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Effectiveness of mechanical debridement with and without adjunct antimicrobial photodynamic therapy in the treatment of periodontal inflammation among patients with prediabetes

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ABSTRACT

Aim: The aim of the present study was to assess the effectiveness of mechanical debridement (MD) with and without adjunct antimicrobial photodynamic therapy (aPDT) in the treatment of periodontal inflammation among patients with prediabetes.
Methods: Demographic information was collected using a questionnaire. Hemoglobin A1c (HbA1c) levels were measured at baseline and at 3 and 6 months' follow-up.
Treatment: Individuals were randomly divided into 2 groups as follows: (a) Group-1, participants underwent full-mouth MD; and Group-2: participants underwent full-mouth MD with adjunct aPDT. In groups 1 and 2, full-mouth plaque index (PI), bleeding on probing (BOP) and probing pocket depth (PPD) were measured at baseline and at 3 and 6 months' follow-up. In both groups, full-mouth digital intraoral radiographs were also taken. Sample-size was estimated and statistical analysis was performed with level of significance set as $P < 0.05$.
Results: In total, 70 prediabetic male individuals (35 patients in group-1 and 35 in group-2) were included. At baseline, PI, BOP, number of sites with PPD ≥4 mm were comparable among individuals in groups 1 and 2. In groups 1 and 2, PI ($P < 0.05$), BOP ($P < 0.05$), number of sites with PPD ≥4 mm ($P < 0.05$) were significantly higher at baseline compared with 3 months' follow-up. There was no statistically significant difference in PI, BOP, number of sites with PPD ≥4 mm at 3 and 6 months' follow-up. At 6 months' follow-up, PI, BOP, number of sites with PPD ≥4 mm were comparable to their respective baseline values. There was no statistically significant difference in CBL in both groups at 3 and 6 months' follow-up. There was no statistically significant difference in HbA1c levels among individuals in groups 1 and 2 at all-time intervals.
Conclusion: In the short-term, MD is effective in reducing periodontal inflammation among patients with prediabetes. The contribution of adjunct aPDT in this regard is insignificant.

1. Introduction

Prediabetes is a state of chronic hyperglycemia (CH) in which, hemoglobin A1c (HbA1c) and fasting blood glucose levels range between 5.7%–6.4% and 100–125 mg/dL (5.6–6.9 mmol/L), respectively [1]. Clinical [2–4] and experimental [5,6] studies have shown that periodontal inflammation is worse among subjects with prediabetes compared with systemically healthy controls. There are a number of events that play a role in aggravating periodontal inflammation among patients with CH (such as those with prediabetes). Firstly, it is hypothesized that CH increases the formation and deposition of advanced glycation end products (AGEs) in periodontal tissues [7]; thereby increasing the interactions between AGEs and their receptors (RAGE) [7]. These AGEs-RAGE interactions have been reported to augment oxidative stress within cells and increase the production of destructive inflammatory cytokines, such as interleukin (IL)-6, IL-1β, matrix metalloproteinases (MMP), which further aggravate the previously existing chronic inflammatory state [8,9]. Moreover, the state of cellular oxidative stress in patients with CH increases the production of reactive oxygen species (ROS) such as superoxide anion, hydroxyl radical, and peroxyl radical

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that have been associated with tissue damage and enhances cell death [10]. These factors contribute in the destruction of periodontal connective tissue attachment and alveolar bone.

Conventionally, non-surgical periodontal therapy (NSPT) in the form of mechanical debridement (MD) using ultrasonic scalers and hand-instruments (such as currettes) is performed for the treatment of periodontal inflammation [11,12]; however, studies [13,14] have shown that NSPT when performed with adjunct therapies such as antimicrobial photodynamic therapy (aPDT) is more effective in the treatment of periodontal inflammation compared with NSPT alone. One explanation in this regard is that aPDT forms free oxygen radicals that damage target cells such as tumor and microbial cells thereby augmenting the overall anti-inflammatory effect of NSPT [15].

Since CH negatively affects periodontal healing [16], it is hypothesized that there is no statistically significant difference in periodontal inflammatory parameters among prediabetic patients that receive US with or without aPDT. Therefore, the aim of the present study was to assess the effectiveness of MD with and without adjunct aPDT in the treatment of periodontal inflammation among patients with prediabetes.

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. Volunteering individuals were requested to read and sign a consent form. All participants were informed that they reserved the right to withdraw their participation at any stage of the investigation without consequences.

2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: (a) patients with medically diagnosed prediabetes (individuals with HbA1c levels ranging between 5.7%–6.4%) [1]; (b) patients with periodontal inflammation (patients with at least 6 periodontal pockets ≥4 mm in depth) [17]; (c) signing the consent form. Third molars, pregnant and/or lactating females, habitual tobacco smokers, smokeless-tobacco product users and alcohol users, patients with self-reported systemic diseases such as diabetes mellitus, acquired immune deficiency syndrome and renal disorders and patients who reported to have used antibiotics, corticosteroids and/or nonsteroidal anti-inflammatory drugs within the past 90 days were excluded.

2.3. Grouping and randomization

Treatment wise, individuals were randomly divided into 2 groups as follows: (a) Group-1, participants underwent full-mouth MD using an ultrasonic scaler (VV DENTA, Guangxi, China); and Group-2: participants underwent full-mouth MD using an ultrasonic scaler (VV DENTA, Guangxi, China) with adjunct aPDT. Randomization was done by picking a paper from an opaque bag marked either “Group-1” or “Group-2”.

2.4. Questionnaire

Information regarding age, gender, duration of prediabetic state, treatment of prediabetes, family history of diabetes, and daily tooth brushing and flossing was collected using a questionnaire.

2.5. Antimicrobial photodynamic therapy

The aPDT was carried out as described elsewhere [18]. In summary, Methylene blue (0.005%) was used as a photosensitizer and was applied using a blunt needle over and into the periodontal pocket. For irradiation, a 670 nm diode laser was used at 150 mW. Laser irradiation was carried out for 60 s using a flexible tip in each periodontal pocket (depth ≥4 mm). The treatment was applied once (at baseline).

2.6. Assessment of clinical periodontal parameters and radiographic marginal bone loss

All clinical and radiographic examinations were performed by a trained and calibrated investigator. The overall *kappa* for intra-examiner reliability was 0.88. In groups 1 and 2, full-mouth plaque index (PI) [19], bleeding on probing (BOP) [19] and probing pocket depth (PPD) [20] were measured at six sites per tooth (mesiobuccal, midbuccal, distobuccal, distolingual/palatal, midlingual/palatal and mesiolingual/palatal) at baseline and at 3 and 6 months’ follow-up. PPD was measured to the nearest millimeter using a graded probe (Hu-Friedy, Chicago, IL., USA) [21]. In both groups, full-mouth digital intraoral radiographs (4 bitewings of posterior teeth, 5 periapical radiographs in maxillary anterior and posterior teeth and 3 periapical radiographs in the mandibular anterior and posterior teeth) were taken using a digital radiographic machine (GENDEX™, INTRAORAL XRAY SYSTEMS, NOMAD PRO2™, Hatfield, PA., USA). The radiographic technique was standardized by using a film holder as a guiding tool for X-ray beams (Belmont ACURAY 071A Intra Oral X-Ray System, Hudson, FL, USA). Crestal bone loss (CBL) was defined as the linear distance from the cementoenamel junction to the most coronal part of the alveolar crest [22]. CBL was recorded in millimeters using a software program (Scion Image, Scion Corp., Fredrick, Maryland, USA).

2.7. Hemoglobin A1c levels

In groups 1 and 2, hemoglobin A1c (HbA1c) levels were measured using the ion-exchange high-performance liquid chromatography and expressed as percentages [23]. In both groups, HbA1c levels were measured at baseline and at 3 and 6 months’ follow-up.

2.8. Statistical analysis

Statistical analysis was performed using a software program (SPSS Version 18., Chicago, IL., USA). In the test- and control groups, The Kruskal-Wallis test was used to compare the periimplant BOP, PPD and MBL at 6 and 12 months follow-up. Sample size estimation was performed with a computer software (nQuery Advisor 5.0, Statistical Solutions, Saugus, Massachusetts, USA). Power analysis was based on the supposition that a mean difference of 0.5 mm and 1 mm in CBL and PPD, respectively should be detected between patients in groups 1 and 2 at a significance level of 0.05 to attain a desired study power of at least 80%. It was estimated that a sample size of 35 individuals per group will achieve a power of 85% with a 0.05 two-sided significance level. P-values less than 0.05 were considered statistically significant.

3. Results

3.1. General characteristics of the study groups

In total, 70 prediabetic male individuals (35 patients in group-1 and 35 in group-2) were included. The mean ages of individuals in groups 1 and 2 were 42.5 ± 2.6 and 45.7 ± 0.8 years, respectively. The mean duration of a prediabetic state among patients in groups 1 and 2 was 14.5 ± 0.5 and 12.2 ± 0.8 months, respectively. All individuals were recommended to manage their glycemic level via dietary control. A family history of diabetes was reported by 62.8% individuals in Group-1 (n = 22) and 60% individuals in Group-2 (n = 21). Tooth brushing once daily was reported by 82.8% (n = 29) individuals in Group-1 and 77.1% (n = 27) individuals in Group-2. None of the individuals in either group reported to have ever used a dental floss.

3.2. Hemoglobin A1c levels

At baseline, the mean HbA1c levels among individuals in groups 1 and 2 were 6.3% (5.9–6.4%) and 6% (5.8–6.2%), respectively. At 3 months' follow-up, the mean HbA1c levels among individuals in groups 1 and 2 were 6.2% (5.7–6.3%) and 5.8% (5.7–6%), respectively. At 6 months' follow-up, the mean HbA1c levels among individuals in groups 1 and 2 were 6% (5.8–6.2%) and 6.2% (5.9–6.3%), respectively. There was no statistically significant difference in HbA1c levels among individuals in groups 1 and 2 at all-time intervals.

3.3. Periodontal parameters and radiographic marginal bone loss in groups 1 and 2 at baseline and at 3- and 6 months' follow-up

At baseline, PI, BOP, number of sites with PPD ≥4 mm were comparable among individuals in groups 1 and 2. In groups 1 and 2, PI ($P < 0.05$), BOP ($P < 0.05$), number of sites with PPD ≥4 mm ($P < 0.05$) were significantly higher at baseline compared with 3 months' follow-up. There was no statistically significant difference in PI, BOP, number of sites with PPD ≥4 mm at 3 and 6 months' follow-up. At 6 months' follow-up, PI, BOP, number of sites with PPD ≥4 mm were comparable to their respective baseline values. There was no statistically significant difference in CBL in both groups at 3 and 6 months' follow-up (Table 1).

4. Discussion

2 To our knowledge, this is the first study that assessed the efficacy of full-mouth MD with and without adjunct aPDT in the treatment of periodontal inflammation among prediabetic patients. We hypothesized that there is no statistically significant difference in periodontal inflammatory parameters among prediabetic patients that receive full-mouth MD with or without adjunct aPDT. The current results are in agreement with this hypothesis since there was no statistically significant difference in periodontal inflammatory parameters (PI, BOP and PPD) among individuals in groups 1 and 2 at 3 and 6 months' follow-up. One explanation in this regard could be derived from the study by Eick et al. [24]., which showed that although aPDT is effective against pathogenic microbes such as *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*) and *Porphyromonas gingivalis* (*P. gingivalis*), and can reduce viability in biofilms but it is unable to completely destroy complex biofilms. Similarly, in the study by Dörtbudak et al. [25], aPDT significantly reduced the counts of *A. actinomycetemcomitans* and *P. gingivalis* around implant surfaces; however a complete eradication of microbes could not be achieved in this study. Moreover, it has also been shown that mecianical plaque debridement with adjunct aPDT moderately decreases the levels of destructive inflammatory cytokines such as tumor necrosis factor-alpha-α, IL-1β and MMP-8 and -9 in the gingival crevicular fluid compared with mechanical debridement alone [26]. The authors applaud these studies since there was a statistically significant reduction in PI, BOP and number of sites with PPD ≥4 mm among individuals in both groups at 3 months' follow-up.

3 Another factor that may have influenced the results of the present study is the persistent state of CH among individuals in groups 1 and 2. It is noteworthy that at baseline and at 6 months' follow-up, the mean HbA1c levels among individuals in groups 1 and 2 were 6.3% (5.9–6.4%) and 6% (5.8–6.2%) and 6% (5.8–6.2%) and 6.2% (5.9–6.3%), respectively. CH increases the formation and deposition of AGEs in periodontal tissues [7]; and increases the AGEs-RAGE interactions [7]. These AGEs-RAGE interactions augment oxidative stress within cells and increase the production of destructive inflammatory cytokines, such as IL-6, IL-1β, MMPs (such as MMP-8 and −9), which further aggravate the previously existing chronic inflammatory state [8,9]. Moreover, the state of cellular oxidative stress in patients with CH increases the production of reactive oxygen species (ROS) such as superoxide anion, hydroxyl radical, and peroxyl radical that have been associated with tissue damage and enhances cell death [10]. In this regard, it is possible that the persistent state of CH in the study groups may have compromised the outcomes of NSPT (with and without adjunct aPDT) in both groups. The authors support the recent results by Devji T [27] and Akram et al. [28], which reported that there is insufficient evidence to claim that aPDT as an adjunct to mechanical plaque debridement improves periodontal status.

In the present study, all patients with prediabetes despite being instructed by their healthcare providers to maintain glycemic levels via dietary control displayed raised glycemic levels at 3 and 6 months' follow-up examinations. It has been reported that under optimal glycemic control, hyperglycemic individuals can exhibit a periodontal status similar to that of a non-diabetic medically healthy individual [21]. Therefore, it is highly recommended that community-based health awareness programs should routinely be carried out to educate the general public about the detrimental effects of glycemic imbalance and the benefits of regular exercise and glycemic maintenance on overall health.

A limitation of the present study is that aPDT was performed once throughout the study period. It is hypothesized that there is a statistically significant reduction in periodontal inflammation following multiple sessions of aPDT (for example every 3 months) as an adjunct to full-mouth MD compared with a single session. Moreover, in the present study, all participants had CH. It is tempting to speculate that aPDT is more effective in reducing periodontal inflammation under optimal glycemic control in contrast to a state of CH. Further studies are needed to test these hypotheses.

5. Conclusion

In the short-term, MD is effective in reducing periodontal inflammation among patients with prediabetes. The contribution of adjunct aPDT in this regard is insignificant.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Table 1
Clinical periodontal parameters and radiographic marginal bone loss in groups 1 and 2 at baseline and at 3 and 6 months' follow-up.

Periodontal parameters	Group-1 (n = 35)			Group-2 (n = 35)		
	Baseline	3 months' follow-up	6 months' follow-up	Baseline	3 months' follow-up	6 months' follow-up
Plaque index (%)	51.6 ± 7.5*	38.5 ± 4.2	47.2 ± 7.4	54.4 ± 8.4†	32.6 ± 5.2	42.5 ± 6.7
Bleeding on probing (%)	56.4 ± 9.3*	30.6 ± 5.7	44.5 ± 8.2	51.6 ± 7.9†	24.8 ± 4.6	40.3 ± 5.6
Number of sites with PPD ≥ 4 mm	17.2 ± 3.4*	9.3 ± 2.5	13.6 ± 2.8	15.8 ± 3.4†	5.8 ± 2.1	10.4 ± 2.5
Crestal bone loss (in mm)	4.2 ± 0.6	4.3 ± 0.3	4.5 ± 0.4	4 ± 0.4	4.1 ± 0.5	4.3 ± 0.3

* Compared with 3 months' follow-up in group-1 ($P < 0.05$).
† Compared with 6 months' follow-up in group-2 ($P < 0.05$).

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