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ORIGINAL STUDY

OSTEOINTEGRATION OF DENTAL IMPLANTS A CHANCE FOR DIABETIC PATIENTS - SYSTEMATIC REVIEW OF THE LITERATURE -

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ABSTRACT

In the mouth, diabetes is responsible for delayed wound healing, increased alveolar bone resorption, a risk of up to 3.4 higher than non-diabetics to develop periodontal disease, an increase in inflammatory tissue destruction and predisposition to infection. For all these reasons, diabetes was considered a contraindication to insertion of dental implants. However, there are experimental studies and clinical observations showing that the survival rate of dental implants is approximately 90%, approaching that of non-diabetic patients. It is also shown that these results are strictly correlated with the importance of glycemic control to provide predictability of success rates and improve osseointegration of the implants inserted

The aim of this study was to synthesize the literature reviews on the osseointegration of implants in diabetic patients, to evaluate the available clinical results on complications such as wound healing, the peri-implantites, prognosis and survival of implants, and in conjunction with our clinical observations, to formulate recommendations for clinical use of implants in diabetes.

KEYWORDS*: diabetes, alveolar bone resorption, dental implants.*

1. Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia with impaired glucose metabolism as the main symptom. Hyperglycemia can result from a deficiency in insulin secretion, insulin resistance, or a combination of both.

The most common pathogenic types of diabetes are : insulin-dependent diabetes mellitus type 1 and non-insulin dependent type 2. According to current epidemiological studies (U.S.) approx. 5% of the population is affected by diabetes. Of these, most patients are type 2 diabetics (> 90%) and about 5% are type 1 diabetics. Balsham et al in 1999 and Powers in 2005 stated that among patients aged over 65 years, approximately 18.4% and 20.1% had various forms of diabetes.

Fiorellini et al in 2000 stated that diabetes affects bone and mineral metabolism, damaging osseointegration of dental implants.

In several experimental studies on diabetic patients to whom dental implants were inserted, the glycemic control was provided to offer predictability

to success rates and improve osseointegration of the inserted implants. Many of these studies included patients that were "well-controlled" glycemically , but few offer detailed information about the normal level of blood glucose and glycosylated hemoglobin (HbA1c), where implants can be inserted.

2. Material and Methods

The bibliographical study and documentation until May 2010 using the Medline database provided the opportunity to select publications (specialty items) refrerred to and evaluated according to the following objectives:

Studies on the osseointegration of dental implants in diabetes mellitus:

-in vitro and experimental studies on animals;

-clinical studies on humans

Studies on complications and prognosis of dental implants in diabetics:

-experimental studies (in vitro, animal model)

-clinical trials (the real clinical cases)

Overall studies and analyses

Using the EbM level from the "Oxford Centre for Evidence-based Medicine" attempts were made to check publications on clinical outcomes through the systematic evidence. After electronic evaluation a number of 61 publications was found. Of these, 10 articles have presented no relevant data to the purpose of the study and were excluded from the final analysis, 14 publications show comments or heterogeneous reviews and will be approached under results section; a study has provided clarification on certain aspects of the implantology treatment in diabetic patients, which is why it was also excluded. Finally there were considered relevant to the study 36 publications.

3. Results

They identified 17 studies in order to assess the influence of metabolic status in diabetics for healing and osseointegration of titanium implants. In 15 studies animals were used for experiments, , such as rats, and in the remaining two studies, rabbits. Of these 4 studies demonstrated that experimentally induced diabetes significantly reduce contact between bone and implant [1-11].

Experimental Studies

Comparing the effects of diabetes on osseointegration of implants, Nevins et al in 1998 [9] showed that in terms of histometry, the amount of bone formation in diabetic rats compared to non-diabetics is unchanged, but the contact between bone and implant was reduced in diabetic rats compared with control group both at 28 and 56 days.

Fiorellini et al's study from 1999 shows that insulin therapy is able to regulate bone formation around the implant; however the contact between bone and implant is significantly lower in the group of diabetic rats kept under glycemic control with insulin compared with non-diabetic rats control group [3].

McCracken et al in 2000, concludes that diabetic rats exhibited a lower implant osseointegration compared to the control group, especially in the trabecular bone, or spongy bone; however bone volume in diabetic rats was 4 times higher compared to the control group. The study demonstrates that although diabetic animals shows a slightly reduced healing, there is still sufficient osseointegration,provided that a good initial contact between bone and implant is established [11].

The influence of insulin in the healing of osseointegration and bone remodeling was assessed by Siqueira et al and later by Margonar et al in 2003. Siqueira demonstrated that uncontrolled diabetes induced experimentally in rats resulted in a reduction of approximately 50% of the surface contact and bone density around the implant. Insulin administration and proper consecutive adjustment of diabetic metabolism status cancel out these effects, so no significant

differences were found compared with healthy rats.

Regarding the insertion of implants immediately after tooth extraction in patients with diabetes, Styng et al in 2006 demonstrated in an experimental study on rats that diabetic animals shows bone mineralization (initially significantly reduced), osseointegration and bone mineralization normalizing after approx. 20-40 days. Based on these observations, the authors are against immediate implant on diabetic patients.

Clinical studies

Among the studies reviewed, only 4 studies evaluated osseointegration of dental implants in diabetic patients. Three of these are articles such as case reports with a Level 4 EBM. Information provided may be summarized as follows:

Bugea et al, in 2008 extracted a prosthetic implant due after 2 months which they analyzed histomorfologicaly. Implant did not show any signs of failure and histomorphometric evaluation demonstrated a bone to implant contact of 80%. The authors concluded that osseointegration can be achieved if use is made of acidly double-etched surface implants in diabetic patients carefully selected [4].

Balshi et al, in 2007 published a study evaluating 18 immediately loaded implants inserted in a diabetic patient using resonance frequency analysis; all 18 implants were osseointegrated and were in operation throughout the study (2.5 years); implant stability decreased by approximately 13% in the first 30 days, then it started to grow, even at 30 months, mean implant stability continued to grow, without reaching the initial values established since the insertion of implants [1,2].

Oates et al, in 2009 in a clinical trial that assessed the stability of implants using resonance frequency analysis on 10 non-diabetic patients (N = 12 implants) and 20 diabetic patients (N = 30 implants) have concluded the following: changes in implant stability for group with high HbA1c (≥ 8.1%) were significantly different from that of the group with low levels of HbA1c (≤ 8.0%), this classification shows decreased stability at weeks 2 and 4 of the insertion of implants and a much increased cure for high HbA1c group, which may suggest alterations in the biological integration of implants directly related to glycemic control. The differences in stability between the two groups from 6th week to the 12th week were not significant. For low HbA1c group, there were no decreases in the stability of the implant insertion , but there were significant increases in stability at 12 and 16 months post-insertion [5].

In general, survival rates of implants inserted in diabetic patients were over 90%.

Maximo et al, in 2008 assessed the correlation between peri-implant and diabetes mellitus in 113 patients with 347 implants inserted; for good glycemic control patients, there were no significant correlations between peri-implant soft tissue condition and diabetes, but there were significant correlations between peri-implant soft tissue condition and diabetes mellitus but positive statistically significant correlations are reported for implants with mucositis and periimplantite, in relation to the time of implant loading. The authors concluded that this may be associated with increased time loading and generalized periodontal bone loss [6].

Since 2006, Ferreira et al reported increased frequency of peri-implantite (24%) in diabetic patients in comparsison with the healthy patient control group (7%);

Also the presence of periodontal disease and diabetes were statistically associated with an increased risk of peri-implantite.

Systematic evaluation of the results of clinical and experimental studies demonstrate that there is no meta-analytic assessment due heterogeneous studies and the absence of randomized controlled trials.

Klokkevold and Han, in 2007 aggregate

survival rates of implants inserted in patients with type II diabetes presented in four studies using the test Forest-Plot, demonstrating that there is a 91.7% survival rate in patients with diabetes compared with 93.2% in healthy patients. They concluded that Type II diabetes can influence implant survival, but this observation must be based on extensive studies and a systematic review [7].

Figure 1. *Clinical case of insulin-dependent Insertion of 6 implants*

Mellado-Valero et al, also in 2007, said that after the evaluation of literature, the survival rates of implants in diabetic patients ranged between 88.8% and 97.3% at one year post-insertion and between 85.6% and 94.6% at one year after functional loading of implants [8].

Figure 2. *Lower right hemi arch, 46-47Prosthetic restorations on implants*

Also, as in other studies reported in the literature, the authors argued that most implant failures occur after phase II of surgery and in the first year of functional loading, which may indicate an impaired microvascular implant active site , this damage leading to a diminished immune response and a reduction in bone remodeling.

Figure 3. *Higher left hemi arch, 25 – 27 Prosthetic restorations on implants*

Figure 4. *Clinical case after 5 years with a very good evolution, with a balanced occlusion*

4. Discussions

From the above, it follows that the average survival rate of implants inserted in diabetic patients is over 90%, most failures occur in the first years of insertion, incorrectly controlled hyperglycemia and

diabetes have negative influence on osseointegration and stability of implants, as well as for healing of wounds and soft tissue around implants.

Pathogenic mechanisms in diabetes are represented by changes in the synthesis of proteins, lipids, extracellular matrix, collagen structure of the bone, bone cells (osteoclasts activation, inhibition of osteoblasts) and inhibition of wound healing and immune defence.

A number of studies have demonstrated reduced contact area between bone and implant in case of hyperglycemia. Goodman et al showed that osteopenia in animals receiving induced diabetic condition can be reversed by insulin; ultra-structural characteristics of the bone-implant interface in diabetic animals may become similar to those in the control group (non-diabetic) following the administration of insulin (Siqueira et al) [1,2]. However Fiorellini et al in 1999 concluded that although the administration of insulin can regulate bone formation around the implant, and the total volume of bone formation is greater in the animals treated with insulin, there is still a bone- to- implant contact significantly reduced compared with non-diabetic animals [3].

As presented, in uncontrolled diabetes, bone quality measured by the degree of mineralization was significantly reduced. These negative effects of hyperglycemia were more strongly present in spongy bone than cortical regions. However, despite the compromised bone metabolism, it was demonstrated a sufficient osseointegration and healing of wounds, so that a diabetic mellitus can no longet be considered an absolute contraindication to insertion of implants. Moreover, these significant adverse effects were observed only in case of hyperglycemia with very high values.

All observations synthesized following this laborious study are very valuable, but mention must be made and we should also consider its limitations, given the fact that most of them are made on small laboratory animals; it remains debatable whether the tests are transferable from animal to clinical situation of the people. Also most of these studies fail to describe how it was investigated and assessed glucose and especially what are the criteria of a well-controlled status. There are only two studies (Dowell et al and Olson et al), who reported an objective assessment of glycemic control by glycated hemoglobin in diabetic patients.

On the other hand, in the studies published by Beikler & Flemming, Hwang & Wang, Ktsovilis et al, Melado-Valero et al and Javed & Romanos there is consensus on the recommendations of preoperative, perioperative and postoperative procedures, as follows:
-performing adequate control of the glucose metabolism and providing suffiecient anti-diabetes therapy by by GP or diabetologist [5,6,11];
- medium and long term control parameter is the value of glycosylated hemoglobin (HbA1c), it should be at approximately 7% or within 6-8%;
- short-term control parameter is the blood glucose value, the target value is a jeun glucose less than 130mg/dl and post-prandial blood glucose less than 180mg/dl;

Mandatory prophylactic broad spectrum antibiotics (eg, amoxicillin, amoxicillin + clavulanic acid generation cephalosporins II and III - Cefaclor, Cefuroxime, Clindamycin), some authors argue administering the day before surgery Others say that surgery is sufficient administration one hour before surgery;

Upon implant insertion the patient must have normoglycemia. Before surgery, the patient should rinse his mouth with a solution of 0.12% chlorhexidine gluconate (eg Corsodyl), Morris et al found that the rate of infectious complications in type 2 diabetic patients is reduced from 13.5% to 4.4 %;

Continue rinsing with chlorhexidine mouthwash until the end of primary wound healing for about 5-7 days;

Continued antibiotic treatment until the fifth, seventh or tenth postoperative day;

Integration of a patient into a dispensary strict program with regular professional sanitation of teeth and implants to prevent periimplant infections.

In conclusion, the results observed in clinical studies regarding insertion of implants in diabetic patients can be summarized as follows:

- survival rate of dental implants is approximately 90%, approaching that of non-diabetic patients;
- the basic criterion of diabetes is properly controlled by HbA1c of 7% or in the range 6-8%,higher values of HbA1c (> 8%) may lead to changes in implant stability;

5. Conclusions

Improperly controlled diabetes leads to significant reduction of contact between bone and implant; insulin therapy is able to regulate bone formation around the implant;

The critical period for implant loss is the first 12 months since the implant, particularly the discovery and initial loading stage;

Use of mouth disinfectant solutions in pre-operative and postoperative stages decreases the inflammatory complications rate during wound healing and even improves survival in the first few weeks; -pre and post-operative antibiotic therapy is a protective factor against the primary disorders of wound healing; in the treatment of diabetic patients with implants it should be considered possible aggravating factors associated with age, sex, tobacco, periodontal disease, and influence of dispensary program of patients;

Increased frequency of periimplantites in diabetic patients compared to non-diabetics;

Correct adjustment of diabetes before, during and after surgery by the patient's doctor, so that HbA1c be <7% and a jeun blood glucose <120 mg / dl; Antibiotic therapy should be initiated one hour before surgery and continued until the completion of the healing process; mouthwash before and after surgery with an oral solution of 0.12% chlorhexidine gluconate; Patient strict dispensary and professional cleaning for diagnosing of periimplant infections.

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