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Efficacy of periimplant mechanical debridement with and without adjunct antimicrobial photodynamic therapy in patients with type 2 diabetes mellitus

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ABSTRACT

Objective: There are no studies that have assessed the efficacy of mechanical debridement (MD) with and without adjunct antimicrobial photodynamic therapy (aPDT) in the treatment of periimplant inflammation in patients with type 2 diabetes mellitus (T2DM). The aim of the present 12-month follow-up study was to assess the efficacy of MD with and without adjunct aPDT in the treatment of periimplant inflammation in patients with T2DM.

Methods: Sixty-seven patients with diagnosed periimplant inflammation and T2DM were included. Treatment-wise, the patients were divided into 2 groups: (a) test-group (n = 34): patients received MD+ aPDT; and (b) control group (n = 33): patients received MD only. Periimplant bleeding on probing (BOP), probing depth (PD) ≥4 mm and mesial and distal marginal bone loss (MBL) were measured at baseline and after 6 and 12 months of therapy in both groups. The Kruskal-Wallis test was used to compare the periimplant BOP, PD, MBL and HbA1c levels in both groups. P-values less than 0.05 were considered statistically significant.

Results: Mean preoperative hemoglobin A1c (HbA1c) for patients in the control group and test group were 8.5% and 8.8%, respectively. In the control group, there was no significant difference in HbA1c levels at all follow-up durations. Among patients in test group, there was a significant decrease ($P < 0.05$) in HbA1c levels at 6 and 12 months of follow-up. Both PD and BOP were significantly lower in the test group compared to the control group at all follow-up durations. At 6 and 12 months of follow-up, there was no significant difference in MBL in both groups.

Conclusion: In patients with T2DM, MD with adjunct aPDT is more effective in the treatment of periimplant inflammation compared with MD alone.

1. Introduction

According to the consensus report from the 11th European Workshop on Periodontology consensus conference, periimplant diseases are an emerging public health issue [1]. Periimplant diseases are categorized into two types namely, periimplant mucositis (inflammation of the soft tissues surrounding the implant without any signs of bone loss) and periimplantitis [2]. Several risk factors such as, previous history of periodontitis, excess cement accumulation in the periimplant tissues, poor oral hygiene, smoking and poorly controlled diabetes mellitus (DM) are associated with the etiology of periimplant diseases [3–5]. It is well known that patients with poorly controlled DM present increased risk of delayed healing, microvascular complications, tissue damage and infections, that could impair and compromise the implant osseointegration leading to higher failure rates [6,7].

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Ideally, the treatment of periimplant diseases focuses on infection control, detoxification of implant surfaces, regeneration of lost tissues and plaque control regimes via mechanical debridement (MD) [8]. However, another approach that has been used for the treatment of periimplant diseases is the use of antimicrobial photodynamic therapy (aPDT) as an adjunct to MD. The aPDT involves interactions between a light source of a specific wavelength (630–830 nm) and chemical dye or photosensitizer such as methylene blue and toluidine blue (TBO) in the presence of oxygen [9,10]. This interaction produces reactive oxygen species [10,11] that cause oxidative damage to microbial cell walls and pre-malignant and malignant cells [12–14]. It has been shown that MD of periimplant surfaces with adjunct therapies such as aPDT is more effective in the treatment of periimplant diseases compared with MD alone [15]. In an experimental study, Hayek et al. [16] compared the effects of aPDT and conventional MD technique on microbial reduction in dogs with induced periimplantitis. The results showed PDT caused significant reduction in the scores of pathogenic microbes (*Prevotella*, *Fusobacterium* and *Streptococci* species) [16]. Likewise, a clinical study by Schär et al. [17] concluded that MD with adjunct PDT may represent an alternative treatment modality in the non-surgical management of initial periimplantitis. It is however worth mentioning that the efficacy of MD with and without aPDT in the treatment of periimplant inflammation in patients with type 2 DM (T2DM) is not yet reported. The present study was based on the hypothesis that MD with adjunct PDT is more effective in the treatment of periimplant inflammation compared with MD alone.

The aim of the present longitudinal 12-month follow up clinical study was to assess the efficacy of MD with and without aPDT in the treatment of periimplant inflammation in patients with T2DM.

2. Materials and methods

2.1. 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 prior to the initiation of the study. All participants were given the liberty to retire from the study at any stage without any form of penalty.

2.2. Eligibility criteria

The inclusion criteria were as follows: (a) Patients diagnosed with periimplant inflammation (periimplant bleeding on probing [BOP] in at least 30% sites and/or periimplant marginal bone loss [MBL] of at least 2 mm); (b) Patients with medically diagnosed T2DM (hemoglobin A1c [HbA1c] levels ≥8%) [18]. Self-reported tobacco smokers and smokeless tobacco chewers, individuals with systemic diseases other than T2DM (such as, acquired immune deficiency syndrome, cancer, hepatic disorders, and renal disorders) and patients with a history of antibiotics, steroid and/or non-steroidal anti-inflammatory drug use within the past six months were excluded.

2.3. Study grouping

Treatment-wise, the patients were divided into 2 groups: (a) test group (n = 34): patients received MD + aPDT; and (b) control group (n = 33): patients received MD alone using an ultrasonic scaler (VV DENTA, Guangxi, China).

2.4. Assessment of periimplant clinical and radiographic parameters

In both groups, periimplant BOP and probing depth (PD) ≥4 mm were measured at 6 sites per implant (mesiobuccal, mid-buccal, distobuccal, distopalatal, mid-palatal, and mesiopalatal) and presented as mean percentages per individual. MBL was defined as the vertical difference in millimeters (mm) between the original periimplant bone level at baseline and that at follow-up [19,20]. The radiographic technique was standardized by using a film holder as a guiding tool for X-ray beams. In each group, the mean mesial and distal MBL were recorded in millimeters on digital radiographs (Belmont ACURAY 071A Intra Oral X-Ray System, Hudson, FL, USA) using a software program (Scion Image, Scion Corp., Fredrick, Maryland, USA). The radiographic technique was standardized by using a film holder as a guiding device for X-ray beams. All measurements were done by one trained investigator at baseline (after implant loading) and after 6 and 12 months of follow-up.

2.5. Photodynamic therapy protocol

In the test group, PDT was performed after MD using a standard PDT setup (HELBO®; Photodynamic Systems GmbH, Wels, Austria). The light source used was a hand-held diode laser (HELBO® TheraLite Laser, HELBO® 3D Pocket Probe; Photodynamic Systems GmbH) with a wavelength of 660 nm and a power density of 100 mW. Phenothiazine chloride (HELBO® Blue Photosensitizer; Photodynamic Systems GmbH) was used as the photosensitizer. The photosensitizer was applied submucosally from the bottom to the top of the periimplant pockets and was left in situ for 120 s. Consequently, periimplant pockets were irrigated with 3% hydrogen peroxide according to the manufacturer's instructions. Each pocket was exposed to the laser light for 10 s.

2.6. Measurement of hemoglobin A1c levels

Venous blood samples were drawn and HbA1c levels were determined using the high-performance liquid chromatography method (Bio-Rad Laboratories Inc., D-10™, Hemoglobin Systems, Hercules, CA, USA) [21]. In both groups, HbA1c levels were measured at baseline and at 6 and 12 months of follow-up.

2.7. Statistical analysis

Statistical analysis was performed using a software program (SPSS Version 18, Chicago, IL, USA). The Kruskal-Wallis test was used to compare the periimplant BOP, PD, MBL and HbA1c levels in both groups. Means and standard deviations of the aforementioned parameters were computed and intergroup and intragroup comparisons were performed. P-values less than 0.05 were considered statistically significant.

3. Results

3.1. General characteristics of the study population

The mean age of patients in the test (n = 34) and control (n = 33) groups was 53.6 ± 9.5 and 51.4 ± 3.7 years, respectively. The male/female ratio in the test and control groups was 19:15 and 17:16, respectively. The mean duration of T2DM among patients in the test and control groups was 11.2 ± 2.7 years and 10.5 ± 0.2 years, respectively. All patients in the test group were using anti-hyperglycemic medications and were also following dietary control regimens for the management of T2DM.

Table 1
Clinical and radiographic periimplant parameters (Mean ± SD) and hemoglobin A1c levels among patients in test (MD + aPDT) and control (MD alone) groups at baseline, 6 and 12 months of follow-up.

	Baseline		6-month follow-up		12-month follow-up	
	Test-group (n = 34)	Control group (n = 33)	Test-group (n = 34)	Control group (n = 33)	Test-group (n = 34)	Control group (n = 33)
BOP (%)	36.3 ± 14.2[a,b,c,d]	31.7 ± 9.4[a,b]	9.2 ± 1.6[b]	15.1 ± 3.4	2.4 ± 0.6[d]	10.5 ± 1.3
PD (%)	16.2 ± 3.7[a,b,c,d]	19.5 ± 2.4[a,b]	3.1 ± 0.8[b]	8.5 ± 1.4	0.4 ± 0.1	4.3 ± 0.7
MBL (in mm)	1.4 ± 0.2	1.3 ± 0.6	1.3 ± 0.1	1.4 ± 0.1	1.3 ± 0.2	1.3 ± 0.1
Hemoglobin A1c levels (%)	8.8 ± 0.4[a,c]	8.5 ± 0.4[a]	6.7 ± 0.2[b]	8.4 ± 0.6	6.1 ± 0.5[d]	7.8 ± 0.2

[a] Compared with the test group at 6 months of follow-up (P < 0.01).
[b] Compared with the control group at 6 months of follow-up (P < 0.01).
[c] Compared with the test group at 12 months of follow-up (P < 0.01).
[d] Compared with the control group at 12 months of follow-up (P < 0.01).

3.2. Periodontal inflammatory conditions among individuals in test and control groups treated with NSPT with and without aPDT

3.2.1. Periimplant inflammatory parameters at baseline

At baseline, there was no statistically significant difference in scores of BOP, PD, and MBL among patients in the test and control groups. However, scores of BOP (P < 0.01) and PD (P < 0.01) were significantly higher in the test and control groups at baseline compared with their respective scores measured at 6 and 12 months of follow-up (Table 1).

3.2.2. Periimplant inflammatory parameters at 6-month follow-up

In the control group, BOP (P < 0.01) and PD (P < 0.01) at all sites were significantly higher at baseline as compared to control sites (P < 0.01) after 6 months of treatment (MD alone). There was no statistically significant difference in the MBL among patients in the control group at baseline and 6-month follow-up. In the test group, BOP (P < 0.01) and PD (P < 0.01) at all sites were significantly higher at baseline as compared to control sites after 6 months of treatment (MD + aPDT). There was no statistically significant difference in the MBL among patients in the test group at baseline and 6-month follow-up. After 6 months of treatment, scores of BOP (P < 0.01) and PD (P < 0.01) were significantly higher in the control group compared with the test group. There was no statistically significant difference in MBL between control sites and test sites after 6 months of treatment (Table 1).

3.2.3. Periimplant inflammatory parameters at 12-month follow-up

In the control group, BOP (P < 0.01) and PD (P < 0.01) at all sites were significantly higher at baseline as compared to control sites (P < 0.01) after 12-months of treatment. There was no statistically significant difference in the MBL among patients in control group at baseline and 12-month follow-up. In the test group, BOP (P < 0.01) and PD (P < 0.01) at all sites were significantly higher at baseline as compared to control sites after 12 months of treatment. There was no statistically significant difference in the MBL among patients in test group at baseline and 12-month follow-up. After 12 months of treatment, scores of BOP (P < 0.01) and PD (P < 0.01) were significantly higher in the control group compared with the test group. There was no statistically significant difference in MBL between control sites and test sites after 12 months of treatment (Table 1).

3.2.4. Hemoglobin A1C levels

At baseline, there was no statistically significant difference in HbA1c levels among patients in the test and control groups. In the control group, no statistically significant difference in the mean HbA1c levels at 6 and 12 months of follow-up compared to baseline. Among patients in the test group, there was a significant decrease (P < 0.01) in HbA1c levels at 6 months and 12 months of follow-up compared to baseline. The mean HbA1c levels were significantly higher (P < 0.01) in the control group compared to the test group after 6 and 12 months of treatment (Table 1).

4. Discussion

Several studies [22,23] have reported that the outcomes of oral surgical interventions are compromised in patients with chronic hyperglycemia. This has been primarily associated with the increase formation and accumulation of advanced glycation end products (AGEs) in the tissues [24]. However, the present study was based on the hypothesis that MD with adjunct aPDT (test group) is more effective in the treatment of periimplant inflammation compared with MD alone (control group) in patients with T2DM. The present results support this hypothesis. It is therefore tempting to consider MD as an adjunct to aPDT is an effective treatment approach for oral infections in healthy as well as immunocompromised individuals because aPDT involves interactions between a light source and a chemical dye (photosensitizer). This interaction results in the formation of free oxygen radicals that have been shown to be lethal against pathogenic microbes, such as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola stronger* [10,11,25]. This is an explanation for the significant reduction in the scores of periimplant PD and BOP. However, it is worth mentioning that other factors may also have contributed significantly in reducing periimplant soft tissue inflammation. One of such factors is the dramatic decrease in the mean HbA1c levels at 6 months follow-up among patients that received MD + aPDT compared with those that received MD alone. It is therefore likely that when MD is performed in conjunction with aPDT, the oral and systemic burden of inflammation is significantly reduced compared with MD alone. This is a possible explanation for the marked reduction in the mean HbA1c levels in the test group compared to the control group in patients with T2DM. Another hypothesis that can be proposed is that aPDT + MD significantly reduced the levels of AGEs in the systemic and periimplant tissues. This reflects that there is a cascade of events that are associated with reduction on periimplant inflammation; however, the contribution of aPDT in this context cannot be overlooked.

Studies [26–28] have shown that non surgical periodontal therapy plays an effective role in minimizing the oral, as well as systemic burden of inflammation. An interesting finding in the present study was that regardless of the type of treatment adopted, there was no significant difference in periimplant MBL at all time intervals in both groups. These results indicate that mechanical eradication of the oral biofilm is sufficient to minimize crestal bone loss around implants. However, the present study had a short follow-up duration (12 months). It is likely that such follow-up duration may be insufficient to predict changes in marginal bone height between both treatment protocols. Since aPDT + MD significantly reduced the clinical parameters of inflammation compared to MD alone, it is hypothesized that the adjunct treatment may also exhibit a bone regenerative capacity as compared to MD

alone. Moreover, aPDT was performed only once throughout the present study. There is a possibility that an increased frequency of aPDT + MD in patients with periimplant inflammation may induce new bone formation around implants. However, further long-term randomized controlled clinical trials are needed in this regard.

A limitation of the present study is the short follow up duration, which might have revealed different results if it was for a longer period of time. The exclusion of smokers and smokeless tobacco products users presents another limitation. It is well-known that tobacco consumption is associated with enhanced periodontal inflammation, impaired healing, and can also jeopardize outcomes of periodontal therapy [29,30]. Moreover, in a recent study [31] periodontal treatment with MD or MD + PDT was not able to reduce levels of 40 subgingival species in smokers. Therefore, it is possible that the favorable effects of MD and PDT would be compromised in tobacco products users compared to individuals not using tobacco. In addition, assessment of MBL was based on the evaluation of 2-dimentional radiographs. Additional studies based on three-dimensional computed tomography analysis may yield valuable information regarding the patterns of alveolar bone remodeling. Furthermore, the present study was conducted in patients with a mean age around 50-year-old. It is hypothesized that periodontal tissues of elderly patients with age-associated factors (such as systemic diseases, medications and changes in behavior, motor function and cognitive function, poor oral hygiene) [32] may respond differently to periimplant therapy. Further studies are needed in this regard.

5. Conclusion

Within the limits of this 12-month follow-up study, it is concluded that MD with adjunct aPDT is more effective in the treatment of periimplant inflammation compared with MD alone in patients with T2DM.

Disclosure

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