a personal computer using the "STATISTICA" 99 software package (Version: 6.1 "Statsoft Inc., USA, № AGAR 909e415822FA). We used the Student-Fisher' exact two-tailed method to estimate the level of reliability of differences in the results obtained; a confidence level of at least 95 is generally accepted for biological and medical research ($p<0.05$). Quantitative data are presented as arithmetic mean (M) and standard error of the mean (m). Qualitative data are presented as percentages. The normality of the distribution was determined using the Shapiro-Wilko method, according to the results of which it was established that the data of the distribution are symmetrical. The reliability of differences in relative indicators was assessed using the Pearson Chi-square test (χ^2). Differences were considered statistically significant at $p<0.05$ [21].

RESULTS AND DISCUSSION

As markers of effectivity of bone metabolism we used markers of osteoresorption – tartrate-resistant acid phosphatase (TRACP) and C-terminal telopeptide (CTX) of type I collagen (β-CL), and levels of the bone isoenzyme of alkaline phosphatase (BAP) and bone gamma-carboxyglutamate protein (osteocalcin) (BGLAP), which were determined as an indicator of the activity of osteoblasts, reflecting bone formation processes around the implants. When the initial balance of bone remodeling markers changes, the opposite is true: the rate of osseointegration slows

down, and disintegration of implants often occurs. According to the results of the research and comparing the groups during dental implantation in patients of the first group, a sharp increase in the content of markers of bone resorption (β-Cl and TRACP) was established in the blood serum, and at the same time, the lowest levels of bone tissue restoration markers (BGLAP and BAP) were recorded. This shows that in patients with type 2 diabetes with systemic osteoporosis in combination with rapidly progressing generalized periodontitis, osseointegration is manifested against the background of a high level of bone resorption and inhibition of osteogenesis processes (Table 1).

Table 1

Indicators of markers of bone metabolism in patients of group I (M±m)

Indicators of markers of bone remodeling	Group I						
	healthy patients (control group (n=19)	baseline indicators (before implantation)	immediately after implantation	1 month after implantation	3 months after implantation	6 months after implantation	12 months after implantation
TRACP (Unit/L)	3.7±0.3	8.8±0.3	9.1±0.2	5.1±0.4*; **	4.0±0.2*; **	3.4±0.6**	3.2±0.3**
β-CL (ng/ml)	1.16±0.31	5.89±0.41*	6.68±0.3***	3.6±0.32*; **	1.68±0.39*; **	1.27±0.32*; **	1.21±0.43*; **
BAP (Unit/L)	36.9±0.9	14.7±0.9*	10.4±0.8***	28.3±0.9*; **	34.6±1.4**	33.8±1.4*; **	32.4±1.2*; **
BGLAP (mg/ml)	19.5±0.4	9.9±0.3*	6.2±0.2*	12.6±0.3*	18.7±0.6	18.8±0.8	17.9±0.9*

Notes: * – $p<0.05$ statistically significant difference from the indicators of the healthy group; ** – $p<0.05$ statistically significant difference from indicators before dental implantation.

In the patients of the group I, after the installation of dental implants, a sharp increase in blood serum β-Cl and TRACP was observed (Table 1). At the same time, low concentrations of osteocalcin were registered. A slight increase in blood serum levels of BAP compared to baseline values was observed, which means that surgical installation of dental implants and the course of the early postoperative period in patients with type 2 diabetes with systemic osteoporosis causes a significant adverse effect on bone metabolism.

Against the background of complex medical treatment, 1 month after dental implantation, positive dynamics of the levels of markers of bone metabolism was observed. Thus, the concentration of β-Cl and TRACP significantly decreased in 54.1% of patients, and in 37.5% of cases their level in the blood decreased compared to the initial values, being found in the range of low normal limits. During these observation periods, in 8.4% the intensity and direction of bone remodeling was fixed at the previous limits, close to the baseline ones.

One month after surgery and pharmacocorrection of bone metabolism processes, patients of group I showed an increase in the content of BAP and BGLAP ($p<0.05$), while the levels of the analyzed markers were taken as the original values obtained before dental implantation. As can be seen from Table 1, the recovery of bone metabolism took place in group I only in 3 months after dental implants instalation, and when the terminals were reached in 6-12 months, markers of osteoresorption and osteogenesis practically approached the values obtained in patients of the control group. This confirms that the osseointegration of the implants ended in the analyzed patients successfully 3 months after implantation, and the markers of bone metabolism stabilized later. This fact is of great interest, as it proves the possibility of restoration of full-fledged osseointegration of dental implants by adequate pharmacocorrection of bone remodeling processes in patients with systemic osteoporosis caused by type 2 diabetes.

In patients of group II, signs of damage to the metabolism of bone tissue in the early period after dental implantation were associated with diabetic osteopathy, as in patients of the main group (Table 2).

Table 2

Indicators of bone tissue remodeling markers in patients of group II (M±m)

Indicators of markers of bone remodeling	Group II						
	healthy patients (control group (n=19)	baseline indicators (before implantation)	immediately after implantation	1 month after implantation	3 months after implantation	6 months after implantation	12 months after implantation
TRACP (Unit/L)	3.7±0.3	8.8±0.3	9.2±0.3*	8.0±0.3*; **; ***	6.2±0.3*; **; ***	4.8±0.2*; **; ***	4.3±0.3*; **; ***
β-CL (ng/ml)	1.16±0.31	5.77±0.43*	6.79±0.32*; **	5.21±0.31*; ***	3.61±0.23*; **; ***	2.69±0.61*; **; ***	2.09±0.43*; **
BAP (Unit/L)	36.9±0.9	13.9±0.8*	10.2±0.8*; **	16.9±0.4*;**; ***	20.2±0.4*; **; ***	29.5±1.2*; **; ***	20.8±1.2*; **; ***
BGLAP (mg/ml)	19.5±0.4	9.7±0.3*	6.4±0.2*; **	10.3±0.4*; **; ***	12.7±0.2*; **; ***	14.2±0.2*; **; ***	13.0±0.2*; **; ***

Notes: * – $p<0.05$ statistically significant difference from the indicators of the healthy group; ** – $p<0.05$ statistically significant difference with indicators before dental implantation; *** – $p<0.05$ statistically significant difference from the indicators of the I group (see Table 1).

After correction of bone turnover with only calcium preparations, positive changes in the dynamics of bone remodeling markers were less pronounced, especially in the early days after dental implantation. Practical confirmation of this position is the fact of slow restoration of the composition of collagen breakdown products β-Cl, TRACP, BAP and BGLAP in blood serum. Even during the 1st and 3rd months after dental implantation in 73% of cases, such studied indicators did not correspond to the initial values and were almost unchanged ($p<0.05$). Subsequently, a slight decrease in the levels of β-Cl was noted, and the content of TRACP in the blood did not show significant positive dynamics.

Accordingly, the recovery of bone metabolism in patients of group II under the influence of the drug osteogenon at all stages of osseointegration was noted in only 4% of cases, while in others it was hardly noticeable and corresponded to the baseline data. Moreover, the increase in the levels of BGLAP and from BAP reached statistical differences the initial values in patients with positive dynamics only closer to 6 months, which confirmed the completion of osseointegration processes in the bone tissue around dental implants. Similar dynamics of bone metabolism characterizes the slower course of osseointegration processes, after the installation of implants, under the influence of traditional pharmacocorrection, than in patients of the group I.

In patients of the group III with rapidly progressing periodontitis, not complicated by diabetic systemic osteoporosis, the dynamics of the content of markers of bone resorption and osteogenesis in blood serum after dental implantation, under the influence of osteogenon, similar to that of group I was noted (Table 3).

Analysis of initial levels of markers of bone metabolism revealed that patients with rapidly progressing generalized periodontitis are characterized by an imbalance of bone remodeling: the predominance of bone resorption processes against the background of some inhibition of osteoblastosis.

In group III patients, after the installation of dental implants, a sharp increase in blood serum β-Cl and TRACP was noted (Table 3). At the same time, low concentrations of osteocalcin (BGLAP) were observed. A slight increase in serum of TRACP levels and significant increase of β-Cl compared to the baseline values was observed, from which follows that surgical intervention for the installation of dental implants in patients with rapidly progressive generalized periodontitis affects bone metabolism. During the first 3 days after the operation, activation of bone resorption occurs, as well as subsequent inhibition of bone tissue restoration processes.

One month after the operation, under the influence of the selected pharmacocorrection of bone metabolism, the patients of the analyzed group had an increase in the content of BGLAP and BAP, while the BAP level changed more significantly, reaching normal values in 85.2% of cases. The level of collagen degradation products and especially TRACP in blood serum decreased reliably and more significantly ($p<0.05$) and approached the limits of the conventional norm in 76.4% of cases. By the 3rd

month, the levels of markers of bone tissue remodeling in blood serum in comparison with the values of the control group had no differences in 91.2% of patients and were at the achieved level in six months and longer.

The above allows us to think that in patients with rapidly progressing generalized periodontitis after dental implantation, the completion of osseointegration under the influence of osteogenon occurs closer to 3 months after surgery.

Table 3

Indicators of bone tissue remodeling markers in patients of group III (M±m)

Indicators of markers of bone remodeling	Group III						
	healthy patients (control group (n=19)	baseline indicators (before implantation)	immediately after implantation	1 month after implantation	3 months after implantation	6 months after implantation	12 months after implantation
TRACP (Unit/L)	3.7±0.3	5.9±0.2*; ***; ****	6.6±0.3*; **; ***; ****	4.4±0.4 ****	4.0±0.3 **; ****	3.9±0.4**; ****	4.1±0.3**; ***
β-CL (ng/ml)	1.16±0.31	4.69±0.32 ***; ****	5.59±0.29*; **; ***; ****	1.89±0.33*; **; ***; ****	1.23±0.42**; ****	1.33±0.34**; ****	1.21±0.45**; ****
BAP (Unit/L)	36.9±0.9	19.7±0.4*; ***; ****	12.7±0.7*; **; ***; ****	30.3±0.9*; **; ****	37.6±1.2**; ****	34.8±1.4*; **; ****	34.4±1.3*; **; ****
BGLAP (mg/ml)	19.5±0.4	14.2±0.3*; ***; ****	10.4±0.2*; **; ***; ****	13.6±0.3*; ****	17.1±0.4*; **; ***; ****	18.9±0.3**; ****	18.2±0.3*; **; ****

Notes: * – p<0.05 statistically significant difference from the indicators of the healthy group; ** – p<0.05 statistically significant difference from indicators before dental implantation; *** – p<0.05 statistically significant difference from the indicators of group I (see Table 1); **** – p<0.05 statistically significant difference from the indicators of group II (see Table 2).

CONCLUSIONS

1. The heterogeneity of the functioning of bone remodeling was established in both patients with rapidly progressive generalized periodontitis combined with diabetic systemic osteoporosis and in patients with similar periodontal lesions without background pathology: in the former, an imbalance of bone metabolism due to a significant increase in bone resorption with a simultaneous strong decrease in bone formation was revealed; in the latter, the predominance of resorption processes over of osteogenesis.
2. To increase the effectiveness of dental implantation under diabetic osteopathy and rapidly progressing generalized periodontitis, it is advisable to use complex and adequate pharmacotherapy, which has a pronounced anti-resorptive effect and simultaneously stimulates bone formation, before and after the installation of dental implants.
3. Inclusion of recombinant morphogenetic protein (rhBMP-2) in a concentration of 10 μg/ml in a complex with osteogenon in a daily dose of 830 mg for 1.5 months in the protocols of dental implantation in patients with diabetic osteopathology contributes to the completion of osseointegration of dental implants within a period of up to 3 months , and the appointment of monotherapy in the form of osteogenon in patients with rapidly progressing generalized periodontitis has a similar effect on the osseointegration process – it accelerates the recovery of bone tissue around dental implants.

Contributors:

Gudarian O.O. – conceptualization, methodology, resources, data curation;

Cherednyk D.O. – conceptualization, methodology, resources, data curation.

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REFERENCES

1. Gudaryan OO, Kucherenko TO. [The state of bone metabolism in patients with various variants of the course of generalized periodontitis]. Visnyk problem biolohii i medytsyny. 2020;3:314-8. Ukrainian.

2. Gudaryan OO, Mashchenko IS, Kucherenko TO. [Treatment of aggressive (rapidly progressing) generalized periodontitis with the use of systemic enzyme therapy in combination with osteoinductive means]. Medicni perspektivi. 2020;25(3):144-52. Ukrainian. doi: https://doi.org/10.26641/2307-0404.2020.3.214852

3. Alghamdi HS, Jansen JA. The development and future of dental implants. Dent Mater J. 2020;39(2):167-72. doi: https://doi.org/10.4012/dmj.2019-140

4. Prots H, Rozhko M, Pjuryk V, Nychyporchuk H, Pavelko N. Efficiency of dental implantation in prosthetic rehabilitation of patients with generalized periodontitis. Georgian Med News. 2021 May;(314):77-82. PMID: 34248031.

5. Do TA, Le HS, Shen YW, Huang HL, Fuh LJ. Risk Factors related to Late Failure of Dental Implant-A Systematic Review of Recent Studies. Int J Environ Res Public Health. 2020 Jun 2;17(11):3931. doi: https://doi.org/10.3390/ijerph17113931

6. Camps-Font O, Martín-Fatás P, Clé-Ovejero A, Figueiredo R, Gay-Escoda C, Valmaseda-Castellón E. Postoperative infections after dental implant placement: Variables associated with increased risk of failure. J Periodontol. 2018 Oct;89(10):1165-73. doi: https://doi.org/10.1002/JPER.18-0024

7. Liaw K, Delfini RH, Abrahams JJ. Dental Implant Complications. Semin Ultrasound CT MR. 2015 Oct;36(5):427-33. doi: https://doi.org/10.1053/j.sult.2015.09.007

8. Aghaloo T, Pi-Anfruns J, Moshaverinia A, Sim D, Grogan T, Hadaya D. The Effects of Systemic Diseases and Medications on Implant Osseointegration: A Systematic Review. Int J Oral Maxillofac Implants. 2019 Suppl;34:s35-s49. doi: https://doi.org/10.11607/jomi.19suppl.g3

9. Mashchenko IS, Kucherenko TO. [Clinical, immunological and metabolic features of acute and rapidly progressing variants of generalized periodontitis]. Suchasna stomatolohiia. 2020;4:26-32. Ukrainian. doi: https://doi.org/10.33295/1992-576X-2020-4-26

10. Germanchuk SM. [Morphobiochemical changes in periodontal tissues in experimental diabetes]. Ukrainskyi zhurnal medytsyny, biolohii ta sportu. 2018;3(4):13-9. Ukrainian. doi: https://doi.org/10.26693/jmbs03.04.013

11. Jiang X, Zhu Y, Liu Z, Tian Z, Zhu S. Association between diabetes and dental implant complications: a systematic review and meta-analysis. Acta Odontol Scand. 2021 Jan;79(1):9-18. doi: https://doi.org/10.1080/00016357.2020.1761031

12. Sgolastra F, Petrucci A, Severino M, Gatto R, Monaco A. Periodontitis, implant loss and peri-implantitis. A meta-analysis. Clin Oral Implants Res. 2015 Apr;26(4):e8-e16. doi: https://doi.org/10.1111/clr.12319

13. Monje A, Alcoforado G, Padial-Molina M, Suarez F, Lin GH, Wang HL. Generalized aggressive periodontitis as a risk factor for dental implant failure: a systematic review and meta-analysis. J Periodontol. 2014 Oct;85(10):1398-407. doi: https://doi.org/10.1902/jop.2014.140135

14. Patel RM. Dental Implants for Patients with Periodontitis. Prim Dent J. 2020 Jan 29;8(4):54-61. doi: https://doi.org/10.1308/205016820828463898

15. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, et al. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022 Oct;33(10):2049-102. Epub 2022 Apr 28. Erratum in: Osteoporos Int. 2022 Jul 28. PMID: 35478046. PMCID: PMC9546973. doi: https://doi.org/10.1007/s00198-021-05900-y

16. Chiodini I, Bolland MJ. Calcium supplementation in osteoporosis: useful or harmful? Eur J Endocrinol. 2018 Apr;178(4):D13-D25. doi: https://doi.org/10.1530/EJE-18-0113

17. Mohsin S, Baniyas MM, AlDarmaki RS, Tekes K, Kalász H, Adeghate EA. An update on therapies for the treatment of diabetes-induced osteoporosis. Expert Opin Biol Ther. 2019 Sep;19(9):937-48. doi: https://doi.org/10.1080/14712598.2019.1618266

18. Castelo-Branco C, Dávila Guardia J. Use of ossein-hydroxyapatite complex in the prevention of bone loss: a review. Climacteric. 2015 Feb;18(1):29-37. doi: https://doi.org/10.3109/13697137.2014.929107

19. Johnson TB, Siderits B, Nye S, Jeong YH, Han SH, Rhyu IC, et al. Effect of guided bone regeneration on bone quality surrounding dental implants. J Biomech. 2018 Oct 26;80:166-70. doi: https://doi.org/10.1016/j.jbiomech.2018.08.011

20. James AW, LaChaud G, Shen J, Asatrian G, Nguyen V, Zhang X, et al. A Review of the Clinical Side Effects of Bone Morphogenetic Protein-2. Tissue Eng Part B Rev. 2016 Aug;22(4):284-97. doi: https://doi.org/10.1089/ten.teb.2015.0357

21. Mitra S. Multiple Data Analyses and Statistical Approaches for Analyzing Data from Metagenomic Studies and Clinical Trials. Methods Mol Biol. 2019;1910:605-34. doi: https://doi.org/10.1007/978-1-4939-9074-0_20

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