Photodiagnosis and Photodynamic Therapy 25 (2019) 247–252

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

Effectiveness of scaling and root planning with and without adjunct antimicrobial photodynamic therapy in the treatment of chronic periodontitis among cigarette-smokers and never-smokers: A randomized controlled clinical trial

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ARTICLE INFO

Keywords:
Chronic periodontitis
Inflammation
Periodontal debridement
Photochemotherapy
Smoking
Antimicrobial photodynamic therapy

ABSTRACT

Objective: The aim of the present short-term randomized clinical trial was to assess the efficacy of scaling and root planing (SRP) with and without adjunct antimicrobial photodynamic therapy (aPDT) in the treatment of chronic periodontitis (CP) among cigarette-smokers and never-smokers.

Materials and methods: Demographic information was collected using a questionnaire. Cigarette-smokers (group-1) and never-smokers (group-2) with CP were included. Treatment wise, these individuals were divided into two subgroups as follows: (a) SRP alone and (b) SRP with adjunct aPDT. Periodontal parameters (plaque index [PI], bleeding on probing [BOP], clinical attachment loss [AL] and probing pocket depth ≥ 4 mm [PD] were measured at baseline and at 1 month and 3 months' follow-up. Group comparisons were done using the Kruskall-Wallis test.

Results: Eighty-three male patients with CP (Group-1: 42 cigarette-smokers and; Group-2: 41 never-smokers) were included. In group-1, individuals that received SRP alone and SRP with adjunct aPDT had a mean history of cigarette smoking of 11.7 ± 0.3 and 12.5 ± 0.4 pack years. At baseline, PI, BOP, PD and clinical AL were comparable among all individuals in groups 1 and 2. At 1 month and 3 months' follow-up, PI ($P < 0.05$), PD ($P < 0.05$) and clinical AL ($P < 0.05$) were higher among all individuals in group-1 compared with group-2. In Group-2, PI, BOP, PD and clinical AL were comparable among all individuals at 1 month and 3 months' follow-up.

Conclusion: Outcomes of SRP with or without aPDT for the treatment of CP are compromised in cigarette-smokers. Among never-smokers with CP, outcomes of SRP with or without aPDT are comparable. The significance of aPDT in this regard remains questionable.

1. Introduction

Scaling and root planing (SRP) (synonym, non-surgical periodontal therapy) using hand instruments (such as curettes) is usually done for the treatment of chronic periodontitis (CP) [1–3]. It has however been reported that SRP alone is sometimes an insufficient protocol for the treatment of CP [1,4,5]. Studies [5–7] have reported that SRP when done with adjunct therapies, such as use of antibiotics, ozonated olive oil therapy and antimicrobial photodynamic therapy [aPDT]) is more effective in the treatment of CP compared with SRP alone. In a recent double-blinded clinical study by Theodoro et al. [8], SRP with adjunct aPDT was shown to be more effective in improving clinical attachment loss (AL) among patients with CP compared with SRP with adjunct antibiotic cover (amoxicillin combined with metronidazole). Similarly 3-months follow-up results from a split mouth randomized clinical trial (RCT) showed a statistically significant reduction in plaque index (PI)

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https://doi.org/10.1016/j.pdpdt.2019.01.006
Received 13 December 2018; Received in revised form 29 December 2018; Accepted 4 January 2019
Available online 06 January 2019

pocket depth (PD) and gingival index among individuals with CP that underwent SRP with adjunct aPDT compared with individuals that received SRP alone [9]. However, controversial results have also been reported. In the study by Al-Askar et al. [10], there was no statistically significant difference in PI, bleeding on probing (BOP) and PD at 3 and 6 months' follow-up among individuals that received SRP either with or without adjunct aPDT. Garcia et al. [11] assessed the influence of systemic nicotine administration for the treatment of experimental periodontitis using SRP with adjunct aPDT in ovariectomized rats. The results showed that SRP with adjunct aPDT is more effective in the treatment of EP than SRP under experimental nicotine exposure [11]. However, from an immunological aspect, the efficacy of SRP with or without adjunct aPDT in reducing the expression of destructive inflammatory cytokines such as interleukin (IL) 1-beta, IL-6 and tumor necrosis factor-alpha in oral fluids remains debatable [12,13].

Studies [14,15] have shown that CP is more often manifested among habitual cigarette smokers compared to never-smokers. Moreover, it has also well-known that outcomes of periodontal therapy are compromised in cigarette smokers compared with individuals that do not use any form of tobacco products [16,17]. One explanation for this is that habitual smoking increases the expression of advanced glycation endproducts (AGEs) in the oral tissues (including periodontal tissues) [18,19]. Interactions between AGEs and their receptors (RAGE) increases the oxidative stress and incites an inflammatory response in the periodontal tissues [18,19]. These events may compromise healing following periodontal therapy among smokers compared with never-smokers with CP. In the present study we hypothesize that the efficacy of SRP with and without adjunct aPDT are compromised in cigarette-smokers compared with never-smokers.

The aim of the present short term follow-up RCT was to assess the efficacy of SRP with and without adjunct aPDT in the treatment of CP among cigarette-smokers and never-smokers

2. Study population and methodology

2.1. Ethical approval

This study was a 12-week parallel-arm, randomized controlled clinical trial which was designed, conducted and reported following the Consolidation Standards of Reporting Trials (CONSORT) Statement and registered at www.clinicaltrials.gov, ClinicalTrials.gov Identifier: NCT03308019. The study was approved by the Research Ethics Review Board at 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 could withdraw their participation at any stage of the investigation without consequences.

2.2. Eligibility criteria

The following inclusion criteria were entailed: (a) Self-reported habitual cigarette-smokers; (b) self-reported never-smokers; (c) patients with CP (presence of at least 30% sites with ≥ 3 mm of clinical AL and PD ≥ 3 mm [20,21]. The exclusion criteria were as follows: (a) patients with systemic diseases such as acquired immune deficiency syndrome/HIV and diabetes mellitus; (b) habitual use of other forms of tobacco such as waterpipe, cigars and pipe; (c) use of electronic-nicotine-delivery-systems; (d) habitual smokeless tobacco product and alcohol users; (e) third molars and fractured teeth with embedded root remnants and edentulous individuals; (f) patients with misaligned teeth; and (g) patients that reported to have used antibiotics, non-steroidal anti-inflammatory drugs and/or steroids within the past 90 days.

2.3. Study participants and groups

Participants were recruited from the Oral health Care Unit of a local hospital in Riyadh, Saudi Arabia. Treatment wise, individuals in each group were randomly divided into two subgroups as follows: (a) SRP alone and (b) SRP with adjunct aPDT. Randomization was done by tossing a coin.

2.4. Questionnaire

Information regarding age, gender, family history of smoking, duration of cigarette-smoking habit (in pack years), daily frequency of smoking (number of cigarettes smoked daily) and daily tooth brushing was collected using a questionnaire.

2.5. Scaling and root planing

In both groups, SRP was performed in one session under local anesthesia using handheld Gracey curettes No. 5/6 (Hu-Friedy Co., Chicago, IL). One trained dental hygienist blinded to the study groups and subgroups made 9–10 strokes in a vertical (apico-coronal) direction and the inclination between scaler tips and roots was maintained as zero [22]. When the curved explorer indicated a smooth and hard dental surface, SRP was judged as completed. In all individuals, SRP was done in one session without any assigned time limit for completion.

2.6. Photodynamic therapy

In groups 1 and 2, aPDT was performed after SRP. The protocol for aPDT is described elsewhere [10]. Briefly, using a blunt needle, 0.005% of Methylene blue was applied into the periodontal pocket and left in place for 10 s. The dye was then irradiated with a diode laser (660 nm) at 150 mW. The fiber diameter, power density of the laser used and duration of irradiation were 600 μm, 75 mW per square centimeters and 60 s, respectively. In each dye filled periodontal pocket, laser irradiation was performed for one minute using a flexible tip. In the present study, aPDT was performed once, at baseline, by a trained investigator.

2.7. Periodontal parameters

One trained and calibrated dental hygienist blinded to the study groups and sub-groups performed the clinical periodontal examination. The overall kappa value for intra-examiner reliability was 0.88. Full-mouth PI [23,24], BOP [23,25], PD [23,26] and clinical AL [21] were measured at 6 sites (mesiobuccal, midbuccal, distobuccal, distolingual/distopalatal, midlingual/midpalatal and mesiolingual/mesiopalatal) per tooth on all maxillary and mandibular teeth. A graded probe (Hu Friedy, IL., Chicago, IL) was used to measure PD in millimeters (mm) [23,27]. Periodontal parameters were measured at baseline and at 1 and 3 months' follow-up.

2.8. Statistical analysis

Statistical analysis was performed using the SPSS software (SPSS Version 18, Chicago, IL). The Kruskall-Wallis test was used to compare the changes in periodontal inflammatory parameters from baseline to 1- and 3-months of follow-up and between treatment modalities among individuals in groups 1 and 2. The primary outcomes was change in PI, BOP, PD and clinical AL. For multiple comparisons, the Bonferroni *post hoc* test was used. It was estimated that with the inclusion of at least 40 individuals per group (assuming a standard deviation of 1.0%), the study would achieve a power of 85% at a two-sided significance level of 0.05.

3. Results

3.1. General characteristics of the study population

In total, 83 male patients with CP (Group-1: 42 cigarette-smokers

Table 1
Characteristics of the study population.

Demographic information	Group-1 (n = 42) (Cigarette-smokers with CP)		Group-2 (n = 41) (Non-smokers with CP)	
	SRP alone	SRP + aPDT	SRP alone	SRP + aPDT
Number of patients (*n*)	22	20	21	20
Gender (male)	22	20	21	20
Mean age ± SD (in pack years)	45.2 ± 3.6	48.4 ± 2.8	44.2 ± 2.4	49.6 ± 3.3
Family history of smoking (%)	72.7%	70%	23.8%	30%
Mean ± SD of duration of cigarette smoking (in pack years)	11.7 ± 0.3	12.5 ± 0.4	NA	NA
Tooth brushing once daily (%)	81.8 %	80 %	80.9 %	75 %
Tooth brushing twice daily (%)	18.2 %	20 %	19.1	25 %

NA: Not applicableSD: Standard deviation*Compared to individuals in Group-2 ($P < 0.01$).

and; Group-2: 41 never-smokers) were included. There was no statistically significant difference in the mean ages of individuals in groups 1 and 2 and their respective subgroups. In group-1, individuals that received SRP alone and SRP with adjunct aPDT had a mean history of cigarette smoking of 11.7 ± 0.3 and 12.5 ± 0.4 pack years. A family history of tobacco smoking was more often reported by individuals in group-1 compared with group-2. At least 80% individuals ingroups 1 and 2 reported to brush their teeth once daily (Table 1). At 3 months' follow-up, 73.8% and 80.5% individuals in groups 1 and 2, reported to brush their teeth twice daily. None of the participants reported any adverse events after both the treatment.

3.2. Periodontal inflammatory parameters among individuals in groups 1 and 2 at 1 and 3 months' follow-up

3.2.1. Group-1

At baseline PI, BOP, PD and clinical AL were comparable among individuals that underwent SRP alone and SRP + aPDT. Compared with 1 month follow-up, baseline PI ($P < 0.05$) was statistically significantly higher among individuals that underwent SRP alone and SRP + aPDT. There was no statistically significant difference in BOP, PD and clinical AL at 1 and 3 months' follow-up among individuals that underwent SRP alone and SRP + aPDT. There was no statistically significant difference in PI, BOP, PD and clinical AL at 1 and 3 months follow-up among individuals that underwent SRP alone and SRP + aPDT (Table 2).

3.2.2. Group-2

At baseline PI, BOP, PD and clinical AL were comparable among individuals that underwent SRP alone and SRP + aPDT. Compared with 1 and 3 month' follow-up, baseline PI ($P < 0.05$), BOP ($P < 0.05$) and PD ($P < 0.05$) was statistically significantly higher among individuals that underwent SRP alone and SRP + aPDT. There was no statistically significant difference in PI, BOP, PD and clinical AL at 1 and 3 months' follow-up among individuals that underwent SRP alone and SRP + aPDT. There was no statistically significant difference in clinical AL at 1 and 3 months follow-up among individuals that underwent SRP alone and SRP + aPDT (Table 3).

3.2.3. Group-1 versus group-2

3.2.3.1. Baseline. PI, PD and clinical AL were comparable among individuals in group-1 compared with group-2. BOP was statistically significantly higher among individuals in group-2 compared with group-1 (Fig. 1a and b).

3.2.3.2. 1 month follow-up. PI was statistically significantly higher and BOP was comparable among individuals in group-1 compared with group-2 among individuals that received SRP alone. PD ($P < 0.05$) and CAL ($P < 0.05$) was statistically significantly higher among individuals in group-1 that underwent SRP alone and SRP + aPDT compared with their counterparts in group-2 (Fig. 1a and b).

3.2.3.3. 3 months' follow-up. PI ($P < 0.05$) was statistically significantly higher and BOP was comparable among individuals in group-1 compared with group-2 among individuals that received SRP alone and SRP + aPDT. PD ($P < 0.05$) and clinical AL ($P < 0.05$) were statistically significantly higher among individuals in group-1 that underwent SRP alone and SRP + aPDT compared with their counterparts in group-2 (Fig. 1a and b).

4. Discussion

The present convenient sample short-term follow-up clinical study was based on the hypothesis that the efficacy of SRP with and without adjunct aPDT is compromised in cigarette-smokers compared with never-smokers. The present results are in accordance with this hypothesis as at 3-months' follow-up, periodontal inflammatory parameters (PI, PD and clinical AL) were statistically significantly higher among individuals in group-1 (cigarette smokers with CP) compared with group-2 (never-smokers with CP). One explanation for this outcome is that the host resistance is altered among individuals in group-1 compare with group-2. Experimental results by Katz et al., [19] showed

Table 2
Mean ± standard deviation of periodontal parameters among individuals in group-1 at baseline and 1 and 3 months' follow-up.

Periodontal parameters	Group-1 (n = 42)					
	SRP alone			SRP + aPDT		
	Baseline	1 month follow-up	3 months' follow-up	Baseline	1 month follow-up	3 months' follow-up
Plaque index (%)	52.6 ± 9.3*	34.9 ± 8.4	38.5 ± 5.6	55.2 ± 5.6*	30.3 ± 5.1	35.2 ± 3.9
Bleeding on probing (%)	35.3 ± 6.9	30.6 ± 6.4	32.7 ± 2.4	31.6 ± 4.5	28.7 ± 2.8	28.2 ± 1.6
Probing pocket depth (in mm)	6.1 ± 0.5	5.4 ± 1.1	5.5 ± 1.2	6.4 ± 0.8	5.7 ± 0.4	5.8 ± 1.1
Clinical attachment loss (in mm)	7.1 ± 0.7	6.3 ± 0.6	6 ± 0.4	7.4 ± 0.7	6.4 ± 0.9	6.2 ± 0.5

* Compared with 1 month follow-up in the same subgroup ($P < 0.05$).

Table 3
Mean ± standard deviation of periodontal parameters among individuals in group-2 at baseline and 1 and 3 months' follow-up.

Periodontal parameters	Group-2 (n = 41)					
	SRP alone			SRP + aPDT		
	Baseline	1 month follow-up	3 months' follow-up	Baseline	1 month follow-up	3 months' follow-up
Plaque index (%)	57.3 ± 8.4*	20.2 ± 3.6	23.5 ± 4.1	54.8 ± 6.6*	21.6 ± 6.2	22.3 ± 4.1
Bleeding on probing (%)	61.2 ± 9.6*	17.3 ± 4.5	20.3 ± 4.7	65.4 ± 8.2*	19.4 ± 8.1	21.6 ± 5.4
Probing pocket depth (in mm)	6.6 ± 0.4*	4.4 ± 0.8	4.1 ± 0.5	6.4 ± 0.5*	4.6 ± 1.1	4.2 ± 0.8
Clinical attachment loss (in mm)	7.2 ± 0.5	5.2 ± 0.3	4.9 ± 0.6	7.1 ± 0.3	5 ± 0.6	5.2 ± 0.4

* Compared with 1 and 3 months' follow-up in the same subgroup ($P < 0.05$).

that the expression of AGEs and RAGE is higher in the periodontal tissues of cigarette-smokers with periodontal disease compared with never-smokers. Moreover, nornicotine, a metabolite of nicotine, upregulates the expression of RAGE in the gingival tissues of cigarette-smokers [18]; which in turn provokes a proinflammatory response by increasing the production of destructive inflammatory cytokines and reactive oxygen species that directly damage the periodontal apparatus [18]. Furthermore, other mechanisms associated with a compromised periodontal healing among cigarette-smokers compared with never-smokers include decreased proliferation of lymphocytes, decreased immunoglobulin G production, altered function of neutrophils and fibroblasts, and increased periodontal pathogens in the oral biofilm [17,28].

In the present study, periodontal inflammatory parameters continued to be higher at 1 month and 3 months' follow-up in group-1 compared with group-2. It is pertinent to mention that in the present study, individuals in group-1 continued to smoke at least up to 3 months of follow-up. The authors applaud the study by Türkoğlu et al. [28] in which, levels of LL-37 (an polypeptide derived from neutrophils, which interferes with innate immune defense) in the gingival crevicular fluid (GCF) were assessed among cigarette-smokers and never-smokers after SRP. The study concluded that SRP is effective in decreasing GCF LL-37 levels in non-smokers with CP but not in cigarette-smokers with CP [28]. This is one explanation for the raised periodontal inflammatory parameters (PI, PD and clinical AL) among cigarette smokers compared with never-smokers. It is also noteworthy that PI was statistically significantly higher at 1 month and 3 months' follow-up among all individuals in group-1 compared with the corresponding

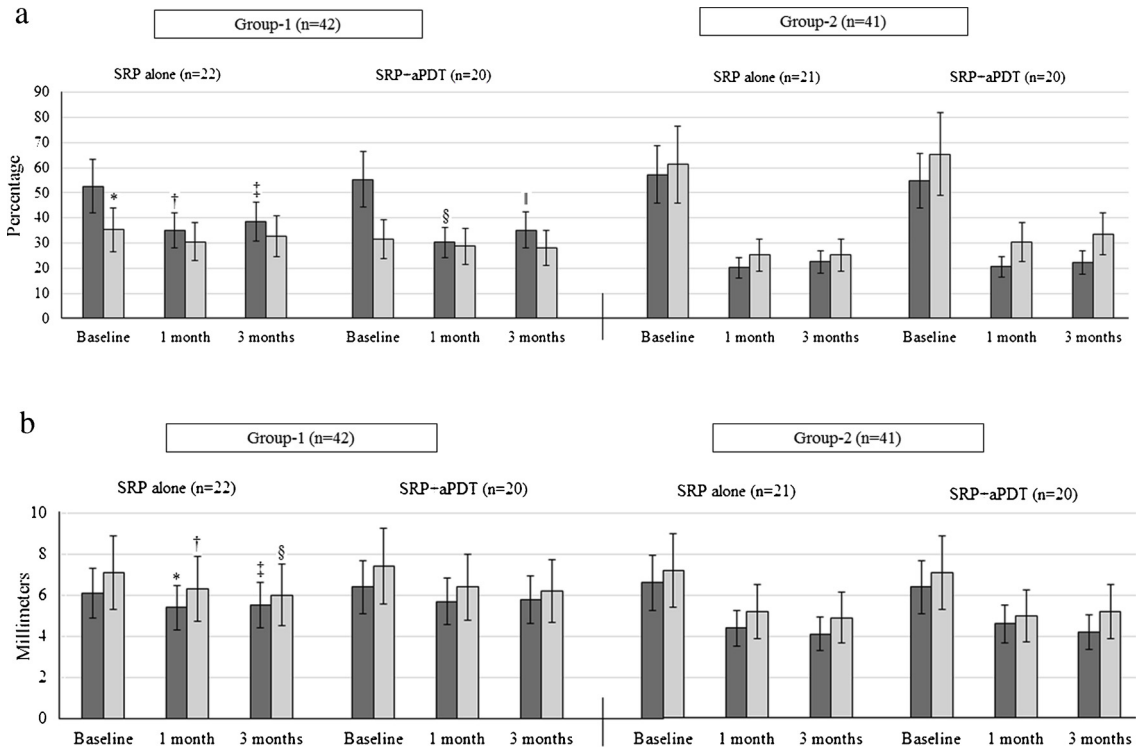

Fig. 1. (a) Mean ± standard deviation of plaque index (dark grey bars) and bleeding on probing (light grey bars) among individuals in groups 1 and 2 at baseline and at 1 and 3 months' follow-up. *Compared with bleeding on probing among individuals that received SRP alone ($P < 0.05$) and SRP + aPDT ($P < 0.05$) in group-2 ; †Compared with plaque index at 1 month follow-up among individuals that received SRP alone ($P < 0.05$) and SRP + aPDT ($P < 0.05$) in group-2; ‡Compared with plaque index at 3 months' follow-up among individuals that received SRP alone ($P < 0.05$) and SRP + aPDT ($P < 0.05$) in group-2; §Compared with plaque index at 1 month follow-up among individuals that received SRP + aPDT ($P < 0.05$) in group-2; and ‖Compared with plaque index at 3 months' follow-up among individuals that received SRP + aPDT in group-2 ($P < 0.05$). (b) Mean ± standard deviation of probing pocket depth (dark grey bars) and clinical attachment loss (light grey bars) among individuals in groups 1 and 2 at baseline and at 1 and 3 months' follow-up. *Compared with probing pocket depth among individuals that received SRP alone ($P < 0.05$) and SRP + aPDT ($P < 0.05$) in group-2; †Compared with clinical attachment loss among individuals that received SRP alone ($P < 0.05$) and SRP + aPDT ($P < 0.05$) in group-2; ‡Compared with probing pocket depth among individuals that received SRP alone ($P < 0.05$) and SRP + aPDT ($P < 0.05$) in group-2; §Compared with clinical attachment loss among individuals that received SRP alone ($P < 0.05$) and SRP + aPDT ($P < 0.05$) in group-2.

time durations among individuals in group-2. One explanation is this regard is that nicotine (a major constituent in cigarette smoke) increases the accumulation of the oral biofilm on oral tissues thereby exposing the periodontal apparatus to periodontopathogenic microbes such as *Aggregatibacter* actinomycetemcomitans, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Treponema denticola* [29,30]. The authors support the results by Kim et al. [31], which showed that reduction in PD and clinical AL are compromise in patients who smoked at least one cigarette per day compared to never-smokers. Despite the significantly high PI and PD in group-1, BOP at baseline was significantly higher among individuals in group-2 compared with group-1. This is most likely associated with the vasoconstrictive effect of nicotine on gingival blood vessels as reported elsewhere [32,33]. This factor may also have contributed towards the compromised periodontal healing among individuals in group-1 than group-2.

The present results showed no statistically significant difference at 1 month and 3 months' follow-up in periodontal parameters among individuals in both groups that received either SRP alone or SRP with adjunct aPDT. With respect to group-1, it is arguable that the non-significant difference in periodontal parameters at both follow-up durations is associated with the detrimental effects of cigarette-smoking (as stated above) on wound healing. Interestingly, among individuals in group-2, there was no statistically significant difference in periodontal parameters among individuals that received SRP alone and SRP with adjunct aPDT for the treatment of CP. This result suggests aPDT is ineffective in reducing periodontal inflammation; however, it is notable that aPDT was done only once (at baseline) throughout the study period. It is hypothesized that if there were additional sessions of SRP with adjunct aPDT (for example at 1-month follow-up), there could have been significant difference in periodontal inflammatory parameters among individuals that received SRP alone and SRP with adjunct aPDT at 3 months' follow-up. Further studies are needed to test this hypothesis.

One limitation of the present study is that systemic diseases such as diabetes mellitus (DM) were excluded. It is known that poorly-controlled DM is a risk-factor of CP [23]. Therefore, it is hypothesized that the outcomes of SRP (with or without aPDT) are worse among diabetic than non-diabetic smokers. Moreover, studies [34–36] have shown that periodontal inflammation is poorer in habitual alcohol and smokeless tobacco (ST) product users. There is a likelihood that outcomes of SRP (with or without adjunct therapies such as aPDT) are compromised in habitual alcohol and ST-product users. Furthermore, patients in the present study were approximately 45 years old. According to Javed et al. [23], CP is worse in older individuals (> 60 years old) compared with younger individuals (< 50 years old). It is therefore speculated that the outcomes of SRP (with or without aPDT) are compromised in older compared with younger patients with CP. Studies [37,38] have shown that hormonal fluctuations during menstruation are associated with an increased expression of destructive inflammatory cytokines including IL-1β, TNF-α and IL-6 in the oral fluids, which make trigger periodontal inflammatory conditions. In the present study, all participants were male. It is speculated that hormonal alterations in females may affect periodontal healing after SRP with or without aPDT. In the present study, aPDT was performed once. There is a possibility that multiple episodes of aPDT following SRP is more effective in reducing periodontal inflammation compared with a single episode of aPDT with adjunct SRP. Assessments of these hypotheses warrants further research.

5. Conclusion

Outcomes of SRP with or without aPDT for the treatment of CP are compromised in cigarette-smokers than never-smokers. Among never-smokers with CP, outcomes of SRP with or without aPDT are comparable. The significance of aPDT in this regard remains questionable.

Conflict of interest statement

The authors declare that they have no conflict of interest and all authors have read and approved the final draft.

Acknowledgement

The authors extend their appreciation to the International Scientific Partnership Program ISPP at King Saud University, Riyadh, Saudi Arabia for funding this research work through ISPP#0075.

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