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Peri-implant evaluation in type 2 diabetes mellitus patients: a 3-year study

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Abstract

Objective: The aim of this study was to analyze the changes produced in peri-implant tissues in type 2 diabetes mellitus patients with different glycemia levels, measured by monitoring glycated hemoglobin A1c (HbA1c), over a period of 3 years following dental implant placement.

Materials and methods: Sixty-seven patients were divided into four groups according to their HbA1c levels: 21 patients in Group 1 (<6); 24 patients in Group 2 (6.1–8); and 11 patients in Group 3 (8.1–10) and Group 4 (>10.1). Each patient received one implant. All implants were placed in the anterior zone of the maxilla. The variables selected to assess the general state of patients' peri-implant health were as follows: probing depth, bleeding on probing, and marginal bone loss.

Results: Marginal bone loss was found to increase in relation to increases in HbA1c levels. Bleeding on probing showed statistically significant differences between groups. When the peri-implant area was probed, mean levels of bleeding varied from 0.43 in Group 1 at 1 year after implant surgery to 0.62 in Group 4 ($P = 0.042$ between the four study groups). After the second year, greater bleeding on probing was observed in Group 4 (0.63) in comparison with groups with lower HbA1c levels. Peri-implant pocket depths presented values that were too low to be considered pathological and without statistically significant differences between the study groups.

Conclusion: Implant therapies for diabetic patients can be predictable, providing these patients fall within controlled ranges of glycemia over time, assessed by monitoring HbA1c levels.

Diabetes mellitus is defined as a "group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both" (Puavilai et al. 1997; Retzepi & Donos 2010). It is one of the main causes of morbidity and mortality in contemporary society and has become an alarming public health problem. A decade ago, diabetes affected approximately 140 million individuals, over 220 million in 2010, and it is estimated that it will affect over 300 million by 2025 (Zimmet et al. 2003; Mella-Valero et al. 2007).

Type 2 diabetes mellitus is a condition characterized by impaired insulin function, that is, resistance to insulin action, combined with inadequate compensatory insulin secretion response. Glycated hemoglobin A1c (HbA1c), the major form of stable glycated hemoglobin, is the product of a slow and

largely irreversible reaction that occurs throughout the life span of the erythrocyte. Since the 1970s, it has been understood that HbA1c reflects mean blood glucose (BG) levels over the previous 2–3 months and has been proposed as a diagnostic criterion for diabetes. HbA1c monitoring has therefore become an accepted means of assessing glycemia and a standard part of diabetes management (Koenig et al. 1976; Bunn et al. 1978; Davidson et al. 2000; American Diabetes Association 2003; Derr et al. 2003).

Because of its characteristics, this disease demands special attention in dental treatment, particularly when dental implants are to be inserted. Diabetics are more susceptible to periodontal disease than non-diabetic patients because these patients have vascular complications associated with the disease. (Takeda et al. 2006; Javed et al. 2007;

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Offenbacher et al. 2008]. The underlying physiopathology that increases the risk of periodontal disease in subjects with diabetes remains largely unknown, but it has been associated with different metabolites produced by an excess of glucose in the blood. These final products reduce the production, by gingival and periodontal fibroblasts, of matrix proteins such as collagen and osteocalcin (Yamamoto et al. 2001; Javed & Romanos 2009).

The aim of this study was to analyze the changes produced in peri-implant tissues in type 2 diabetes mellitus patients with different glycemia levels, measured by monitoring HbA1c, over a period of 3 years following dental implant placement.

Material and methods

Ethical guidelines

This study was performed following guidelines established by the Declaration of Helsinki as revised in 2002 for experimentation involving human subjects. Possible side effects of surgical therapy were handled according to the current standards in private practice.

Patients

Research subjects were recruited among patients referred to the Department of General Dentistry and Master Degree in Implant Dentistry at the Faculty of Medicine and Dentistry (University of Murcia, Spain) and Master of Periodontology and Implant Dentistry at the Faculty of Dentistry (University of Granada, Spain) during a 48-month period. The study analyzed a total of 67 subjects. Only patients treated with one-piece implants were included, so that variations in prosthetic design would not alter crestal bone resorption values or the state of the peri-implant soft tissues. Diagnosed or suspected type 2 diabetes mellitus patients receiving dental implant treatments supplied the relevant analyses, which were used to divide

patients into four groups according to HbA1c levels: Group 1 (control group without diabetes), values lower than 6; Group 2, HbA1c levels of 6.1–8; Group 3, HbA1c levels of 8.1–10; and Group 4, HbA1c levels higher than 10.1 (Oates et al. 2009; Fig. 1). All patients with type 2 diabetes mellitus remained in the care of the doctor prescribing oral hypoglycemics, and participation in the present study did not interfere with this regime. All participants gave their informed consent before the study commenced. In all cases, implants were inserted at sites that had undergone at least 4 months healing after dental extraction, and the bone dimensions were adequate for implant placement without the need for any type of bone implant.

Inclusion and exclusion criteria

Additional inclusion criteria applied were as follows: sufficient bone height (at least 5 mm of bone height) and width to allow the placement of implants with a minimum diameter of 3.3 mm and a minimum length of 10 mm, and an occlusal pattern that allowed for the stability of teeth adjacent to the implant. All study subjects also needed to have at least 3 mm of soft tissue, to allow for the establishment of an adequate biologic width and to reduce bone resorption. Diabetes was assessed using HbA1c values 2 weeks before implant surgery and repeating the test 3–5 months after implant placement and prior to loading of the implant-supported prosthetic restoration, after 1 year and 3 years following surgery.

Exclusion criteria established at the start of the study were as follows: severe maxillo-mandibular skeletal discrepancies, hemophilia, metabolic bone disorders, a history of renal failure, radiation treatment to the head or neck region, current chemotherapy, pregnancy, drug or alcohol abuse, poor oral hygiene, insufficient bone volume at the recipient site, and the need for bone-augmentation procedures during surgery, a history of

bone implants at or near to the implant site and smokers. Any patients with a history of microvascular or macrovascular complications arising from diabetes were also excluded, as well as those who failed to attend one or more of the checkup appointments established in advance.

Surgical protocol

All implants were placed at the bone crest level. The implant bed was prepared following the manufacturer's instruction for the placement of Straumann bone level implant (Straumann AG, Basel, Switzerland), 10–14 mm long and 3.3–4.1 mm in diameter. All implants were placed with a submerged protocol and topped with a closure screw to avoid loading during the healing process. After implant insertion, radiographs were taken at the moment of prosthetic placement following standardized parameters to compare crestal bone levels at later study times. Each patient received one implant. All implants were placed in the anterior zone of the maxilla.

Postoperative care

After implant placement and suturing, each patient received amoxicillin 875 mg and clavulanic acid 125 mg to be taken twice daily for 7 days, 600 mg of ibuprofen to be taken as needed, and 0.12% chlorhexidine mouthwash (Perio-Aid; Dentaid, Barcelona, Spain) to be used twice daily for 2 weeks. Patients were also asked to brush gently with chlorhexidine toothpaste. Sutures were removed 8–10 days after surgery. All surgery was performed under local anesthesia, following the manufacturers' protocol. Sulcus incisions were made at the buccal and lingual part of the teeth.

Clinical parameters

The variables measured were selected to assess the general state of patients' peri-implant health and the two periodontal pathologies established by the Consensus of the Seventh European Workshop on Periodontology in 2011: peri-implant mucositis and peri-implantitis (Lang & Berglundh 2011). Each checkup ensured that patients were maintaining adequate hygiene levels for oral biofilm control. As established by the VII European Workshop on Periodontology for routine implant monitoring, probing was performed to evaluate both the state of the peri-implant mucosa and probing depth. Bleeding on probing around the implant was evaluated and by so doing, the presence or absence of peri-implant mucositis. In cases of a probing depth greater than 6 mm, a radiograph was

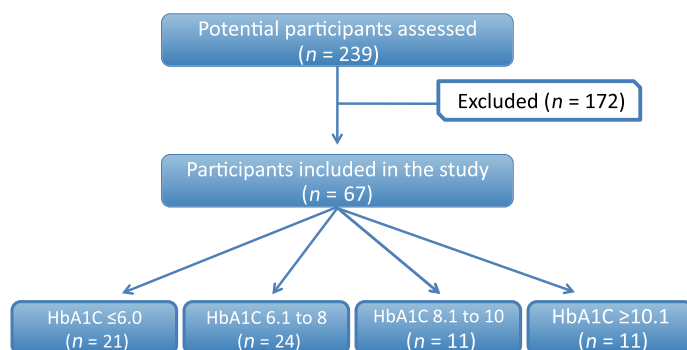


Fig. 1. Flow chart describing the derivation of the study sample.

taken to evaluate bone loss and so the severity of peri-implantitis (Lindhe & Meyle 2008; Lang & Berglundh 2011). In this way, the parameters analyzed were as follows: (i) probing depth (PD); periodontal pocket depth was measured to the nearest millimeter with a plastic periodontal probe, and a mean probing depth value was calculated for each implant; (ii) bleeding on probing (BOP); this was measured at six points per implant (three on the vestibular aspect and three on the palatine/lingual aspect); the measurement was calculated as the number of points where bleeding occurred out of the total number of points probed (Tatarakis et al. 2013); and (iii) marginal bone loss (MBL); periapical radiographs were taken immediately after implant placement, and after 1, 2, and 3 years at sites where bleeding on probing had been observed. Standardized radiographs were taken using an individualized X-ray film holder device with the film placed parallel to the implant axis and the X-ray beam directed perpendicular to the implant. The radiographs were digitized as JPEG files and imported to Image J 1.43 open source software (National Institute of Health, Bethesda, MD, USA). MBL was assessed on the mesial and distal aspects of each implant by measuring the distance between the implant shoulder and first point of bone-to-implant contact. The known distance between implant threads was used for image calibration.

Statistical analysis

Data analysis was performed by the SPSS 20.0 software (New York, NY, USA). Probing depth, bleeding on probing, and marginal bone loss were analyzed to identify any associations with HbA1c levels and the time following implant placement (baseline, 1, 2 and 3 years). Between-group comparison of means was verified with Kruskal–Wallis test. Statistical significance was established as $P < 0.05$.

Results

The 67 patients who took part in the study were divided into four groups according to

their HbA1c levels (Table 1). Average age did not show statistically significant differences between groups, mean age ranging between 59 and 64 years. With regard to gender distribution, Groups 1 and 2 showed a slight prevalence of women, while Groups 3 and 4 included slightly more men than women. Results for the three variables analyzed (probing depth, bleeding on probing, and marginal bone loss) are shown in Table 2. It should be noted that marginal bone loss was found to increase in relation to increases in HbA1c levels. In this way, control group levels varied from 0.41 mm after the first year, reaching 0.53 mm ($P = 0.074$) after 3 years, while in Group 4 (consistently the highest levels of blood sugar), crestal bone loss values went from 0.54 mm after 1 year to 0.70 mm ($P = 0.073$) at the end of the 3-year study (Table 2). Only bleeding on probing showed statistically significant differences between groups (Table 2). When the peri-implant area was probed, mean levels of bleeding varied from 0.43 in Group 1 at 1 year after implant surgery to 0.62 in Group 4 ($P = 0.042$ between the four study groups). After the second year, greater bleeding on probing was observed in Group 4 (0.63) in comparison with groups with lower HbA1c levels, a relation that was repeated at the 3-year follow-up. Lastly, peri-implant pocket depths presented values that were too low to be considered pathological and without statistically significant differences between the study groups. After 1 year following implant surgery, mean probe depth ranged from 2.19 mm in Group 1 to 2.33 mm ($P = 0.072$) in Group 4, values that rose only slightly during the subsequent study periods (Table 2).

Discussion

Dental implant therapy has been shown to be safe and has a high success rate, although there are certain conditions that can affect the predictability of outcomes; one of these is when a patient who is to receive implants is diabetic due to the

particular characteristics of the disease in the osseointegration process. (Kotsovilis et al. 2006; Mombelli & Cionca 2006; Alsaadi et al. 2007). Some diabetic patients fail to maintain adequate glycemic control, showing mean HbA1c values of between 8.5% and 9% (Kirk et al. 2005).

This study analyzed a number of variables related to peri-implant tissue response in relation to the level of glycemic control assessed by means of HbA1c levels and their evolution over time. The data obtained are concurrent with several earlier studies, which have shown that hyperglycemic conditions lead to alterations to osseous physiology (Funk et al. 2000; Amir et al. 2002; Lu et al. 2003; Oates et al. 2009). Furthermore, other transversal and retrospective studies have also identified disturbances in bone healing associated with hyperglycemia (Loder 1988; White et al. 2003). The present study observed that crestal bone resorption showed a proportional relation to glycemia levels, whereby greater marginal bone loss was seen in Group 4 (with higher HbA1c levels) compared with Group 1 (control group), which showed physiological HbA1c levels. These findings agree with previous studies that have found increased alveolar bone loss among diabetic patients compared with non-diabetic subjects (Taylor et al. 1998; Javed et al. 2007). This can be explained by increased production of proinflammatory cytokines (such as interleukin [IL]-1B and -6 and tumor necrosis factor alpha [TNF- α]) in the serum and gingival crevicular fluid (GCF) due to the accelerated interaction of glycation products in diabetic patients. (Cochran 2008; Graves 2008).

An increase in proinflammatory cytokine expression has been observed in bone tissue, supporting the idea that the bone itself produces an inflammatory response in diabetic patients (Iacopino 2001). It is likely that mechanisms of this type bring about augmented osteoclast formation and loss of bone mass, which would explain the bone alterations found in the present study (Javed & Romanos 2009). However, increased bone resorption was not statistically significant over the three study periods analyzed, a finding that agrees with Tatarakis et al. whose diabetic patients did not show higher rates in the progression of the disease according to evaluation of changes in clinical attachment level (CAL) or mean crestal bone level measured radiographically (Tatarakis et al. 2013).

It should be noted that for patients in the present study, mean peri-implant pocket

Table 1. Number of participants, gender, and age of each group

HbA1c levels	Number of participants	Gender	Age
≤6.0	21	W:12 M: 9	Mean $\pm$ SD: 60 $\pm$ 7.2 Median: 56
6.1–8	24	W:13 M:11	Mean $\pm$ SD: 59 $\pm$ 8.1 Median: 60
8.1–10	11	W:5 M:6	Mean $\pm$ SD: 62 $\pm$ 6.8 Median: 59
≥10.1	11	W:4 M:7	Mean $\pm$ SD: 64 $\pm$ 5.6 Median: 63

Table 2. Values of HbA1c, MBL, BOP, and PD at 1, 2, and 3-year follow-up

HbA1c levels	MBL (mm)			BOP (0/1)			PD (mm)		
	1-year			2-year			3-year		
	1-year	2-year	3-year	1-year	2-year	3-year	1-year	2-year	3-year
≤6.0	0.41 ± 0.18 Mesial: 0.39 ± 0.21 Distal: 0.42 ± 0.22	0.48 ± 0.15 Mesial: 0.47 ± 0.14 Distal: 0.50 ± 0.22	0.53 ± 0.17 Mesial: 0.51 ± 0.21 Distal: 0.54 ± 0.18	0.43 ± 0.05	0.47 ± 0.05	0.45 ± 0.06	2.19 ± 0.22	2.21 ± 0.20	2.26 ± 0.19
6.1–8	0.45 ± 0.15 Mesial: 0.43 ± 0.13 Distal: 0.46 ± 0.20	0.52 ± 0.18 Mesial: 0.51 ± 0.20 Distal: 0.54 ± 0.17	0.57 ± 0.16 Mesial: 0.56 ± 0.13 Distal: 0.59 ± 0.20	0.52 ± 0.06	0.54 ± 0.06	0.56 ± 0.07	2.24 ± 0.20	2.27 ± 0.23	2.30 ± 0.23
8.1–10	0.51 ± 0.16 Mesial: 0.48 ± 0.20 Distal: 0.52 ± 0.17	0.59 ± 0.16 Mesial: 0.58 ± 0.12 Distal: 0.60 ± 0.22	0.64 ± 0.17 Mesial: 0.63 ± 0.21 Distal: 0.66 ± 0.15	0.59 ± 0.07	0.60 ± 0.05	0.62 ± 0.06	2.29 ± 0.18	2.31 ± 0.21	2.34 ± 0.20
≥10.1	0.54 ± 0.12 Mesial: 0.52 ± 0.14 Distal: 0.55 ± 0.13	0.63 ± 0.16 Mesial: 0.62 ± 0.13 Distal: 0.64 ± 0.23	0.70 ± 0.19 Mesial: 0.69 ± 0.12 Distal: 0.71 ± 0.16	0.62 ± 0.06	0.63 ± 0.07	0.72 ± 0.06	2.33 ± 0.28	2.37 ± 0.26	2.40 ± 0.25
Significance	$P = 0.074$	$P = 0.068$	$P = 0.073$	$P = 0.042^*$	$P = 0.043^*$	$P = 0.037^*$	$P = 0.072$	$P = 0.075$	$P = 0.068$

BOP, bleeding on probing; PD, probing depth.

Values are means ± SEM.

MBL, marginal bone loss between baseline and at 1, 2, and 3-year follow-up. Determination of mesial and distal values.

*Significant difference ($P < 0.05$).

depth did not exceed the values that establish pocket depth as pathological. However, bleeding on probing values were the only variable that showed statistically significant differences when the study groups were compared, a difference that was maintained over the three study periods. In this way, the values obtained are compatible with findings by Tawil et al. (2008), who did not find significant differences in peri-implant pocket depth between diabetic and non-diabetic patients over a 12-year follow-up (Tawil et al. 2008). Nevertheless, the importance of periodontal maintenance for tissue stability around implants has been confirmed in a 5-year study that showed that a lack of preventative measures among subjects with pre-existing peri-implant mucositis was associated with a higher incidence of peri-implantitis (Costa et al. 2012). The pioneering element of the present study lies in its analysis of the evolution of tissues, both hard and soft, surrounding dental implants, and the fact that it relates analysis to different degrees of severity of type 2 diabetes mellitus. In this way, the study provides a new overview of peri-implant tissue responses among diabetic patients, which permits an assessment of an important risk factor for dental implant failure.

For this reason, control and treatment of periodontal infections should be a key element in the overall care of patients with diabetes mellitus and could play an important role in ensuring the success of implant therapy. However, treatment with dental implants remain contraindicated in diabetic patients – who often suffer obesity and cardiovascular disease – due to the negative effects of hyperglycemia associated with vascular microangiopathy accumulation in hard and soft peri-implant tissues (Javed & Romanos 2009). Morris et al. showed that the use of a chlorhexidine mouthwash reduces implant failure rates in diabetes mellitus type 2 patients from 13.5% to 4.4% (Morris et al. 2000). Furthermore, pre-operative antibiotic coverage reduced implant failure rate among the same population from 13.4% to 2.9%. In other similar research among non-diabetic patients, Simpson et al. found a higher implant failure rate when patients were not prescribed antibiotics (Simpson et al. 2010).

In conclusion, implant therapies for diabetic patients can be predictable, providing these patients fall within controlled ranges of glycemia over time, assessed by monitoring HbA1c levels.

Conflict of interest

The authors declare that they have no conflict of interest.

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