

Features of Dental Implantation in Patients with Type II Diabetes

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Abstract

The aim of this review article is to consider the features of dental implantation in type II diabetes mellitus. Diabetes mellitus is defined as a metabolic disorder of various etiologies, chronic hyperglycemia with impaired carbohydrate, fat, and protein metabolism as a result of defects in insulin secretion, the action of insulin, or both.

A systematic review of the literature in the electronic databases Google Scholar and Pubmed was conducted. Articles concerning the features of dental implantation in type II diabetes mellitus and factors affecting the outcome of treatment are considered and included.

Results: 120 articles were reviewed during the analyze. After making the selection based on the exclusion criteria, the number of included studies was 69.

According to the studied publications, the main recommendations that must be followed to achieve successful osseointegration in type II diabetes were compiled.

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Keywords: Dental implantation, diabetes mellitus 2 type, osteopenic syndrome, secondary osteoporosis, diabetes, dental implants, periimplantitis, glucose level, hyperglycemia, complications, vitamins, minerals, vitamin d.

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Introduction

One of the most common endocrine diseases in the world is diabetes mellitus. It is a group of endocrine diseases associated with impaired glucose uptake and developing due to absolute or relative insulin insufficiency, leading to hyperglycemia. According to the latest data, more than 500 million people worldwide suffer from diabetes. In the 65+ population group, this prevalence reaches 25%¹. Type 2 diabetes is characterized by muscle and liver immunity to insulin and its reduced secretion. The results of research conducted in recent decades indicate that there is an Association between the level of vitamin D availability and the risk of developing both diabetes itself and its chronic complications².

Changes in the activity of the vitamin D receptor or changes in the concentration of extracellular and intracellular calcium in

conditions of vitamin d deficiency can have an adverse effect on the functional state of pancreatic β cells and lead to a decrease in the synthesis and secretion of insulin². It was found that vitamin D stimulates the expression of the insulin receptor gene and thus participates in the transmembrane transport of glucose². It was also found that normal vitamin D levels maintain the concentration of intracellular Ca^{2+} in a narrow range, and changes in its level observed in conditions of vitamin d deficiency negatively affect the activity of intracellular glucose-4 transporters (GLUT-4) and lead to the development of insulin resistance in peripheral tissues^{3,4}.

Inflammatory processes in periodontal tissues against the background of diabetes mellitus are characterized by significant changes, in the pathogenesis of which a special significance is given to generalized microangiopathy, characterized by destruction of the basement membrane, plasma impregnation and the development of hyalinosis, which occurs due to an attempt to remove under-oxidized metabolic products outside the vascular wall. When insulin is deficient, the processes of

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mineralization and bone remodeling are disrupted. In saliva, the level of calcium ions increases, the level of phosphate ions decreases, which leads to resorption, demineralization, up to the lysis of bone tissue. Problems of osteosynthesis are also caused by the energy deficit of osteoblasts⁵. Also, against the background of the above mechanisms, patients with type II diabetes may develop both osteopenic syndrome and secondary osteoporosis⁶.

Clinical assessment of hyperglycemia occurs through regular determination of the level of hemoglobin HbA 1c (also known as glycohemoglobin). HbA 1c values are evaluated in the long term (8-12 weeks) by determining the average blood sugar level, which also helps to assess the effectiveness of antihyperglycemic therapy and patient compliance with the regimen^{7,8,9,10}.

Materials and methods

To write this review article, we conducted a search in the electronic databases PubMed and Google scholar and in the literature, lists indicated in the found studies and articles.

The following terms were selected for the search: «dental implantation», «diabetes mellitus 2 type», «osteopenic syndrome», «diabetes», «dental implants», «periimplantitis», «glucose level», «hyperglycemia», «Zahnimplantation», «vitamin d».

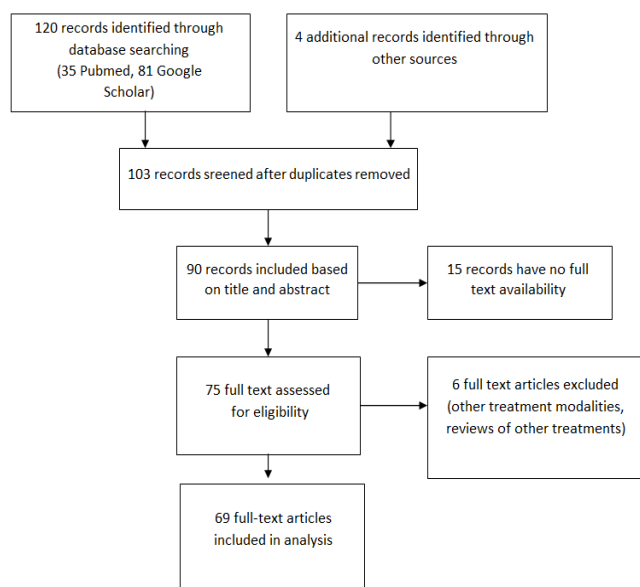


Table 1. Article selection process.

The research was filtered in two stages. At the first stage, the title and summary of publications were analyzed. At the second stage, the content was reviewed, and full-text versions of the selected articles were reviewed. When selecting the sources, preference was given to more recent publications. The earliest publication dates to 1976, the latest to 2019. The search was performed on 13.06.2020 and 2.07.2020.

Results

120 articles were reviewed, including 35 from the PubMed database, 81 from Google Scholar, and 4 article links. After making the selection based on the exclusion criteria, the number of included studies was 69.

Based on the publications we have studied; we present you the results of some studies describing the factors that affect the prognosis of dental implantation in type II diabetes:

1. Preclinical studies have shown a negative effect of hyperglycemia on BIC and implant osseointegration and highlighted the importance of glycemic control³¹⁻³³.

2. Data from prospective and retrospective studies confirm successful osseointegration of dental implants installed in patients with diabetes mellitus with good / normal metabolic control, in the range from 85.5 to 100%³⁴.

3. Some studies have shown a higher percentage of early implant loss in diabetic patients compared to late loss^{35,42,43} and an increased risk of perimplantitis⁴⁵.

4. With inadequate metabolic control were identified a higher percentage of loss of the implants⁴⁶, but a recent survey of Oates et al.⁴⁷ found that data on the effect of uncontrolled carbohydrate metabolism is still insufficient, since most of the studies obtained indirectly reported control of glycemia, which should be evaluated by measuring HbA1c glycohemoglobin³¹, and they were able to find only two prospective studies and one prospective series of cases that meet this requirement.

In two of these publications, implant loss was not recorded during the four-month period before recovery⁴⁶ and after one year, respectively⁵³. The third study involved 45 patients with diabetes, with 44 of them having HbA1c levels up to 9% (22 with well-controlled

and 22 with fairly well-controlled) and only one patient with a level of more than 9% (with poorly controlled). The following results were obtained: the frequency of loss was 9.1% in patients with uncompensated diabetes mellitus over a period of 42.4 months⁴⁸. When combining the results of all groups of patients, the cumulative frequency of implant loss was 3.9%. The authors concluded that implantation therapy can be successful even in patients with poor glycemic control, while creating favorable conditions for good osseointegration.

5. However, it is also important to emphasize that hyperglycemia can lead to serious complications such as macro / microangiopathy, neuropathy, and an increased risk of bacterial infections, so strict control of glycemia before and after implantation is strongly recommended^{31,51,52}. Working with patients with diabetes, the doctor should consider the possibility of antibiotic prophylaxis as necessary and be sure to prescribe the use of antiseptics before and after surgery to reduce the potential risk of secondary infections. In addition, Smoking cessation, a strict regime of maintenance therapy and prevention are important, and regular preventive dental examinations with oral hygiene control are recommended to reduce the risk of periodontal infections and peri-implantation complications⁵³.

6. Despite the contradictory data, most experts tend to believe that a normal level of vitamin D is necessary to prevent the development of metabolic disorders⁶¹. This is confirmed by research results indicating that among participants with a level of 25 (OH)D in the serum corresponding to the highest, the risk of metabolic disorders is 43% lower than in those with the lowest 25(OH)D levels, and an increase in the concentration of 25 (OH)D for every 25 nmol/l is accompanied by a 13% reduction in the risk of developing metabolic syndrome. Thus, vitamin d deficiency can be considered as a separate independent risk factor for the development of metabolic disorders, including DM2.

7. Research conducted at Shanghai University has shown that there is a relationship between level 25 (HE)D in blood serum and the severity of neuropathy in patients with DM2, namely, the greatest changes were detected in individuals with level 25 (OH)D less than 16 ng / ml⁴⁷. A possible Association of vitamin d

deficiency with Pro-inflammatory cytokines in patients with DM2 and DPN was also demonstrated by the results of a study conducted in Turkey. It was revealed not only an increase in the concentration of interleukins (IL-13 and IL-17) in patients with DM2 and DPN, but also correlations between the level of 25 (OH)D in blood serum and IL values⁴⁷.

8. the question remains Whether vitamin D should be used and in what doses to compensate for its deficiency or deficiency in patients with DM2. And one study evaluated the effect of vitamin D therapy at a dose of 200,000 IU per month for 3 months on reducing the level of glycated hemoglobin (HbA1c) in patients with newly diagnosed DM2 AND asymptomatic vitamin D deficiency⁵¹. It turned out that vitamin D therapy improved glycemic control, but the decrease in HbA1c was statistically insignificant in both groups. In another study, there was a significant reduction in symptoms of painful DPN in patients with DM2 20 weeks after a single intramuscular injection of 600,000 IU of vitamin D⁵².

9. using frequency-resonance analysis of implant stability and bone quality assessment using the Haunsfield scale units, it is possible to prevent complications associated with an unreasonable early load on the implant. The use of hyaluronic acid activates inhibitors or retarders of metalloproteinases and effectively counteracts tissue destruction. This effect is achieved by slowing down cytokines that cause inflammation (for example, TNFa). Thus, hyaluronic acid can help to stabilize the structure of tissues⁵⁵.

10. In the survey by Dr. R. BeliauskiiP and Mingazeva A. Z. it was found that the use of a drug based on ossein-hydroxyapatite complex provides a preventive effect, reducing the frequency of postoperative perimplantitis by 1.9 times⁵⁵.

11. Unsuccessful implantation outcomes are closely associated with impaired calcium metabolism and are observed in individuals with a total serum calcium level of 2 mmol/l or less and concomitant reciprocal changes in the level of phosphates and parathyroid hormone. Preventive administration of "Osteogenon" during preimplantation preparation reduces the frequency of postoperative perimplantitis and unsuccessful outcomes by 2.7 times⁵⁹.

Discussion

Previously, the presence of type II diabetes mellitus (uncompensated form) in a patient was an absolute contraindication for dental implantation, but now, with rapidly developing trends in optimizing the conditions for preoperative preparation and postoperative rehabilitation, dental implantation in patients with this disease has become possible while maintaining normal blood glucose levels.

A mandatory component of preoperative preparation of patients with type II diabetes is a comprehensive examination not only by a dentist, but also by an endocrinologist. When preparing for dental implantation in this pathology, an interdisciplinary approach is important. In addition to standard tests, patients are assigned additional tests: free calcium in the blood, paratharmon level, 25-OH vitamin D in the blood, as well as analysis for the presence of biochemical markers of osteoporosis (osteocalcin, bone alkaline phosphatase, oxyproline).

At the stage of preoperative preparation, one of the main tasks of the endocrinologist is to bring glucose indicators to acceptable standards (fasting glucose level should not exceed 6.1 mmol/l, and two hours after eating — not to be higher than 7.8 mmol / l, HbA1c — no more than 6 %), good results can be achieved by hypoglycemic therapy.

Increased blood glucose levels have a direct impact on the successful achievement and long-term maintenance of osseointegration¹⁸⁻²⁰, which must be considered for effective treatment with dental implants. Diabetes mellitus impairs protein synthesis at the sites of surgery and delays the healing process of tissues^{21,22}. Also, in diabetes mellitus, the formation of extracellular matrix around the dental implant is inhibited by accumulated glycosylation end products (AGEs), which are formed during irreversible molecular interactions with glucose degradation products (GDP)^{19,20}. Diabetes mellitus suppresses osteoblastic activity and maturation, causing serious defects in bone remodeling, formation, and mineralization^{22,23}. In diabetes mellitus, the incidence of postoperative infection and perimplantitis increases due to a violation of the periodontal status and a decrease in the immune response, which leads to implant rejection²³⁻²⁵.

As for foreign authors, most of the literature agreed that implant survival is

comparable in diabetic patients with proper metabolic control with healthy patients^{37,38}.

However, impaired implant osseointegration was also observed in patients with diabetes³⁹. In animal studies, it was found that hyperglycemia inhibits osteoblast differentiation and affects the regulation of phosphorus and calcium metabolism mediated by parathyroid hormone, as well as negatively affects the growth and accumulation of extracellular matrix of bone tissue^{9,29,39,40}. In addition, it was also noted that the inflammatory response around dental implants was higher in diabetic rats than in control rats, which appeared to lead to increased bone resorption in the group with endocrine pathology^{14,41}. Given the negative impact of hyperglycemic conditions on bone healing, it is recommended to conduct pre-and post-operative preparation, as well as strict glycemic control before and after dental implantation. These patients are also encouraged to practice maintaining good oral hygiene, applying antiseptic mouthwash, and so on to avoid secondary periodontal and perimplantitis infections.

At the next stage of diagnosis, it is necessary to determine whether the patient has osteopenic syndrome or secondary osteoporosis. For this purpose, there is a special x-ray method aimed at determining the bone mineral density (densitometry). Densitometry is performed to assess the risk of developing osteoporosis and determine the effectiveness of therapy that slows down bone demineralization as an additional diagnostic method. To assess the state of bone tissue, ultrasound densitometry is used on the Omnisense 7000S device (Sunlight Medical, Israel).

According to who recommendations and guidelines of the International society of clinical densitometry (ICCD), the diagnosis of osteoporosis was performed using the T-criterion in the form of standard deviations (SD) from the norm: 1) up to 1 SD norm, 2) from 1 SD to 2.5 SD osteopenia, 3) less than 2.5 SD without fractures osteoporosis, 4) less than 2.5 SD + 1 fracture complicated osteoporosis⁵⁸.

If this pathogenetic unit is detected, it is recommended to conduct appropriate pharmacotherapy. There are many pharmacological drugs that inhibit the process of bone resorption (calcitonin, bisphosphonates), activate mineralization (calcium salts), bone

formation (fluorides), or have a polymodal effect on resorption and bone formation (vitamin D, ossein-hydroxyapatite complexes)⁵⁴. Drug therapy should be carried out for a long time: for 6 months before surgery and 2 years after dental implantation.

Tovmasyan A. M., Panin A. M., et al. in their work, we studied the effect of osteopenic syndrome on osteointegration during dental implantation in people with type II diabetes. The authors noted an extension of the healing time of surgical wounds in the presence of osteopenia and the duration of the disease for more than 5 years. At the beginning of the disease, with a lack of systemic signs of remodeling processes according to blood biochemical parameters, the acceleration of bone metabolism with the predominance of the resorption phase is highlighted, which must be taken into account before surgery in order to reduce the number of complications. It is believed that today there are reasons for dentists to consider the selection of patients with type II diabetes for dental implantation, subject to additional examination and preoperative preparation⁸.

In diabetes, polyhypovitaminosis is observed, so it is recommended to detail vitamin therapy, which includes not only vitamin D, but also group B, folic acid, but also vitamin C. Great importance in preparing patients for implantation is given to vitamin D, since it lowers the level of glucose in the blood. A recently published meta-analysis of 24 controlled trials evaluated the effects of vitamin D therapy on HbA1c, fasting plasma glucose, and a homeostatic model for evaluating insulin resistance (HOMA-IR) in diabetic patients. It was found that taking vitamin D in a daily dose of at least 4000 IU statistically significantly reduces fasting plasma glucose, HbA1c and HOMA-IR. In these studies, the daily dose of vitamin D was significantly higher than the daily requirement and began with 4000 IU per day, which allowed more effective control of the glycemic response and improved tissue sensitivity to insulin in patients with DM2. Vitamin therapy plays an important role in preventing the development of microangiopathy 5 mg / day of folic acid in combination with vitamins B12 (6 mg/day) and B6 (4 mg/day) leads to a decrease in the average level of homocysteine in the blood serum by 34%⁵⁹.

Women entering the age of menopause are recommended to additionally check the level

of estradiol, as well as the level of thyroid hormones. If there are abnormalities, additional corrective therapy is recommended before dental implantation⁵⁷.

Preoperative preparation in addition to the rehabilitation of the patient's oral cavity with subsequent constant monitoring of oral hygiene, the patient's motivation for hygiene, controlled brushing of teeth, it is also necessary to assess the condition of the periodontal, study the history of chronic periodontitis, make sure that its clinical course is in therapeutic remission. In addition to the proposed comprehensive approach, there is an obvious need for an individual plan of dental implantation with the choice of the optimal Protocol and type of implantation, considering clinical indicators and the state of bone tissue. In diabetes mellitus, it is recommended to perform minimally invasive prosthetics methods, such as transgingival implantation, single-stage implantation. When choosing, you must consider the type of bone tissue. According to the Misch classification, the following types of bone were observed. 1) 1150 units of the Haunsfield scale or more according to the Misch classification corresponded to the D1 bone type (dense homogeneous compact bone substance, little spongy tissue); 2) 840-1150 the Haunsfield scale units – type D2 bone (dense homogeneous compact bone substance, the coarse cancellous tissue, with a pronounced trabecular structure); 3) 330-840 scale units Haunsfield – bone type D3 (a thin layer of cortical bone, fine-meshed spongy substance with a pronounced trabecular structure); 4) 145-330 scale units Haunsfield – type D4 bone (very thin layer of cortical bone and loose cancellous)⁵⁵.

Precise algorithms of three-dimensional dental computed tomography when planning and performing dental implantation prevent violations of the integrity of the closure cortical plate of the bottom of the maxillary sinuses, nasal cavity, damage to the mandibular nerve, vestibular or oral walls of the alveolar process in the area of intended implantation in somatic patients⁵

The modification of the surgical Protocol should also include the control of the consistency of sutures in the postoperative period. Planning for orthopedic treatment should begin before surgery and include a full analysis of the patient's local status with the identification of dental risk factors, in addition to the risks of concomitant disease. Introduction to the occlusal load should

only be performed in accordance with the progressive load Protocol in order to prevent additional occlusal trauma of the installed dental implants. The immediate orthopedic load Protocol is rational for use in limited cases. When rehabilitating fully adentic patients with antagonistic splinting permanent restorations, or with signs of bad habits and parafunctions, it is preferable to manufacture removable structures with integrated voltage dampers on an enough supporting implants.

During the operation, the surgeon-implantologist should minimize surgical trauma, and it is also recommended to additionally treat the surface of the implant. There are many processing methods: "BCS"(machine processing), "NIKO"(coarse-grained sandblasting and acid etching), "ENDURE"(sandblasting and acid etching), "RADIX"(intense plastic deformation), "SGS" (electrochemically deposited calcium-phosphate bonite surface). Sand-blasted, Large grit, Acid-etched" (S. L. A.) - coarse-grained sandblasting and acid etching is the most popular. As a result of treatment, primary stabilization is provided and there is no micro-displacement of the implant. This treatment gives a higher contact area of osteoblasts with the implant surface and a higher rate of bone formation on the implant surface.

After surgery, the patient is recommended to prescribe rinsing with antiseptic solutions (chlorhexidine 2%, etc.), if necessary, prescribe antibiotic therapy, HELBO therapy and immunomodulatory therapy as a prevention, in order to reduce postoperative hyperemia, edema and soreness.

To determine the primary stability of implants and analyze the long-term results of osseointegration of intraosseous dental implants, use the device "Osstell ISQ" manufactured by Integration Diagnostics (Sweden), configured for frequency-resonance analysis RFA (Resonance Frequency Analysis), which determines the stability coefficient of the implant. All patients during and after surgery are recommended to measure the ISQ (Implant stability Quotient) / CI (implant stability coefficient) during surgery, before closing the wound, and through 1, 2, 4, 6, 9, 12 and 24 months. The results of research have shown that the density of bone tissue depends on the age of implantation and the functional load on the implant. Within a year after directed bone regeneration, the growth of bone

tissue reaches 95%⁵⁵.

Implant loss can occur up to a year after implant placement - "early implant loss" and a year after implantation - "delayed implant loss", which is primarily associated with the development of a pronounced inflammatory reaction in the tissues surrounding the osteointegrated implant. The absence of osseointegration of the installed implant leads to early loss of the implant²¹. Smoking²², bone quality²³, osteoporosis¹⁹, systemic diseases²⁴, or chemotherapy²⁵, along with surgical trauma or bacterial infection, are the most important causes of early implant loss²⁶. Perimplantitis is the most common cause of late implant loss²⁷.

Conclusions

When analyzing all the above studies, certain patterns were identified that should be considered in the Protocol of dental implantation in patients with type II diabetes, presented for convenience in the format of recommendations:

1. Regular monitoring of blood glucose levels is of paramount importance. Patients with HbA1c <8% are suitable for implantation therapy. Patients with uncompensated diabetes mellitus should be informed of the risks of incomplete osseointegration, up to implant rejection. Before starting dental implantation, it is necessary to conduct a comprehensive examination and comprehensive treatment together with specialists of other profiles. At the initial stage, an interdisciplinary approach to the management of patients with type II diabetes is very important, bringing glucose, vitamin D, and bone metabolism indicators to normal before implantation, as well as continuing therapy and monitoring indicators after surgery.

2. Before working with a patient, it is recommended to evaluate the periodontal status of patients, oral hygiene and the history of periodontitis. It is important to make sure that the clinical course of chronic generalized periodontitis is in therapeutic remission. Preventive periodontal therapy twice a year is necessary to maintain the health of the tissues around the implant and ensure long-term operation of the implant.

3. It is Recommended to prescribe a preventive course of antibiotic therapy and antiseptic mouthwash as additional therapy to avoid postoperative infection.

4. It is Recommended to perform surface treatment of implants, such as hydroxyapatite and SLA (sandblasting, coarse graining, acid etching), as they help to improve the indicators of osseointegration of implants.

5. When using methods of directed tissue regeneration using bone grafts are possible, it is recommended to avoid excessive surgical trauma, thereby facilitating the processes of wound surface repair and minimizing the occurrence of postoperative infection.

6. The immediate loading Protocol can be applied to patients with compensated diabetes mellitus, while normal loading is adequate for use in patients with uncompensated diabetes mellitus.

7. Administration of complex multivitamin therapy with the use of antihypoxants in order to improve glucose and blood parameters both in the preoperative period and in postoperative rehabilitation.

The analysis also revealed the effect of hyperglycemia on the prognosis of treatment, but its role in the osseointegration of implants is subject to further investigation. There is no doubt that a safe and adequate bone metabolism is necessary for the osseointegration of dental implants, and the presence of osteopenia or osteoporosis significantly reduces the effectiveness of this surgical intervention. The issue of the appointment of modulators of bone metabolism before and after treatment is also relevant.

Declaration of Interest

The authors report no conflict of interest.

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