CLINICAL ORAL IMPLANTS RESEARCH

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Effect of oral hygiene maintenance on HbA1c levels and peri-implant parameters around immediately-loaded dental implants placed in type-2 diabetic patients: 2 years follow-up

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Abstract

Objective: The aim of the present 2-year follow-up study was to assess the effect of oral hygiene maintenance on hemoglobin Alc (HbA1c) levels and peri-implant parameters around immediately-loaded dental implants placed in type-2 diabetic patients with varying glycemic levels.

Material and methods: Ninety-one individuals were divided into three groups. In group 1, 30 systemically healthy individuals were included (HbA1c < 6%). Patients in group 2 and 3, comprised of 30 patients with T2DM (HbA1c 6.1–8%); and 31 patients with T2DM (HbA1c 8.1–10%) respectively. In all groups, patients received immediately loaded bone level implants. All participants were enrolled in a 6 monthly periodontal/peri-implant maintenance program. Peri-implant bleeding on probing (BOP), probing depth (PD), and marginal bone loss (MBL) were measured at 6, 12, and 24 months of follow-up.

Results: Mean preoperative HbA1c levels in patients in groups 1, 2, and 3 were 4.5%, 6.8%, and 8.7% respectively. In group-1, there was no significant difference in HbA1c levels at all follow-up durations. Among patients in groups 2 and 3, there was a significant decrease in HbA1c levels at 24-months follow-up than 6-months follow-up. At 6 months follow-up, BOP, PD, and MBL were significantly higher among patients in group-3 than group-1. At 12 and 24 months follow-up, there was no significant difference in BOP, PD, and MBL in all groups.

Conclusions: Oral hygiene maintenance reduces hyperglycemia and peri-implant inflammatory parameters around immediately loaded dental implants placed in type 2 diabetic patients.

Placement of dental implants in patients with diabetes mellitus (DM) was previously avoided due to the increased risk of delayed healing, microvascular complications, tissue damage and infections in these patients (Delamaire et al. 1997; Ebersole et al. 2008; Javed & Romanos 2009). However, under optimal glycemic control, dental implants can osseointegrate and remain functionally and esthetically stable in patients with DM in a manner similar to non-diabetic individuals (Javed & Romanos 2009; Fenner et al. 2015; Hoeksema et al. 2015). It has been proposed that optimal glycemic control levels may help to improve the function of osteoblasts, and retard the progression of periodontal inflammation and bone loss (Aguilar-Salvatierra et al. 2015; Ghiraldini et al. 2015). Glycosylated hemoglobin Alc (HbAlc) is a form of stable glycosylated hemoglobin, the product of a slow and largely irreversible reaction produced during the red blood cell life cycle. For more than four decades, measurement of HbAlc levels has been acknowledged as a precise approach to determine and monitor glycemic status in diabetic patients as it reflects average blood glucose levels during the previous 2–3 months (Koenig et al. 1976).

It has been reported that non-surgical periodontal therapy (NSPT) improves periodontal status and lower glycemic levels in patients with type-2 diabetes mellitus (T2DM) (Rodrigues et al. 2003; Al-Zahrani et al. 2009; Koromantzos et al. 2011; Auyeung et al. 2012; Sgolastra et al. 2013) by reducing the systemic burden of inflammatory mediators (such as interleukin-1beta and tumor necrosis factor-alpha) that aggravate the existing metabolic disorder in patients with

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hyperglycemia (Nishimura et al. 2003; Pontes Andersen et al. 2006). The same logic may be related to dental implants as closely resemble natural teeth with the exception that the former lacks a periodontal ligament. In a recent 2 year follow-up study, Aguilar-Salvatierra et al. (2015) evaluated the implant survival rates of immediately loaded implants that were placed in diabetic patients with varying HbA1c levels. In this study, each patient received implant in the maxillary anterior zone. The results showed that marginal bone loss (MBL) and peri-implant bleeding on probing (BOP) increased in relation with higher HbA1c levels; however, differences in peri-implant probing depth (PD) with reference to varying HbA1c levels did not reach statistical significance (Aguilar-Salvatierra et al. 2015). It is pertinent to mention that this study primarily focused on the variations in clinical and radiographic peri-implant parameters with reference to variations in HbA1c levels in the study population. It is hypothesized that routine peri-implant hygiene maintenance reduces hyperglycemia and clinical and radiographic peri-implant parameters around immediately loaded dental implants placed in type 2 diabetic patients with varying glycemic levels.

The aim of the present 2-year follow-up study was to assess the effect of oral hygiene maintenance on HbA1c levels and peri-implant parameters around immediately-loaded dental implants placed in type-2 diabetic patients with varying glycemic levels.

Material and methods

Ethical guidelines

The study was approved by the research ethics review committee of the College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia. Consenting individuals were requested to read and sign a consent form.

Inclusion criteria

The eligibility criteria were as follows: (a) patients with medically diagnosed T2DM; (b) measurement of HbA1c levels at the time of implant placement and at follow-up (c) measurement of peri-implant BOP, peri-implant probing depth (PD) and MBL and (d) use of guided bone regeneration in the surgical site. Type 2 diabetic patients with a history of tobacco smoking and/or tobacco chewing and individuals with other systemic disorders, such as acquired immune deficiency syndrome, cancer, hepatic disorders, and/or renal disorders were not sought.

Participants and grouping

In total, 91 partially edentulous male patients (30 non-diabetic controls and 61 patients with medically diagnosed T2DM) were recruited from an oral healthcare center in Riyadh, Saudi Arabia. Hospital records were explored to confirm the systemic health status of these individuals. Participants receiving single one-piece implants were recruited. This was done to avoid the possibility that prosthetic design might influence the peri-implant parameters investigated. Absence of female patients in the study population was a coincidence most probably due to the predominance of males attending the oral healthcare center. All patients with T2DM were using oral hypoglycemic agents with similar doses for the management of T2DM.

Participants were divided into three groups based on their HbA1c levels. In group 1, 30 systemically healthy individuals were included (HbA1c < 6%; Control group). Patients in group 2, comprised of 30 patients with T2DM and HbA1c levels between 6.1% and 8%; and in group-3, 31 patients with T2DM and HbA1c levels 8.1–10% were included.

Hemoglobin A1c levels

Among individuals in each group, HbA1c levels were measured at baseline (preoperatively) and at 6, 12 and 24 months follow-ups using an HbA1c analyzer kit (Quo-Test, EKF Diagnostics, Magdeburg, Germany).

Surgical protocol

In all groups, patients received bone level implants (Straumann Bone Level implants Straumann AG, Basel, Switzerland) with lengths and diameters ranging between 10–14 mm and 3.3–4.1 mm respectively. All implants were placed at the level of crestal bone in the anterior maxilla using an insertion torque of 35Ncm. All implants were immediately loaded and a postoperative digital periapical radiograph was taken after suturing to determine the levels of crestal bone for prospective radiographic assessments between the groups.

All patients were prescribed antibiotics (amoxicillin 500 mg three times daily for 7 days) and analgesics (ibuprofen 600 mg for as long as required). None of the participants in all groups had any known allergies to the prescribed medications. Oral hygiene instructions were given and the patients were advised to start rinsing with an essential-oil based mouthwash (Listerine Zero, Johnson & Johnson Middle East FZ – LLC) twice daily for 2 weeks, after 24 h of surgery.

Non-surgical periodontal therapy and oral hygiene instructions

In each group, participants were enrolled in a 6 monthly periodontal/peri-implant maintenance program in which, full mouth scaling was performed around all natural teeth and implant surfaces using an ultrasonic scaler. Oral hygiene instructions regarding regular tooth brushing were given and patients were encouraged to floss the teeth and peri-implant surfaces daily.

Assessment of peri-implant clinical and radiographic parameters

In each group, peri-implant BOP and PD ≥ 4 mm were measured with reference to the Consensus report of the Seventh European Workshop on Periodontology-2011 (Lang & Berglundh 2011). These parameters were measured at six sites per implant (mesiobuccal, mid-buccal, distobuccal, distopalatal, mid-palatal, and mesiopalatal) and presented as mean percentages per individual. In each group, the mean mesial and distal marginal bone loss was recorded in millimeters on digital peri-apical radiographs (Belmont ACURAY 071A Intra Oral X-Ray System, Hudson, FL, USA) using a software program (Scion Image, Scion Corp., Fredrick, Maryland, USA). These radiographs were taken at baseline and after 6, 12, and 24 months of follow-up. All clinical and radiographic assessments were performed by one experienced and calibrated investigator blinded to the study groups.

Statistical analysis

Statistical analysis was performed using the Kruskal–Wallis test (SPSS Version 18, Chicago, IL, USA). Peri-implant clinical (BOP and PD) and radiographic (MBL) parameters were statistically evaluated to determine their association with HbA1c levels in the respective groups and also with the follow-up durations. Means and standard deviations of the aforementioned parameters were computed and intergroup and intragroup comparisons were performed. For multiple intragroup comparisons, the Bonferroni *post hoc* test was performed. Box plots were also made to demonstrate the HbA1c levels among patients in groups 1, 2, and 3 after 6, 12, and 24 months of follow-up. *P*-values less than 0.05 were considered statistically significant.

Results

General characteristics of the study population

At the time of implant placement, the mean age of the patients in groups 1, 2, and 3 were 48.5 years (range 45–52 years), 50.1 years (range 46–55 years), and 50.5 years (range 45–59 years) respectively. The mean preoperative HbA1c levels in patients in groups 1, 2, and 3 were 4.5% (range 4.1–5.4%), 6.8% (range 6.4–8%), and 8.7% (range 8.2–9.7%) respectively (Table 1).

Hemoglobin A1c levels among patients in groups 1, 2, and 3 after 6, 12, and 24 months of follow-up

There was no statistically significant difference in the mean HbA1c levels at 6, 12, and 24 months of follow-up among patients in group-1. Among patients in groups 2 ($P = 0.01$) and 3 ($P = 0.003$), there was a significant decrease in HbA1c levels at 24-months follow-up as compared to 6-months follow-up (Figure 1).

Peri-implant clinical parameters and marginal bone loss among patients in groups 1, 2, and 3 after 6, 12, and 24 months of follow-up

At 6 months follow-up peri-implant BOP was significantly higher among patients in group-3 as compared to group-1. There was no significant difference in BOP among patients in groups 2 and 3 at 6-months follow-up. At 12 and 24 months of follow-up, there was no statistically significant difference in peri-implant BOP in all groups. In group-3, peri-implant BOP was significantly higher at 6-months follow-up compared to 24-months follow-up (Table 2).

At 6 months follow-up, peri-implant PD was significantly higher among patients in group-3 as compared to group-1. There was no significant difference in PD among patients in groups 2 and 3 at 6 months follow-up. At 12 and 24 months of follow-up, there was no statistically significant difference in peri-implant PD in all groups. In group-3, peri-implant PD was significantly higher at 6-months follow-up compared to 24-months follow-up (Table 2).

At 6 months follow-up peri-implant MBL was significantly higher among patients in group-3 as compared to group-1. At 12 and 24 months of follow-up, peri-implant MBL was significantly higher among patients in group-3 as compared to group-1 ($P = 0.02$). There was no statistically significant difference in peri-implant MBL among patients in all groups at 24 months follow-up (Table 2).

Discussion

The present study was based on the hypothesis that routine peri-implant hygiene maintenance reduces hyperglycemia and clinical and radiographic peri-implant parameters around immediately loaded dental implants placed in type 2 diabetic patients with varying glycemic levels.

An interesting finding in the present study was that there was a significant decrease in HbA1c levels at 24-months follow-up as compared to 6-months follow-up among patients in groups 2 and 3. A number of factors could have been associated with this difference in HbA1c levels. It is noteworthy that all participants were enrolled in a 6-monthly oral hygiene maintenance program in which they received full mouth scaling around teeth and implant surfaces. Studies (Beck et al. 1996; Page 1998; Grossi 2001; Javed et al. 2014, 2015a,b,c) have reported that bacteria and their products (such as lipopolysaccharides) enter systemic circulation from infected periodontal pockets that may in turn worsen insulin resistance by potentially increasing low-grade inflammation. This suggests that the systemic load of bacteria and their products is higher in individuals with persistent hyperglycemia compared to patients with well-controlled glycemic levels. Moreover, leakage of proinflammatory cytokines into the main blood stream from inflamed periodontal tissues may also result in deterioration of the hyperglycemic state, which may in turn further aggravate periodontal inflammation (Loos et al. 2000). It is therefore possible that mechanical debridement of plaque from teeth and implant surfaces helps reduce the overall burden of systemic inflammation thereby reducing hyperglycemia in patients with T2DM. This hypothesis has been supported by previous studies (Javed et al. 2014, 2015a,b,c). Also, throughout the study period, all patients with T2DM continued to use the hypoglycemic medications prescribed by their healthcare physicians. Since these individuals were recalled biannually for mechanical debridement, it is likely that this motivated them to continue using their hypoglycemic medications, which in turn reduced their hyperglycemic state. It is tempting to speculate that had the type 2 diabetic individuals been followed for longer durations, they would have had their glycemic levels within normal limits as observed in group-1 (non-diabetic controls). However, the preset results are in contradiction to a randomized clinical trial in which, Engebretson et al. (2013) assessed whether or not NSPT reduces HbA1c in patients with T2DM and moderate to advanced chronic periodontitis. The results showed that NSPT did not improve glycemic control in patients with T2DM and

Table 1. **Number of participants, mean age and hemoglobin A1c-levels in the study groups**

	Group-1	Group-2	Group-3
Number of participants (*n*)	30	30	31
Mean age in years (range)	48.5 (45–52)	50.1 (46–55)	50.5 (45–59)
Preoperative mean hemoglobin A1c (range)	4.5% (4.1–5.4)	6.8% (6.4–8)	8.7% (8.2–9.7)

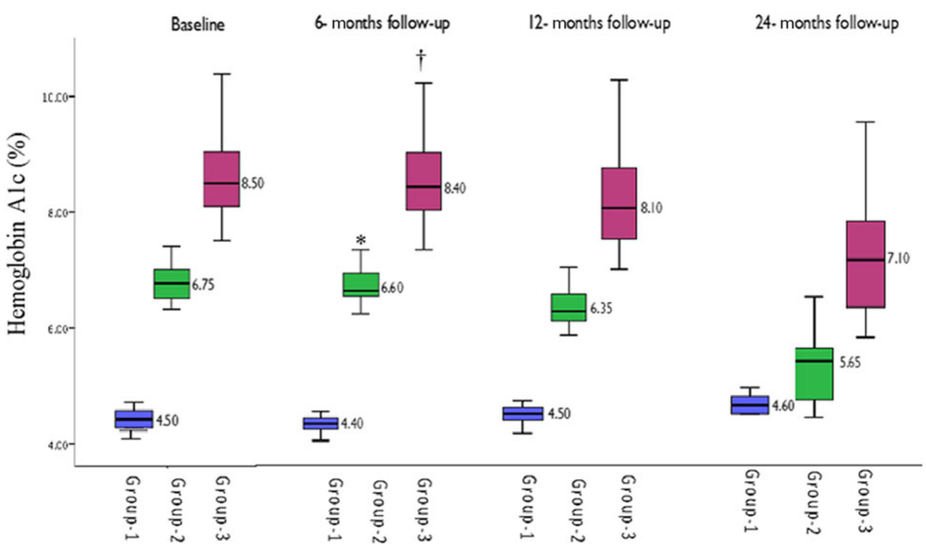

Fig. 1. Box plots showing the median hemoglobin A1c levels among patients in groups 1, 2, and 3 after 6, 12, and 24 months of follow-up. *In Group-2, there was a significant decrease in HbA1c levels at 24-months follow-up as compared to 6-months follow-up ($P = 0.01$). †In Group-3, there was a significant decrease in HbA1c levels at 24-months follow-up as compared to 6-months follow-up ($P = 0.003$).

Table 2. **Clinical peri-implant parameters and marginal bone loss (Mean ± SD) among patients in groups 1, 2 and 3 at 6, 12 and 24 months follow-up**

	Bleeding on probing (%)			Probing depth (in millimeters)			Marginal bone loss (in millimeters)		
Follow-up	6 months	12 months	24 months	6 months	12 months	24 months	6 months	12 months	24 months
Group-1	0.42 ± 0.05*	0.4 ± 0.02	0.4 ± 0.06	2 ± 0.5†	1.9 ± 0.04	1.6 ± 0.05	Mesial: 0.32 ± 0.12 Distal: 0.35 ± 0.12 Total: 0.33 ± 0.1¶	Mesial: 0.45 ± 0.08 Distal: 0.46 ± 0.05 Total: 0.45 ± 0.06‖	Mesial: 0.45 ± 0.25 Distal: 0.51 ± 0.13 Total: 0.46 ± 0.16**
Group-2	0.63 ± 0.06	0.6 ± 0.04	0.62 ± 0.07	2.5 ± 0.18	2.3 ± 0.26	2.3 ± 0.15	Mesial: 0.51 ± 0.05 Distal: 0.53 ± 0.04 Total: 0.52 ± 0.02	Mesial: 0.54 ± 0.23 Distal: 0.55 ± 0.17 Total: 0.54 ± 0.12	Mesial: 0.56 ± 0.24 Distal: 0.59 ± 0.08 Total: 0.58 ± 0.15
Group-3	0.71 ± 0.05‡	0.63 ± 0.02	0.62 ± 0.05	3.3 ± 0.21§	2.4 ± 0.35	2.3 ± 0.62	Mesial: 0.54 ± 0.15 Distal: 0.56 ± 0.21 Total: 0.55 ± 0.06	Mesial: 0.56 ± 0.05 Distal: 0.58 ± 0.1 Total: 0.57 ± 0.07	Mesial: 0.58 ± 0.18 Distal: 0.61 ± 0.22 Total: 0.59 ± 0.2

*Comparison of bleeding on probing at 6-month follow-up in group-1 with 6-month follow-up in group-3 ($P = 0.02$).
†Comparison of probing depth at 6-month follow-up in group-1 with 6-month follow-up in group-3 ($P = 0.03$).
‡Comparison of bleeding on probing at 6-month follow-up in group-3 with 24-months follow-up in the same group ($P = 0.01$).
§Comparison of probing depth at 6-month follow-up in group-3 with 24-months follow-up in the same group ($P = 0.03$).
¶Comparison of marginal bone loss at 6-month follow-up in group-1 with 6-month follow-up in group-3 ($P = 0.03$).
‖Comparison of marginal bone loss at 12-month follow-up in group-1 with 12-months follow-up in group-3 ($P = 0.02$).
**Comparison of marginal bone loss at 24-month follow-up in group-1 with 24-months follow-up in group-3 ($P = 0.02$).

moderate to advanced chronic periodontitis. It is notable that the follow-up duration for study by Engebretson et al. (2013) was up to 6-months compared to the present study in which, the patients were followed up to 24 months. It is possible that if patients in the study by Engebretson et al. (2013) were followed for longer durations, a significant difference in HbA1c levels following NSPT may have been observed.

A chronic hyperglycemic state increases the formation and accumulation of advanced glycation endproducts (AGEs) in periodontal tissues that impair the chemotactic and phagocytic function of polymorphonuclear leukocytes and produces destructive inflammatory cytokines in the serum and gingival crevicular fluid (Javed et al. 2012; Gurav 2013). This leads to periodontal inflammation and MBL in patients with T2DM. Furthermore, function of potential cells involved in immunoinflammatory responses is also sabotaged in a chronic hyperglycemic state (Mealey 2006). It is noteworthy that at 24 months of follow-up, there was no significant difference in peri-implant BOP, PD, and MBL in patients with T2DM (groups 2 and 3) and controls (group-1). It is likely that reduction in the hyperglycemic state in patients in groups 2 and 3 also reduced the production of AGEs in the peri-implant tissues and minimized oxidative stress in the peri-implant tissues.

There is a dearth of published research with reference to the immediate loading of dental implants in patients with T2DM. The present results are in contradiction to those reported by Michaeli et al. (2009) in which, the authors claimed that since hyperglycemia compromise bone remodeling, immediate loading is less effective in diabetic patients as compared to delayed loading. The present study supports the 15 year follow-up results of a randomized clinical trial with split mouth design and immediately vs. delayed loaded implants by Romanos et al. (2014) in which, the authors reported no significant differences between immediately and delayed loaded implants.

A limitation of the present study is that tobacco smokers and smokeless tobacco product users were excluded. Studies have reported that tobacco habits (such as tobacco smoking and smokeless tobacco consumption) enhance periodontal inflammation and alveolar bone loss and also jeopardize the outcomes of periodontal therapy (Javed et al. 2015a,b; Kotsakis et al. 2015). Therefore, it is likely that the beneficial effects of mechanical plaque debridement (as observed in the present results) would be compromised in type 2 diabetic smokers and smokeless tobacco product users as compared to individuals not using tobacco in any form. Moreover, peri-implant microbial and immunological profile (such as assessment of microbes in the peri-implant plaque and proinflammatory cytokines in the peri-implant crevicular fluid) remained uninvestigated. Therefore, in the present study it remained unclear whether the MBL primarily occurred due to microbial action, inflammation or other factors such as biological width establishment. Furthermore, the present study was based on outcomes limited to 24-months of follow-up. It is hypothesized that the type 2 diabetic population, which continued to exhibit higher glycemic levels at the end of the study would have had well-controlled T2DM in case these individuals were followed for longer durations and oral hygiene maintenance protocols were continued. Further studies are needed in this regard.

Conclusion

Oral hygiene maintenance reduces hyperglycemia and peri-implant inflammatory parameters around immediately loaded dental implants placed in type 2 diabetic patients.

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