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Impact of tooth-related factors on photodynamic therapy effectiveness during active periodontal therapy: A 6-months split-mouth randomized clinical trial

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ABSTRACT

Background: The persistence of periodontal pockets > 5 mm after periodontal treatments increases the risk of periodontitis recurrence and the need of periodontal surgery. This study evaluated the impact of tooth-related factors on the effectiveness of adjunctive photodynamic treatment (PDT) in the reduction of pockets > 5 mm during active periodontal treatment.

Methods: Thirty-six patients suffering from severe chronic periodontitis were evaluated in a 6-months split-mouth randomized clinical trial. Each quadrant was assigned to test (scaling and root planing (SRP) + PDT) or control (SRP alone) group. PDT was conducted using the toluidine blue O and a light-emitting diode (LED) with a red spectrum. PDT applications were performed immediately after SRP, 7 days later and at 3 months. Plaque index (PI), bleeding on probing (BOP), periodontal pocket depth (PPD), and clinical attachment level (CAL) were recorded at baseline, 3 and 6 months.

Results: Multilevel analysis showed a significant reduction of pockets > 5 mm in test group in comparison with control group at 3 (OR = 0.69) and 6 months (OR = 0.77). This effect was mainly observed at 6 months in initially deep sites (PPD > 6 mm) with BOP (OR = 0.57). At sites exhibiting PI > 1 no PDT effect was observed. A more moderate PDT effect was observed on mean PPD and BOP reductions at 3 months only.

Conclusions: Repeated applications of PDT significantly improved SRP outcomes, reducing by more than 40% residual pockets > 5 mm in initially deep and bleeding on probing periodontal sites. PDT effect was negatively influenced by dental plaque accumulation.

1. Introduction

Periodontitis is characterized by an imbalance within host-pathogen relationship [1]. Periodontal primary cares aim to restore equilibrium through removal of periodontal pathogens and reduction of inflammation. Scaling and root planing (SRP) has been established as a cornerstone of this cause-related therapy. It has proven its efficacy in reducing periodontal pocket depth (PPD) and improving clinical attachment level (CAL) [2]. However, SRP presents some limitations especially at deep periodontal sites with PPD > 6 mm [2], or around multi-rooted teeth where "pocket closure" (PPD ≤ 4 mm) [3] and the removal of all periodontal pathogens are not easily achieved [4]. To increase SRP efficacy, adjunctive treatments have been developed such as the use of systemic antibiotics [5,6]. However, their frequent use could be responsible for the development of bacterial resistance [5] and may induce adverse side effects [7]. Adjunctive photodynamic therapy (PDT) is a locally administered and a non-invasive antimicrobial approach without side effects recently introduced among the periodontal treatments' arsenal [8,9]. Its antimicrobial properties are based on the production of cytotoxic reactive oxygen species by a photoactivatable agent (or photosensitizer) exposed to a light of compatible wavelength [10].

Clinical improvements associated to PDT during active periodontal treatment of periodontitis have been reported [11–16]. However, additional benefits and clear indications towards the use of this adjunctive therapy remain to be determined [17] due to the high heterogeneity of

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study designs and PDT application protocols as highlighted in several meta-analyses [8,9,18]. For instance, effectiveness of adjunctive antimicrobial treatments has been shown to be influenced by periodontitis severity and PPD levels [5]. Indeed, PDT is highly dependent from the periodontal pocket micro-environment where it is applied (pH, presence of exudates, bleeding) which may vary with PPD [19]. Many investigations on PDT effect were restricted to shallow-to-moderate periodontal pockets [11,20] or deeper periodontal pockets [21] or both [12,16,22]. Moreover, in some cases, selected inflamed sites exhibited bleeding on probing (BOP) [23]. The type of selected teeth and furcation involvements could also influence PDT effects [24]. Furthermore, the main studied periodontal treatment outcomes were the reduction of mean PPD, CAL, and gingival inflammation [9]. However, the improvement of mean PPD or CAL due to PDT could be considered too modest (< 1 mm) to indicate this treatment approach in all cases [17]. From a clinical point of view, the number of residual pockets > 5 mm after active periodontal therapy could be more helpful to determine the benefit of PDT [5,25,26]. Indeed, those residual pockets after active periodontal therapy have been associated to the risk of periodontitis recurrence [27] and to the need of periodontal surgery [28], increasing the cost of periodontal treatment [5]. Finally, other factors such as oral hygiene and smoking have been suggested to influence PDT effectiveness [9,17,29].

Therefore, the aim of this double-blind, randomized, split-mouth controlled clinical trial was to evaluate the effect of repeated PDT on residual pockets > 5 mm during non-surgical treatment of severe generalized chronic periodontitis at 6 months and the influence of tooth-related factors, dental plaque accumulation and smoking using a multilevel analysis.

2. Materials and methods

2.1. Study population and inclusion/exclusion criteria

This study was approved by the Institutional Ethical committee of the University Hospitals of Strasbourg (Registration date: January 8, 2014, ClinicalTrials.gov Identifier: NCT02030470) and was carried out according to the Declaration of Helsinki (2008). All participants received written information about the objectives of this trial and their written informed consent was obtained. Patients attending periodontal consultation at the Department of Periodontology, University Hospitals of Strasbourg, France and diagnosed with severe generalized chronic periodontitis [30] were invited to participate in this study. Patient recruitment extended from June 2014 to June 2017. Age, gender, medical and dental history, and smoking status were obtained by patient self-reporting. The inclusion criteria comprised, (a) ≥ 40 years old, (b) ≥ 20 teeth (excluding third molars), (c) ≥30% of sites with CAL > 5 mm and ≥5 sites with PPD ≥ 5 mm per quadrant (d) ≥ 1 molar per quadrant (except for third molars), (e) radiographic bone loss, and (f) BOP ≥ 30%. The exclusion criteria comprised, (a) aggressive periodontitis, (b) smokers > 10 cigarettes/day, (c) periodontal, antibiotic, anti-inflammatory, anticoagulant treatment in the last 6 months, (d) metabolic, endocrinal or hormonal diseases, (e) medical history likely to compromise treatment outcomes, and (f) pregnant or breastfeeding patients.

2.2. Clinical measurements

Clinical parameters were recorded at six sites per tooth, at baseline, 3 and 6 months. Clinical parameters included Plaque index (PI) [31], BOP, PPD, gingival recession, and CAL. BOP was recorded based on the presence or not of bleeding 30 s after probing. PPD was measured in millimeters from the gingival margin to the depth of the periodontal pocket. Gingival recession was measured in millimeters from the gingival margin to the cemento-enamel junction. CAL was measured in millimeters from the cemento-enamel junction to the bottom of the pocket. A PCPUNC 15 periodontal probe (Hu-Friedy, Chicago, IL, USA) was used.

The difference between groups for the number of pockets with PPD > 5 mm was the primary outcome. The differences between groups for BOP%, mean PPD and CAL were considered as secondary outcomes.

2.3. Randomization

A randomized split-mouth double-blind controlled design (RCt) was used. All investigators were trained periodontists. None of the investigators (LA, AC, AM, CP, JLD) were aware of treatment allocation when they performed examination and SRP at baseline, 3 months or 6 months. At baseline (V1), PDT treatment was performed according to a predefined computer-generated balanced block randomization table with a 1:1 allocation and each of the four quadrants per patients was assigned to either a test group (SRP + PDT) or control group (SRP). Blinding to the randomization was insured using sealed and opaque envelopes numbered in sequence opened only after SRP. Envelopes were resealed until the next visits. At 3 months (V2), the same procedure was repeated with a second investigator, unaware of the randomization before periodontal reevaluation and additional SRP. At 6 months (V3), a third investigator blinded to the previously allocated quadrants, performed the final re-evaluation. The patients were not aware about which quadrant received the PDT treatment.

2.4. Study design and treatments

At the screening visit, all patients received oral hygiene instructions (OHI), including brushing technique instructions and towards use of interproximal hygiene devices, and supra-gingival scaling. At V1, SRP was performed using ultrasonic device (Newtron®, Merignac, France) and manual curets (Deppeler, Rolle, Swiss) under local anesthesia [32]. SRP and PDT were performed in sites with PPD > 3 mm in test quadrants [12]. Three sessions including OHI, SRP and PDT were performed within 3 weeks: first session, SRP of the maxillary arch + randomization + PDT in maxillary test quadrant; second session, SRP of the mandibular arch + randomization + PDT in mandibular test quadrant + 2nd PDT application in the maxillary test quadrant; third session, 2nd PDT application in the mandibular test quadrant. Patients were instructed to rinse with a chlorhexidine mouthwash (0.12%) twice a day for 15 days. At V2, OHI was performed if needed after periodontal reevaluation. SRP and PDT were then performed in residual sites with PPD > 3 mm following the same quadrant allocation described at V1 (Fig. 1).

PDT was performed using FotoSan® device (CMS Dental, Copenhagen, Denmark) [20]. The light source consisting in a light-emitting diode (LED), with a red spectrum (wavelength: 625–635 nm, power peak at 628 nm; maximum output power density: 2000 mW/cm2) used with the photoactivatable agent toluidine blue O (TBO), 0.1 mg/ml (FotoSan® agent medium viscosity). According to manufacturer's recommendations TBO was applied at test sites with a needle for 1 min and then irradiated by the LED for 10–30 s depending on the depth of the pocket with a long specific pocket tip and followed by a 10 s irradiation with a blunt trans-gingival tip. In the control quadrants, sham irradiation was carried out. Hence, two applications of PDT with an interval of 1 week were done in test sites at V1, and 1 application at V2.

2.5. Examiner calibration

Examiners underwent inter-examiner calibration on patients not included in the study. The percentage of agreement within ± 1 mm with another experimented examiner (JLD) had to be at least 80%. The intra-class correlation coefficients were > 0.8.

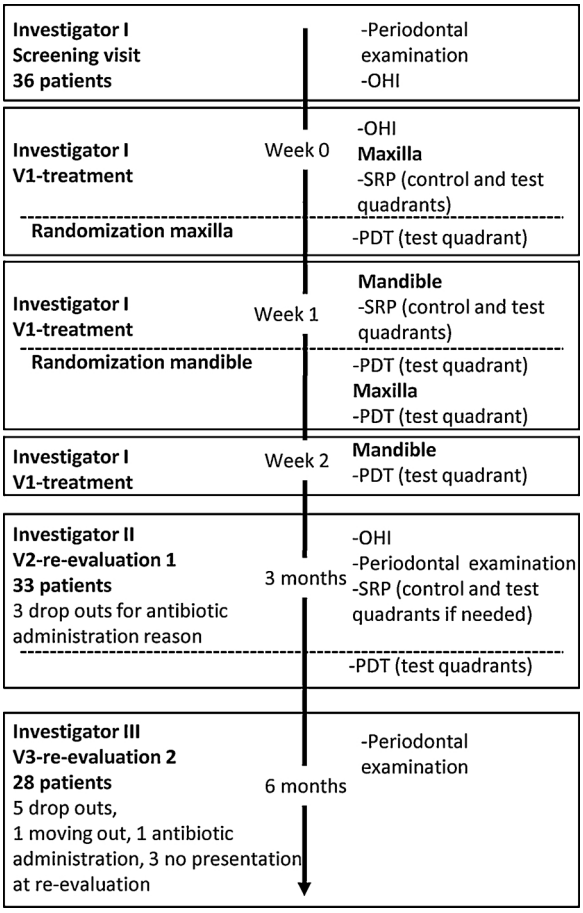

Fig. 1. Study design and flow-chart.
OHI: oral hygiene instructions, SRP: scaling and root planning, PDT: adjunctive photodynamic therapy.

2.6. Calculation of sample size

The objective was to highlight a 25% reduction in the rate of sites with PPD > 5 mm at 6 months between test and control groups with a power of 80% and an alpha risk set at 5%. Based on an average number of 150 sites per patient, a total of 28 patients was required to detect such a difference. Considering 20% of potential missing data, 36 patients were finally included in the study.

2.7. Statistical analyses

The qualitative variables are presented as effectives and percentages. Quantitative variables are described using the mean +/- SD. Comparison of the baseline characteristics was carried out using multilevel regression model including nested random effects (sites / teeth / jaws and subject effects). Gamma distribution was used for quantitative variable and binomial distribution for qualitative variable. The comparison of the principal endpoint (PPD > 5 mm) at 3 and 6 months was performed using multilevel logistic regression model including an interaction term between time (baseline, 3 months and 6 months) and treatment group (SRP or SRP + PDT). All the subgroup analyses were performed by introducing interactions triple in this model (between time, treatment group and the local factor of interest or between the treatment group and two different local factors). The results are presented as odds ratios with their 95% confidence intervals. A *p-value* < 0.05 was considered as statistically significant. All analyses were realized using R software version 3.3.2. R Core Team (R: A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/)) (2015).

Table 1
Demographic characteristics at baseline.

	N = 36
Age (years)	50.25 ± 5.98
Women, n (%)	22 (61.1)
Smoker n (%))	11 (30.5)

3. Results

3.1. Studied population characteristics

At baseline, 36 patients were included in the study corresponding to 2820 and 2802 analyzed sites in test and control groups, respectively. The mean age was 50.25 ± 5.98 years, the percentage of women was 61.1 (22 patients), and the percentage of smokers was 30.6 (11 patients) (Table 1). During the 3-months follow-up, 3 patients were excluded due to the administration of antibiotics (2 following an extraction and 1 for an endodontic abscess). At 6 months, five other patients were lost: one moved out, one received antibiotics for medical reasons, and three did not attend the visit. Thus, 33 subjects were analyzed at 3 months, corresponding to 2556 sites in test and control groups, and 28 subjects at 6 months corresponding to 2160 and 2178 sites in test and control groups, respectively (Fig. 1). None of the patients reported adverse effects after therapies.

3.2. Initial periodontal parameters and treatment outcomes in test (SRP + PDT) and control (SRP) groups

The mean number of teeth and the percentage of molars was 13.0 ± 1.0 and 27.7% in SRP, and 13.1 ± 1.2 and 27.8% in SRP + PDT groups. There was no significant difference between the treatment groups at baseline for pockets > 5 mm, BOP%, mean PPD and CAL, and PI (Table 2).

During treatment, a significant improvement of all clinical parameters was observed in both groups and was more pronounced from baseline to 3 months than from 3 to 6 months. A significant difference in favor of SRP + PDT was observed at 3 months for pockets > 5 mm (OR = 0.69), BOP (OR = 0.86), and mean PPD. This difference was still observed at 6 months for pockets > 5 mm (OR = 0.77) but not for BOP and mean PPD. There was not difference related to PI and CAL changes between groups (Table 3).

3.3. Influence of local factors on residual pockets > 5 mm and PDT effect

The number of deep sites (PPD > 6 mm) at baseline was 226 in SRP + PDT group, and 251 in SRP group. At 3 months, the positive effect of PDT on pockets > 5 mm reduction was mainly observed at sites with initially PPD ≤ 6 mm (OR = 0.74, $p = 0.012$). At 6 months, the opposite trend could be observed as PDT effect appeared more

Table 2
Pockets > 5 mm, BOP, mean PPD, mean CAL and PI at baseline in SRP + PDT and SRP groups.

	SRP + PDT	SRP	*p*-value
Pockets > 5 mm, number (%)	579 (20.58)	609 (21.73)	0.330
BOP number (%)	1830 (64.89)	1804 (64.64)	0.949
Mean PPD, mm (SD)	4.06 ± 1.71	4.10 ± 1.72	0.520
Mean CAL mm (SD)	4.79 ± 2.07	4.77 ± 2.06	0.875
PI > 1 number (%)	612 (21.95)	615 (21.70)	0.369

SRP: scaling and root planing, PDT: adjunctive photodynamic treatment, PI: plaque index, BOP: bleeding on probing, PPD: periodontal pocket depth, CAL: clinical attachment level.

Table 3
Pockets > 5 mm, BOP, mean PPD, mean CAL, and PI at 3 and 6 months in SRP + PDT and SRP groups.

	SRP + PDT	SRP	*p*-value	OR
Pockets > 5 mm number (%)				
3 months	**207 (8.10)**	**273 (10.68)**	< 0.001*	0.69
6 months	**141 (6.53)**	**171 (7.85)**	0.037*	0.77
BOP number (%)				
3 months	**826 (32.39)**	**892 (34.93)**	0.020*	0.86
6 months	**701 (32.48)**	**723 (33.12)**	0.435	0.95
Mean PPD mm (SD)				
3 months	**3.16 ± 1.62**	**3.26 ± 1.61**	< 0.001*	
6 months	**2.93 ± 1.42**	**2.94 ± 1.43**	0.704	
Mean CAL mm (SD)				
3 months	**4.06 ± 2.06**	**4.10 ± 2.03**	0.107	
6 months	**3.94 ± 1.99**	**3.92 ± 1.93**	0.967	
PI > 1 number (%)				
3 months	**395 (15.35)**	**365 (14.35)**	0.115	1.15
6 months	**271 (12.55)**	**247 (11.35)**	0.282	1.12

SRP: scaling and root planing, PDT: adjunctive photodynamic therapy, PI: plaque index, BOP: bleeding on probing, PPD: periodontal pocket depth, CAL: clinical attachment level.
In bold, significant change of clinical parameters ($p < 0.05$) at 3 or 6 months compared to baseline, * significant. difference between SRP + PDT and SRP groups ($p < 0.05$).

Table 4
Subgroup analyses: multilevel logistic regression analysis of local factor influences on PDT effect on the number of residual pockets > 5 mm at 3 and 6 months.

Baseline	Pockets > 5 mm					
	3 months			6 months		
	OR	95% CI	p-value	OR	95% CI	p-value
PPD ≤ 6 mm	0.74	0.59 - 0.94	0.012*	0.91	0.59 - 1.22	0.533
PPD > 6 mm	0.76	0.51 - 1.22	0.157	0.69	0.44 - 1.08	0.111
BOP +	0.77	0.61 - 0.97	0.024*	0.83	0.64 - 1.08	0.161
BOP –	0.68	0.48 - 0.95	0.025*	0.79	0.47 - 1.33	0.368
Molars	0.84	0.63 - 1.12	0.23	0.83	0.59 - 1.17	0.281
Non-molars	0.64	0.49 - 0.83	< 0.001*	0.81	0.58 - 1.13	0.208

BOP+: positive bleeding on probing. BOP-: no bleeding on probing, PPD: periodontal pocket depth, OR: odds ratio, CI: confidence interval.
* significant difference between SRP and SRP + PDT groups (p < 0;05).

pronounced in initially deep sites (PPD > 6mm) (OR = 0.69, p = 0.111). PDT positive effects were similar in sites with or without BOP at baseline. The reduction of pockets > 5 mm was more pronounced in SRP + PDT group in non-molars at 3 months (OR = 0.64, $p < 0.001$) but not at 6 months (Table 4).

When combining baseline local factors, multilevel logistic regression models showed that use of PDT was significantly associated with a reduced number of residual pockets > 5 mm at 3 months in site with initially a PPD ≤ 6 mm, with (OR = 0.72, p = 0.041) or without BOP (OR = 0.62, p = 0.024) at baseline. At 6 months, PDT effect on residual pockets > 5mm was only observed in initially deep sites (PPD > 6mm) with BOP (OR = 0.57 p = 0.033). Regarding the combined influence of deep sites (PPD > 6mm) at baseline and the type of tooth, a PDT effect was significantly observed in non-molar sites with a PPD ≤ 6 mm at 3 months (OR = 0.52, p < 0.001). At 6 months, a tendency to a better reduction of residual pockets > 5mm with PDT was shown in non-molar teeth deep sites (PPD > 6mm) (OR = 0.59, p = 0.108) (Table 5).

Table 5
Subgroup analyses: multilevel logistic regression analysis of the combined influence of initial PPD, BOP and tooth type on the presence of residual pockets > 5 mm at 3 and 6 months.

Baseline	Residual pockets > 5 mm at 3 months					
	BOP +			BOP -		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
PPD ≤ 6 mm	0.72	0.53 - 0.98	0.041*	0.62	0.41 - 0.94	0.024*
PPD > 6 mm	0.64	0.38 -1.06	0.083	1.47	0.51 - 4.23	0.475
	Molars			**Non-molars**		
PPD ≤ 6 mm	0.80	0.44 - 1.46	0.480	0.52	0.37 – 0.72	< 0.001*
PPD > 6 mm	0.66	0.34 -1.29	0.232	0.97	0.66 - 1.42	0.895

Baseline	Residual pockets > 5 mm at 6 months					
	BOP +			BOP -		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
PPD ≤ 6 mm	0.92	0.66 - 1.28	0.625	0.87	0.46 - 1.63	0.657
PPD > 6 mm	0.57	0.34 - 0.96	0.033*	1.45	0.48 - 4.46	0.511
	Molars			**Non-molars**		
PPD ≤ 6 mm	0.84	0.43 - 1.64	0.613	0.87	0.58 - 1.31	0.512
PPD > 6 mm	0.94	0.62 -1.42	0.766	0.59	0.31 - 1.12	0.108

BOP+: positive bleeding on probing, BOP-: no bleeding on probing, PPD: periodontal pocket depth, OR: odds ratio. CI: confidence interval.
* significant difference between SRP and SRP + PDT groups (p < 0;05).

3.4. Influence of oral hygiene, smoking on residual pockets > 5 mm and PDT effects

A dichotomic PI was used in order to distinguish adequate oral hygiene corresponding to visible dental plaque [33]. When PI was ≤ 1 at baseline (78% of sites), PDT was more effective in reducing the number of residual pockets > 5 mm at 3 months (OR = 0.72, p = 0.003). The same trend was observed at 6 months (OR = 0.77, p = 0.060). Adversely, when PI > 1, there was no superiority of PDT over SRP alone in reducing those pockets. Interestingly, when PI was ≤ 1 at 6 months, the same trend was observed for those pockets at 6 months (OR = 0.78, p = 0.068). In non-smokers, PDT was more effective in reducing the number of residual pockets > 5mm at 3 months (OR = 0.66, $p < 0.001$). The same trend was observed at 6 months (OR = 0.74, p = 0.057). In smokers, there was no apparent additional effect of PDT over SRP alone in reducing residual pockets > 5mm at 3 and 6 months (Table 6).

4. Discussion

This double-blind randomized clinical trial aimed to evaluate the

Table 6
Subgroup analyses: multilevel logistic regression analysis of PI and smoking influences on PDT effect on the number of residual pockets > 5 mm at 3 and 6 months.

Baseline	Residual Pockets > 5 mm					
	3 months			6 months		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
PI ≤ 1	0.72	0.58 - 0.89	0.003*	0.77	0.59 - 1.01	0.060
PI > 1	0.81	0.55 - 1.19	0.281	0.98	0.61 – 1.56	0.931
Non-smokers	0.66	0.52 - 0.83	0.001*	0.74	0.55 - 1.01	0.057
Smokers	0.92	0.66 - 1.28	0.618	0.94	0.65 - 1.34	0.723

PI: plaque index, PPD: periodontal pocket depth, OR: odds ratio, CI: confidence interval.
* significant difference between SRP and SRP1 + PDT groups (p < 0;05).

clinical effectiveness of PDT in the treatment of severe chronic periodontitis. The results showed that PDT could significantly improve non-surgical periodontal treatment outcomes at 3 and 6 months reducing residual periodontal pockets > 5 mm. Interestingly, PDT effects were modulated by tooth-related risk factors, dental plaque accumulation, and smoking.

Repeated applications of PDT significantly decreased the number of pockets > 5 mm by 31% (OR = 0.69) and 23% (OR = 0.77) in comparison with SRP alone at 3 and 6 months, respectively. This effect of PDT on pockets > 5 mm has been previously suggested at 3 months during active periodontal treatment [12,15]. The persistence of those pockets after active periodontal therapy is considered as a failure of periodontal treatment [5] and is associated to periodontitis recurrence during supporting periodontal therapy [27]. An additional 14% (OR = 0.86) reduction of BOP was also observed in PDT subgroup at 3 months suggesting a concomitant reduction of inflammation with residual pocket reduction. This effect of PDT on BOP changes was inconstantly observed in others studies [8]. An additional 15% of BOP reduction due to PDT has been previously described at 3 months in a comparable study [12]. This beneficial effect of PDT on residual pockets and BOP could reduce the perceived need of antibiotic treatment and surgery [2,5,25,34].

The effects of PDT on other periodontal parameters were more limited. A significant 0.1 mm improvement of mean PPD reduction by PDT was also observed but only at 3 months. This modest difference may be explained by the fact that the reduction of mild and moderate pockets (PPD ≤ 5 mm) appeared less influenced by PDT (data not shown), as previously suggested [12]. Such a similar significant small difference of mean PPD has been previously observed for PDT [12]. Mean CAL followed the same trend than mean PPD but there was no significant difference between test and control groups at any time. An attenuation of PDT effect was observed with time for all periodontal parameters. In the study of Goh et al. (2017), PDT application at residual pockets ≥ 5 mm during supporting periodontal treatment significantly improved PPD reduction at 3 months but not at 6 months [35]. These data suggested the existence of a “dose effect” of PDT [13]. During supporting periodontal treatment, two PDT applications within 1 week have been shown to be more efficient than one PDT application to reduce residual pockets [36]. In the present study, the fact that two PDT applications were performed at baseline, but only one at 3 months may explain the attenuated effect of PDT in re-instrumented residual test sites.

Many local and behavioral factors and their combination have been shown to modify SRP effectiveness at short term, such as initial PPD, tooth type, dental plaque accumulation and smoking [3]. The effect of PDT on residual pockets > 5 mm appeared also to be influenced by these factors [9,37]. At 3 months, PDT positive effect on residual pockets > 5 mm was mainly observed in mild and moderate sites with PPD ≤ 6 mm (OR = 0.74). At 6 months, an influence of initially deep sites (PPD > 6 mm) only persisted (OR = 0.69). Furthermore, the effect of PDT was only observed in non-molars (OR = 0.64) at 3 months. The difficulty to access to deep pockets and the presence of furcation on molars may limit PDT antiseptic action, as previously suggested [21]. Indeed, there was no additional improvement of furcation with PDT [24]. Interestingly, effect of PDT was amplified in subsets of periodontal pathologic sites defined by the combinations of local risk factors. The reduction of residual pockets > 5 mm was increased by 43% with PDT (OR = 0.57) in initially deep sites (PPD > 6 mm) with BOP. These data suggested that pocket reduction with PDT was more efficient and beneficial in deep (PPD > 6 mm) and inflamed/bleeding upon probing pockets, as shown for antibiotics [5,6]. Another study did not find a significant effect of PDT in this type of sites at 12 months [21]. However, the difference of protocol, such as the lack of systematic subgingival re-instrumentation and PDT application following active phase, as well as the limited number (four) of selected experimental teeth could explain these different results.

In the present study, the level of oral hygiene at baseline and at 6 months influenced PDT effect. The positive effect of PDT on pockets > 5 mm reduction was only observed at sites with a PI ≤ 1. These data emphasized the importance of good oral hygiene habits before and during treatment to optimize PDT results, as shown for SRP [3]. Smoking was also a major risk factor of periodontal treatment failure [38]. In the studied population, patients smoking not more than 10 cig/day have been included and they smoked a mean number of 7 cigs/day. In spite of this relative low tobacco consumption, the positive effect of PDT on pockets > 5 mm reduction was not observed in smokers but only in non-smokers. These results are in accordance with studies performed with heavy smokers (≥ 10cigarettes per day) at 3 months [29] where not significant intergroup clinical differences regarding mean PPD and/or residual pockets were measured. However, a significant reduction of moderate and deep pockets was observed in smokers at 6 months with PDT and not with SRP alone [16]. These data showed that smoking could modify PDT effect and could also explain some discrepancies between our results and results of other studies which were not stratified according to smoking status [20–22,39].

This study was designed as a split-mouth trial, in order to have a strong homogeneity between groups. However, in spite of the high number of investigated sites, the power of multilevel analysis between some subgroups could be limited. Furthermore, the number of included patients could limit the analysis of patient-related factor effects such as smoking effect and the corresponding results could be more considered exploratory. The disadvantage of the split-mouth design was the possible recontamination from the control side or a “carry-across” effect of PDT on the control side [40]. The choice of a 5 mm PPD threshold for residual pockets to determine the need of additional therapy or surgery could also be discussed while other authors having defined this need for sites with PPD > 4 mm and BOP [36].

5. Conclusions

This study showed that PDT efficiency was significantly influenced by tooth-related factors. PDT significantly improved the reduction of residual pockets > 5 mm at 6 months and was especially beneficial for initially deep and inflamed/bleeding on probing periodontal sites. This effect was more important in patients with good oral hygiene and in non-smokers. Thus, considering these influencing factors, the cost/benefit ratio of PDT appeared clinically relevant, reducing the needs of surgery.

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