Dental Implant Treatment Features in Patients with Type 1 Diabetes Mellitus: A Systematic Review

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Abstract

Aim to determine the impact of diabetes mellitus, particularly the type one, on the success of dental implant treatment.

Electronic search of publications in the databases such as Google Scholar, PubMed, Embase in the course of a systematic review of the literature was conducted. Included articles contain information about the impact of type 1 diabetes mellitus (T1DM) on the quality of dental implantation, bone tissue and osteointergation of implants.

88 articles were viewed during the review. After analyzing the literature for inclusion criteria, the total number of publications has become 35.

According to the reviewed literature, uncontrolled type 1 diabetes can negatively affect the quality of implantation. Constant monitoring of glucose levels in compromised patients can increase the success rate of dental implantation.

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Introduction

Diabetes mellitus is a group of endocrine diseases associated with impaired glucose uptake and developing absolute or relative insulin insufficiency which lead to hyperglycemia.

The main classification of this pathology envisages the division of diabetes into two main varieties: type 1 diabetes (insulin-dependent) and type 2 diabetes (insulin-nondependent), also we can distinguish gestational diabetes (diabetes of pregnant women) and impaired glucose tolerance[1]. In patients with type 1 diabetes absolute insulin insufficiency is observed due to the death of the Langerhans islets β-cells, whereas in type 2 diabetes, on the contrary, increased concentrations of this hormone can be observed because of genetic insufficiency of the insulin apparatus and adverse factors such as obesity.

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Tissue hypoxia associated with diabetes can lead to many complications, such as microangiopathies (peripheral arteriosclerosis and atherosclerosis, ischemic heart disease) and microangiopathies (periodontal disease, nephro-, retino- and neuropathy), increased sensitivity to infections[2-4]. It is also important to discuss the changes of bone tissue structure in diabetes mellitus patients. In particular, the manifestation of marginal bone resorption and reduced bone mineral density play a direct role in predicting the success of dental implantation in compromised patients[4-11].

The purpose of this systematic review article is to determine the effects of T1DM on bone tissue, osseointegration and dental implants survival.

Materials and methods

This review article was performed during an electronic search in two databases, such as Google Scholar, PubMed and Embase.

The search terminology included: «dental implants in diabetes patients», «diabetes and osteointegration», «bone microarchitecture in

T1DM», «osteopenic syndrome in T1DM», «survival rate of dental implants in patients with type 1 diabetes», «effects of hyperglycaemia on peri-implant tissues".

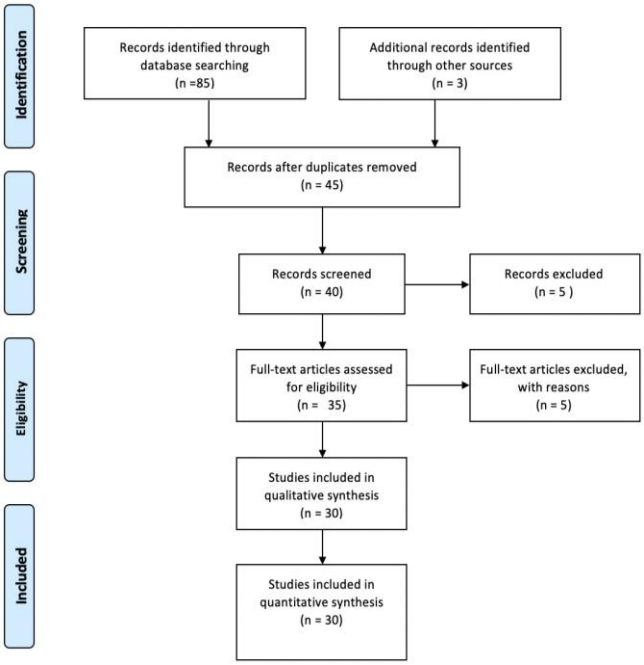

Table 1. Article selection process.

Publications with the following criteria were included:

1. Articles published in 2004 or earlier;
2. Description of type 1 diabetes mellitus in the study;
3. Consideration of the diabetes mellitus effects on bone tissue and metabolic pathways;
4. Articles containing diabetes patient surgical management.

Publications were selected and included in analysis in several stages. The first exclusion criterion was the choice of literature published earlier than 2004. Duplicates were discarded. Then we analyzed the titles and abstracts of publications. The content and full-text versions of selected articles were reviewed at the last stage.
The risk of systematic error was assessed during data extraction. The assessment of systematic error risk was done (for the included studies) with the help of a two-component Cochrane Collaboration's tool. The overall risk of systematic error was assigned to each trial. The levels of systematic error were categorized as follows: low risk if all criteria were done; moderate risk if only one criterion was missing; high risk if two or more criteria were missing; and unclear risk if there were a low number of details to make a decision about a particular risk assessment.

Results

88 articles were reviewed. 17 of them were based on the electronic database PubMed, 28 on Google Scholar and 20 on Embase. There were also 3 dissertations that are freely available. After selection based on the exclusion criteria, the total number of publications has become 30. In observed studies was analyzed the influence of diabetes mellitus, especially type 1, on the quality characteristics of bone tissue and the success of dental implantation.

The discussed studies also described methods that are presumably capable to improve implant osseointegration rates in patients with T1DM:

1. According to the results of this laboratory study, it was found that the use of diabetic serum (obtained by taking a whole blood sample, which then was subjected to centrifugation) predisposes to less favorable conditions for osteoblast adhesion. It was noted that titanium disks treated with diabetic serum before surgery have a smaller number of osteoblasts on their surface than the normoglycemic control group. The surface depleted by osteoblasts can lead to a delay in the process of implant osteiontergation.
2. Ophiopogonin D, a natural substance isolated from Radix O. Japonicas, is able to exert a stimulating effect on the reactivation of the Wnt/ β-catenin signaling pathway, which contributes to improving the biological functions of osteoblasts, including adhesion, proliferation and differentiation. The use of this substance, as a result of a laboratory experiment, led to an improvement in the osseointegration of a titanium alloy implant in diabetic rabbits. Activation of antioxidant protection occurs, which prevents the manifestations of oxidative stress under the action of reactive oxygen species at the bone-implant border in diabetic conditions.
3. During this study, the authors evaluated the effect of low - frequency vibration on bone tissue and the quality of titanium implants

osseointegration in T1DM-induced rabbits. In the DM group, there was a clear deterioration of bone microstructure compared to the control "healthy" group, whereas vibration stimulation (WBV - whole-body vibration) served as an activator of trabecular bone growth in diabetic rabbits. In addition, the WBV group also demonstrated an obvious prevention of cortical bone thickness reduction. [35]

Discussion

Diabetes mellitus is an adverse factor in wound healing after surgery. Previously, dental implantation was contraindicated in diabetic patients due to the presence of an increased risk of complications, such as impaired osseointegration and stabilization of the implant, peri-implantitis. Currently, DM is not an absolute contraindication to implantation, especially in the presence of constant glycemic control.[12]

According to the literature, the average survival rate of implants in diabetes patients is in the range from 85% to 97%[4,15,23,31]. Some authors during clinical researches noted that there was not any statistically significant difference in the frequency of implant failure in diabetic persons and non-diabetic ones.[14-17,40,45,48] At the same time, there is evidence of reduced survival rates of implants in patients with insufficient metabolic control compared with the control group.[17,21,44]

During the analysis of the literature in electronic databases on inclusion signs, there was a marked predominance of publications describing the association of type 2 diabetes mellitus with dental implantation compared with T1DM. It can be because of the greater prevalence of insulin-dependent type of diabetes among populations.

Due to somatic pathology in the form of diabetes mellitus, patients are at a greater risk of premature tooth loss because of the periodontal diseases development, microangiopathies and infections, which dictates the interest in dental implantation procedures. To determine the effect of type 1 diabetes on the success of implantation it is necessary to analyze changes in bone tissue occurring in hyperglycemic conditions and the quality of osseointegration.

Changes in bone tissue.

Type 1 diabetes mellitus causes a disturbance of bone mineral density, inter alia in the jawbones. Studies, in which the effect of experimental streptozocin-induced T1DM in mice on bone metabolism described, have shown a direct effect of this condition on osteoblasts. Noted a significant decrease in the number of osteoblasts and their functional activity, accompanied by a disorder of osteoid formation and bone matrix mineralization, presumably due to oxidative stress caused by increased reactive oxygen species (ROS) formation, increased apoptotic cell death and impaired expression of transcription factors.[7,18,19,41] Also, authors identified an increased number of osteoclasts.[50]

In experimental DM neoosteogenesis can be achieved by applying guided bone regeneration (GBR). However, the presence of a decompensated form of diabetes is associated with a higher incidence of infectious complications and less predictable treatment outcome.[20]

In type 1 diabetes mellitus, lower values of MCW – mandibular cortical width index in the area of the mental foramen (2.06 ± 0.57) and PMI – panoramic mandibular index (0.28 ± 0.07) were observed compared to the control group, while no statistically significant difference between T2DM and T1DM was found. [5] There is also a decrease in the mineral density of trabecular and mixed bone tissue.[4,6,8,11,29,35].

Consequently, the more porous newly formed bone is not able to support the implant properly, which can lead to its failure in patients with hyperglycemia mediated by diabetes mellitus.[29,30]

Disorder of bone mineral density, to one degree or another, is the result of a deficiency of insulin-like growth factor-1, the production of which is significantly reduced in type 1 diabetes mellitus. IGF-1 is one of the main anabolic regulators of bone growth and metabolism. A decrease in the level of this substance in patients with insufficient glucose control may contribute to complications from the bone structure. In the course of a clinical study, the following was found: patients with T1DM had significantly lower concentrations of insulin-like growth factor-1 compared to the control "healthy" group. Also, the authors noted an increase in serum levels of IL-6 and IL-8, which suggested that oxidative stress, glycation-end products and perverted fat metabolism substances are able to activate certain kinases, which leads to greater

production of pro-inflammatory cytokines. Inflammatory cytokines and reduced IGF-1 concentrations seem to play a role in the morphogenesis of microvascular and bone complications in type 1 diabetes, especially with insufficient glycemic control.[51]

In comparison to T2DM, type 1 has a weakened expression of type I collagen and altered concentrations of bone metabolism markers, such as osteocalcin and RANKL. [2, 18] The results of one study showed that when zinc sulfate was injected (0.25 mg/kg/day) to mice with streptozocin-induced DM, some positive effects on the metabolism and bone tissue of animals were observed. The level of trabecular bone mineral density increased, the level of blood glucose and serum RANKL decreased. Meanwhile, a normal number of adipocytes of bone substrate was detected during the evaluation of histomorphological parameters, which indicates a significant inhibition of excessive lipogenesis in DM.[41]

Osseointegration of the implant.

As noted earlier in the text, type 1 diabetes mellitus leads to disorders of bone formation early stages [30], to decreased parameters of bone matrix mineralization, and, apparently, delayed wound healing, which can lead to an impairment of the osseointegration of implants.

The authors noted that such molecules as fibronectin and integrin α5β1 take part in the adhesion of osteoblasts to the implant surface. The action of fibronectin as an osteoclast antagonist is also described, which mediates the prevention of premature bone resorption. Uncontrolled diabetes, in some degree, inhibits osseointegration by delaying the expression of fibronectin and integrin α5β1. [25, 37] It is important to note the fact, that in the presence of uncontrolled type 1 diabetes there is a disorder of osteoconduction due to changes in the adhesive properties of the fibrin matrix and platelet dysfunction, deficiency of PDFG (platelet-derived growth factor) and TGF-β (transforming growth factor beta).[10]

In the study of streptozocin-induced T1DM in mice, there was a disorder of angiogenesis, manifested by a decreased numbers of small blood vessels and expression of platelet/endotheliocyte adhesion molecules (CD31, PECAM-1), NGF (nerve growth factor), VEGF (vascular endothelial growth factor)[18].

These processes can adversely affect the trophism of newly formed tissue, which can negatively reflect the quality of osteointergation. Impairment of angiogenesis in newly formed bone tissue is experimentally eliminated by the injection of calcitonin gene-related peptide (CGRP).[49]

Presumably, the procedure of using osteoinductive mesenchymal stem cells (BMMSCs) can positively affect the degree of implants osseointegration in patients with uncontrolled diabetes mellitus. There was a significant improvement in implant engraftment in rabbits with T1DM subjected to this procedure, compared with a healthy control group and diabetic animals that were not treated with mesenchymal cells.[24]

Summarizing the data of the studied studies, it can be stated that the phenomena of hyperglycemia mediated by uncontrolled type 1 diabetes mellitus adversely affect the differentiation, proliferation and functional activity of osteoproducing cells, which negatively react the processe of bone formation and implant integration. Also, the risk of peri-implantitis should not be excluded.[26,28,37,46]

An important factor for evaluating long-term implantation results is the stability of the intraosseous part of the structure. According to research data, there was no statistically significant difference in the implant stabilization levels in diabetes patients with HbA1c < 7% and control group after 3 months from the date of surgery. Meanwhile, if the patient is not sufficiently motivated to maintain proper blood glucose levels, a deterioration in the implant stabilization indicators, especially in the first year after its installation occurs.[52,53]

The success of dental implantation in diabetes mellitus, including type 1, largely depends on glycemic control. In the presence of a well-controlled metabolic profile of patients, the outcomes of partly/full adentia surgical treatment often have a positive prediction. Moreover, as noted earlier, there was no statistically significant difference between implant failure in diabetic patients with good glycemic control and healthy people.

It is necessary to achieve the following target values: HbA1c < 7%, a fasting plasma glucose of 80-110 mg/dL, maximum post-prandial level of glycaemia < 180 mg/dL to prevent the negative impact of diabetes mellitus

on the postoperative rehabilitation period.[4,29] It is worth to say, that the procedure of dental implantation in patients with insufficient glycemic control should be delayed until the target values of HbA1c and plasma glucose are reached, if it is possible.

Based on the above information, it is important to analyze the impact of carbohydrate metabolism on implant survival. A clinical research study reviewed, in which authors produced the separation of patients into 2 groups. The implant was installed to each participant: 1 – the group of patients with diagnosed prediabetes (HbA1c ≥5.7% to 6.4%, and the level of a fasting plasma glucose ≥126 mg/dL)[37], 2 – control "healthy group". The researchers noted that were observed no statistically significant differences in marginal bone loss between the groups (in groups 1 and 2 the indicators were 0.2 ± 0.1 mm and 0.1 ± 0.01 mm, respectively) after 1 year of monitoring. Therefore, it can be assumed that the prediabetic condition is not a direct factor for reducing the success of dental implantation.[38]

It is particularly important for the doctor to obtain a complete and accurate medical history of the patient. Detailed information about the patient's condition (duration of diabetes, medications used to control glucose levels) obtained during the initial examination should be regularly supplemented with relevant data, including the current glycemic status. Also, you should pay attention to concomitant diseases, in addition to diabetes mellitus, that can affect the results of dental implantation (cardiovascular diseases, blood diseases) and bad habits (smoking).[37]

It is up to the dentist surgeon to choose the optimal implantation systems, surgical techniques, perioperative and further management of the patient. It is desirable to minimize functional mechanical loads, especially during the first year after implantation (there is a 4%failure risk during the period of osseointegration, 3% during the first year of loading).[31,32]

Since hyperglycemia can be the result of stress, diabetic patients may be further advised to take insulin prior to surgery to prevent a stress-induced spike in glucose blood concentration.

In addition, to avoid unexpected hypoglycaemia during surgery and postoperative infections, it is recommended to maintain glucose blood levels below 150 mg/dL in the preoperative period. It is important to provide appropriate emergency care, differentiating hypoglycemic and hyperglycemic symptoms from other clinical signs, to prevent systemic complications.[39]

To prevent the development of infectious complications mediated by a reduced immune response and impaired phagocytosis in patients with T1DM, it is proposed to use broad-spectrum antibiotics. The drug of choice is amoxicillin + clavulanic acid (inhibitor - protected aminopenicillin), because it acts on streptococci, staphylococci, Gr+ and Gr - microorganisms, which are the most frequent pathogens of the infectious process after the implant installation. In addition to the use of antibiotics, oral rinses using disinfecting solutions, such as a 0.12% chlorhexidine, are indicated.[4,36]

The use of less invasive surgical approaches for implant placement, which contribute to a shorter healing period, minimal edema, and pain syndrome, is the method of choice for diabetic patients. Attention is focused on the use of a flapless implant surgery method, which has some advantages over the standard method: achieving shorter healing times for soft tissues, some prevention of marginal bone tissue resorption, minimal interference to the local blood supply systems of the bone.[37,54]

Based on the studied data, guided bone regeneration and sinus lift (SFE) can be considered fairly safe procedures for patients with controlled diabetes mellitus in the presence of alveolar bone loss.[52]

The use of implants with a surface treated with hydroxyapatite, SLA (sandblasting and acid etching) and modified SLAs can positively affect the quality of osseointegration and survival of implants. In presented study, researchers evaluated the degree of implant osteointergation with an experimental SLA-modified surface-SLActive (conditioning of a standard SLA surface of titanium implant in a nitrogen atmosphere and its further content in an isotonic NaCl solution). Presumably, this technique creates optimal conditions for the adhesion of osteoblasts and blood cells to the surface of the implant. There were significant results regarding an increase in the level of BIC (osseointegration index) after 90 days from the date of surgery in diabetic rats using SLActive implants, compared with standard SLA.[53] Nanostructured modification of the hydroxyapatite surface on titanium implants is

also able to prevent the disorder of the osteointergation process in patients with controlled diabetes mellitus due to the potential increase in angio - and osteogenesis.

It is worth to note in needs to teach patients with diabetes the correct method of brushing their teeth to prevent the formation of soft and hard dental deposits[57]. Plaque and tartar are the place of microorganism accumulation that mediate the possible occurrence of periimplantitis and inflammation of the mucous membrane. It is necessary to choose the optimal method of teeth brushing and personal hygiene products, which will lead to the most effective removal of plaque and microorganisms in the process of use.

Summarizing the information considered, it is worth to say the fact that optimal peri - and postoperative management and monitoring of the patient's condition is necessary, since there may be a picture of diabetes mellitus decompensation, impaired implant survival and wound healing associated with emotional stress of the person, type of anesthesia, the operation itself and insufficient glycemic control. Higher glucose levels in the perioperative period lead to a higher risk of complications. If there are data on HbA1c levels below 7%, but above 6.2%, the use of preoperative and postoperative antibiotics (amoxicillin, penicillin, clindamycin, ampicillin/sulbactam) is necessary considered due to an increased opportunity of infectious complications.[36]

We could not exclude from the discussion the possibility of drugs use, including medication for local anesthesia, in influence on carbohydrate metabolism. Thus, the use of barbiturates, inhaled anesthetics and strong vasoconstrictors leads to a disorder of the metabolic pathways normal functioning. Acceptable from the point of view of influence on carbohydrate metabolism are the following drugs used for anesthesia: nitrous oxide, sodium oxybutyrate, narcotic analgesics, droperidol. The use of felipressin as a vasoconstrictor for local anesthesia is more appropriate to avoid the occurrence of hypertension and hyperglycemia due to external effects of epinephrine. In addition, given the fact, that one of the diabetes mellitus targets is the cardiovascular system, circulatory disorders in patients can affect the vessels of the periodont, as a result of its blood vessels excessive narrowing under the influence of adrenaline can adversely affect the healing of soft tissues.[36]

A required condition during the intervention is cardiorespiratory and glycemic monitoring of the patient to control the general somatic state to prevent acute disorders of hemodynamics and glucose levels in the direction of increasing / decreasing plasma concentration. In the presence of intraoperative hyperglycemia symptoms (blood glucose above 200 mg/dL), the authors noted the success of using an electrolyte solution containing rapid-acting insulin.[36]

Stated, that it is preferable to perform surgical manipulations in diabetic patients in the morning, if possible, with a reduction in the time and invasiveness of the operation. The intervention is performed after a meal on the background of insulin therapy. In that case, if the meal is skipped, an intravenous infusion of 5% glucose solution is carried out to prevent hypoglycemia.[36]

Conclusions

Decompensated type 1 diabetes is a systemic disease, possible complication of which is a disorder of bone tissue structure, which can negatively affect the result of implant treatment. In turn, glycemic control, specific preoperative and postoperative antibacterial therapy, optimal choice of surgery intervention methods allows us to achieve a good osseointegration and stabilization of the implant, which is important for reaching success in dental implant treatment.

Declaration of Interest

The authors report no conflict of interest.

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