

Effect of surgical periodontal treatment associated to antimicrobial photodynamic therapy on chronic periodontitis: A randomized controlled clinical trial

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Funding information

This study was financially supported by the São Paulo Research Foundation – FAPESP (protocol number 14/09801-9).

Abstract

Aim: This randomized controlled clinical trial evaluated the effects of an adjunctive single application of antimicrobial photodynamic therapy (aPDT) in Surgical Periodontal Treatment (ST) in patients with severe chronic periodontitis (SCP).

Material and Methods: In a split-mouth design, 20 patients with SCP were treated with aPDT+ST (Test Group, TG) or ST only (Control Group, CG). aPDT was applied in a single episode, using a diode laser and a phenothiazine photosensitizer. All patients were monitored until 90 days after surgical therapy. Levels of 40 subgingival species were measured by checkerboard DNA-DNA hybridization at baseline, 60 and 150 days. Clinical and microbiological parameters were evaluated.

Results: In deep periodontal pockets depth (PPD ≥ 5 mm), Test Group presented a significantly higher decrease in PPD than Control Group at 90 days after surgical therapy ($p < .05$). Test Group also demonstrated significantly less periodontal pathogens of red complex (*Treponema denticola*) ($p < .05$).

Conclusion: A single episode of aPDT used in adjunct to open flap debridement of the root surface in the surgical treatment of SCP: i) significantly improved clinical periodontal parameters; ii) eliminates periodontal pathogens of the red complex more effectively (NCT02734784).

KEYWORDS

antimicrobial photodynamic therapy, chronic periodontitis, microbiology, photosensitizing, surgical treatment

1 | INTRODUCTION

Chronic periodontitis is an infectious disease resulting in inflammation within the supporting tissues of the teeth, loss progressive attachment and bone loss and is characterized by pocket formation and/or gingival recession (Genco & Borgnakke, 2013). Periodontal pockets, a unique environment for colonizing microorganisms, contains at least 400 species of bacteria, which are organized in biofilms (Paster & Dewhirst, 2009). The subgingival biofilm differs markedly in periodontal health and in periodontitis (Slots, 1979). Thus, treatment modalities aimed at

biofilm control are essential for the treatment of periodontitis (Baker, 1995).

Scaling and root planing (SRP) is the most common periodontal treatment which has proven clinical effectiveness in terms of decreasing the probing pocket depth, reducing inflammation and improving the clinical attachment level (CAL) (Haffajee et al., 1997). SRP has some limitations, such as difficulties in accessing deeper pockets, root concavities and furcation areas (Nagarakanti, Gunupati, Chava, & Reddy, 2015; Rabbani, Ash, & Caffesse, 1981) and difficulty to remove microbial pathogens that have penetrated into dentinal tubules

and which are residing in lacunae and concavities (Mombelli, Cionca, & Almaghlouth, 2011).

The limitations of SRP become more evident particularly if the disease has led to the formation of pockets deeper than 5 mm around the affected teeth (Badersten, Nilveus, & Egelberg, 1987; Caffesse, Sweeney, & Smith, 1986; Rabbani et al., 1981). To facilitate scaling and root planing, and to allow direct visual control in deep pockets, the soft tissues can be detached surgically for better access (Deas, Moritz, Sagun, Gruwell, & Powell, 2016; Heitz-Mayfield & Lang, 2013).

Antimicrobial photodynamic therapy (aPDT) is becoming an effective method of antibacterial treatment and may be used as adjunct therapy for the treatment of severe periodontitis (de Oliveira, Schwartz-Filho, Novaes, & Taba, 2007). aPDT has been evaluated in in vitro and in vivo studies (Betsy, Prasanth, Baiju, Prasanthila, & Subhash, 2014; Carvalho et al., 2015; Chondros et al., 2009; Komerik, Wilson, & Poole, 2000; Komerik et al., 2003; Moreira et al., 2015; de Oliveira, Novaes, Taba, de Souza, & Papalexou, 2007; Qin, Luan, Bi, Sheng, et al., 2008; Ramos et al., 2016; Sarkar & Wilson, 1993). This therapy presents the principle of eliminating cells through the use of a photosensitizing agent (optical absorption-dye) and a light source (low-intensity laser with the appropriate wavelength). It may thus promote the elimination of microorganisms present in periodontal tissues (Moreira et al., 2015; Novaes et al., 2012; Petelin, Perkic, Seme, & Gaspirc, 2015; Qin, Luan, Bi, Sheng, et al., 2008).

The use of aPDT presents divergent results on the non-surgical treatments of chronic periodontitis. Some authors achieved better clinical outcomes in favour of aPDT (Andersen, Loebel, Hammond, & Wilson, 2007; Berakdar, Callaway, Eddin, Ross, & Willershausen, 2012; Birang, Shahaboui, Kiani, Shadmehr, & Naghsh, 2015; Braun, Dehn, Krause, & Jepsen, 2008), others only present differences on bleeding on probing (Chondros et al., 2009; Christodoulides et al., 2008) and a significant reduction in the percentage of sites positive for periodontal pathogenic bacteria (Theodoro et al., 2012). On the other hand, some studies failed to show an additional benefit of aPDT on clinical periodontal parameters and subgingival microbial flora (Balata et al., 2013; Polansky, Haas, Heschl, & Wimmer, 2009).

Based on this previous literature, aPDT may be effective as an adjunctive therapy to periodontal mechanical debridement, especially in cases of advanced periodontal disease and in sites where there is a difficult access for complete root surfaces decontamination using manual instruments, as for example teeth with furcation lesions, presence of concavities, narrow and deep periodontal pockets.

The aim of this study was to evaluate the effects of single application of aPDT associated with Surgical Periodontal Treatment (ST) or ST alone in patients with severe chronic periodontitis (SCP) following surgical treatment.

2 | MATERIALS AND METHODS

2.1 | Subject population

Twenty subjects were selected from the population referred to the Periodontal Clinic of the University. Subjects who fulfilled the

Clinical Relevance

Scientific rationale for the study: Patients with severe chronic periodontitis (SCP) may present continuous periodontal attachment loss after non-surgical therapy with scaling and root planing (SRP). As aPDT has emerged as an adjuvant method to SRP in the treatment of SCP, the combined treatment with aPDT and surgical periodontal treatment was investigated.

Principal findings: Single episode of aPDT adjunctive to surgical treatment of SCP significantly improves clinical periodontal parameters and eliminates periodontal pathogens more effectively than Surgical Periodontal Treatment alone.

Practical implications: aPDT can be an alternative to adjunctive treatment to SRP + surgery in the treatment of advanced forms of periodontal diseases.

inclusion criteria were invited to participate in the study (*ClinicalTrials.gov* ID: NCT02734784). All eligible subjects signed an Informed Consent Form. The study protocol was evaluated and approved by the Human Research Ethics Committee of the institution (protocol number 26497414.8.0000.5419).

2.2 | Sample size calculation

The patient was considered the study unit. The sample size was determined to provide 80% power, in order to recognize a significant difference of 1 mm between groups with a 95% confidence interval ($\alpha = 0.05$) and intragroup standard deviation of 2 mm (Novaes et al., 2012) considering the changes in probing pocket depth (PPD) as the primary outcome variable. A sample size of 18 patients was required. However, considering that some patients may be lost during follow-up, the number of subjects enrolled in this study was 20.

2.3 | Inclusion and exclusion criteria

All subjects were diagnosed with SCP (Armitage, 1999). The inclusion quadrant- and site-related criteria were: (i) interproximal attachment loss (horizontal) involving at least 2 contralateral teeth with probing depth (PD) ≥ 5 mm, (ii) Posterior (molar) of opposite sides of the maxilla or mandible teeth with proximal sites (Mesial or distal) presenting probing pocket depth (PPD) and clinical attachment level (CAL) ≥ 5 mm; (iii) surgical access therapy indicated for at least two subsequent contralateral quadrants (iv) bleeding on probing. In addition, other inclusion criteria were adopted: i) age ≥ 35 years; ii) Good general health (patients without systemic involvement and not taking any medication).

The exclusion criteria were: subgingival periodontal therapy or antibiotic treatment in the previous 6 months, functional overload, systemic diseases that could affect the progression of PD, extensive prosthetic involvement, furcation involvement $\geq II$, need of antibiotic

coverage for routine dental therapy, long-term administration of anti-inflammatory medication, smoking and pregnancy.

2.4 | Experimental design, allocation concealment and treatment protocol

Before the study began, all subjects received full-mouth supragingival scaling and instructions on proper home-care techniques. One molar tooth per quadrant with proximal sites presenting PPD and CAL ≥ 5 mm was selected for the clinical and microbiological evaluations. According to a predefined balanced block randomization table with a 1:1 allocation, each tooth selected was randomly assigned to the following treatments: Flap debridement + Sham procedure (Control Group) or Flap debridement associated to a single application of aPDT (Test Group). The randomization scheme was generated by using the Web site Randomization.com (<http://www.randomization.com>). The experimental design was split-mouth.

An investigator (S.L.S.S.) not involved in data collection and treatment performed the enrolment of patients and their assignments into interventions. Sealed non-transparent envelopes were used for allocation concealment and opened just before the interventions. A single trained operator, who was masked to clinical examinations and data collection, undertook the adjunctive treatment. Patients did not receive any information about the adjuvant treatment performed on each tooth selected. All study personnel, including biostatistician and examiner, were blinded to the treatment assignment. The designation of the groups was revealed only after the statistical analysis.

In each group, weekly sessions of SRP were performed using both hand instruments and ultrasonic device, during 30 days before surgery. SRP was conducted by one trained periodontist who was not informed about the treatment allocation. The SRP was performed in sextant, in four weekly interval sessions (1 sextant/week). 30 days after last session of SRP Test Group received flap debridement associated to aPDT protocol, as follows: application of phenothiazine chloride solution 10 mg/ml (Helbo Blue[®], Bredent Medical GmbH & Co, Germany), apico-coronally irrigation of the surgical site, 5 min of pre-irradiation time (Qin, Luan, Bi, He, et al., 2008; Qin, Luan, Bi, Sheng, et al., 2008), followed by irrigation with saline solution (approximately 1 ml per tooth) and irradiation with a red laser (HELBO[®] TheraLite Laser, Bredent Medical GmbH & Co, Germany) for 10 s at each site (mesiobuccal, distobuccal, distolingual, mesiolingual, buccal and lingual) (70 mW of power, and a power density of 28mW/cm²), with an optic fiber angulated 60, 0.06 mm diameter, 8 mm length, delivering a total energy of 2.79J/cm² per site (16.72 J/cm² per tooth). The flap was then repositioned and sutured (Figure 1). A simulation of aPDT (Sham procedure) was performed simultaneously in contralateral teeth (Control Group) (Figure 2). No teeth of the sample had furcation lesions \geq II. The sutures were removed after 7 days on both sides. Patients from both groups received supragingival dental prophylaxis using polishing paste and rubber cups monthly until the third month. All subjects were monitored for more 90 days after the surgical procedures. The study timeline is shown in figure 3.

2.5 | Examiner calibration

All clinical parameters were measured by a single calibrated examiner (M.R.M.). At two separate sessions 48 hr apart, duplicate measurements of PPD and CAL were obtained from ten patients who were not related to this study and presented at least two pairs of contralateral multiple rooted teeth with PPD ≥ 5 mm in proximal sites. Calibration was accepted if percentage agreement between measurements was more than 90%.

2.6 | Clinical measurements

Clinical measurements were collected as previous described (Moreira et al., 2015). Clinical parameters were recorded at baseline, 60 and 150 days. Plaque index (PI) (O'Leary, Drake, & Naylor, 1972) was employed to assess the oral hygiene status of the patients. Bleeding on probing (BOP) (Ainamo & Bay, 1976) was recorded based on the presence or absence of bleeding up to 30 s after probing at the experimental sites. PI and BOP were scored as plaque and bleeding being absent or present (0 or 1, respectively). PPD was measured from the free gingival margin to the bottom of periodontal pocket. CAL was measured from the cemento-enamel junction to the base of periodontal pocket. Gingival recession (GR) was measured from the cemento-enamel junction to the free gingival margin. BOP, PPD, CAL and GR were measured at six sites per tooth (mesio- buccal, buccal, disto-buccal, disto-lingual, lingual and mesio-lingual). All probing measurements were performed using an automated periodontal probe (Florida Probe Corporation, Gainesville, FL, USA).

2.7 | Microbiological monitoring

Subgingival plaque samples were collected at baseline, immediately before surgery and 90 days post-surgical procedure mesial and distal from selected teeth. Plaque Samples were collected as previous described (Moreira et al., 2015). Briefly, supragingival plaque was removed and subgingival samples were collected with individual sterile Gracey curettes (#11-12; #13-14) and immediately placed in separate Eppendorf tubes containing 0.15 ml of buffer solution (10 mM Tris-HCl, 1 mM EDTA, pH 7.6). One hundred microliters of 0.5M NaOH were added to each tube and the samples were dispersed using a vortex mixer. Counts of 40 bacterial species were performed in each sample, using the checkerboard DNA-DNA hybridization technique (Matarazzo, Figueiredo, Cruz, Faveri, & Feres, 2008; Socransky et al., 1994) as previously described (Mestnik et al., 2012). A total of 240 samples were analyzed.

2.8 | Outcome variables

Changes in the median PPD at 90 days post-surgical procedure were defined as the primary outcome variable of the study. Secondary outcome variables were differences between groups in the following parameters: CAL, GR, PI, BOP, counts and proportions of the 40 bacterial species analyzed, numbers of patients requiring additional periodontal treatment, number of residual periodontal pockets.

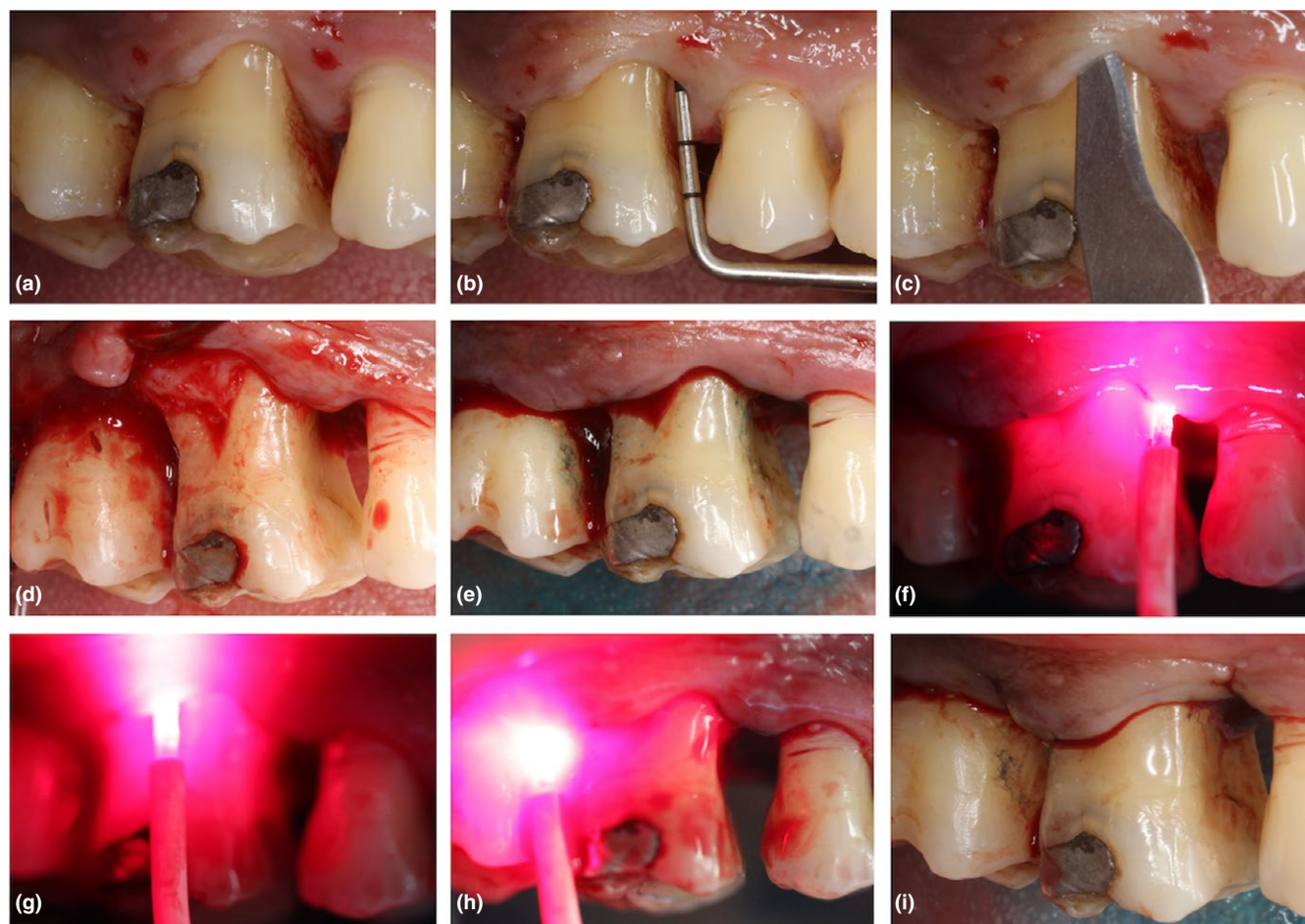


FIGURE 1 Surgical Therapy - Test Group: (a) First molar; (b) Preoperative probing showing PPD ≥ 5.5 mm; (c) Intra-sulcular incision; (d) Mucoperiosteal flap (e) photosensitizer hydrochloride phenothiazine (Helbo Blue, Helbo Photodynamic Systems) application at a concentration of 10 mg/ml - Test Group; (f) Activation of laser diode (670 nm, 75 mW, 0.25 W/cm², 2.49 J/cm², 10 s per point); (g) Nylon 5.0 sutures

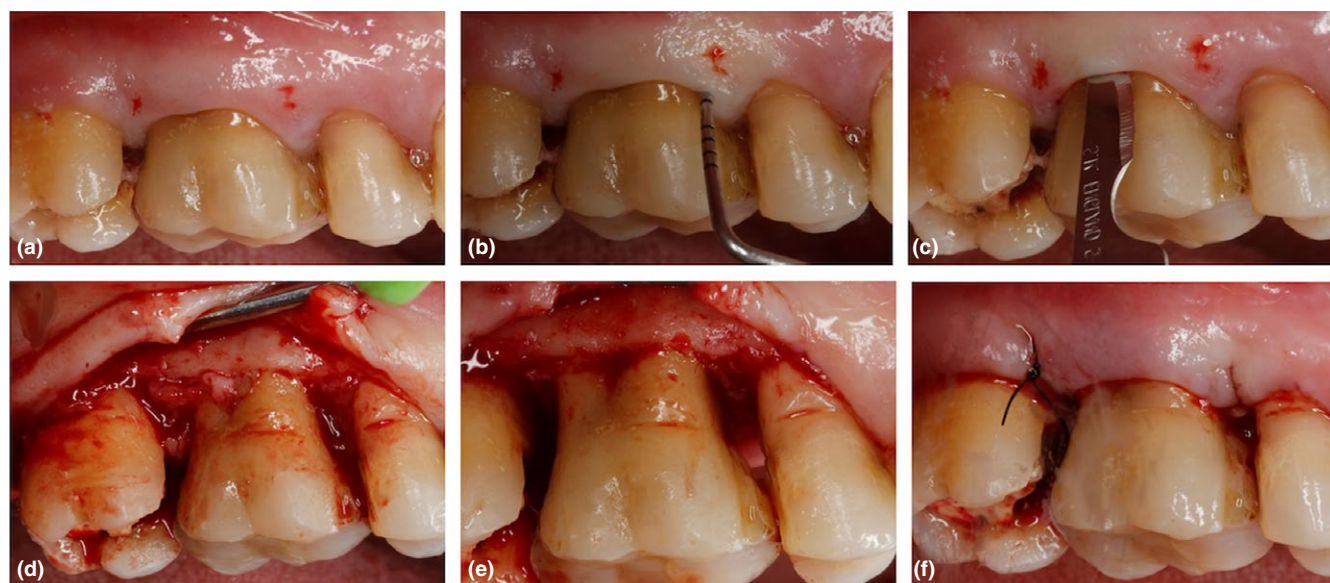
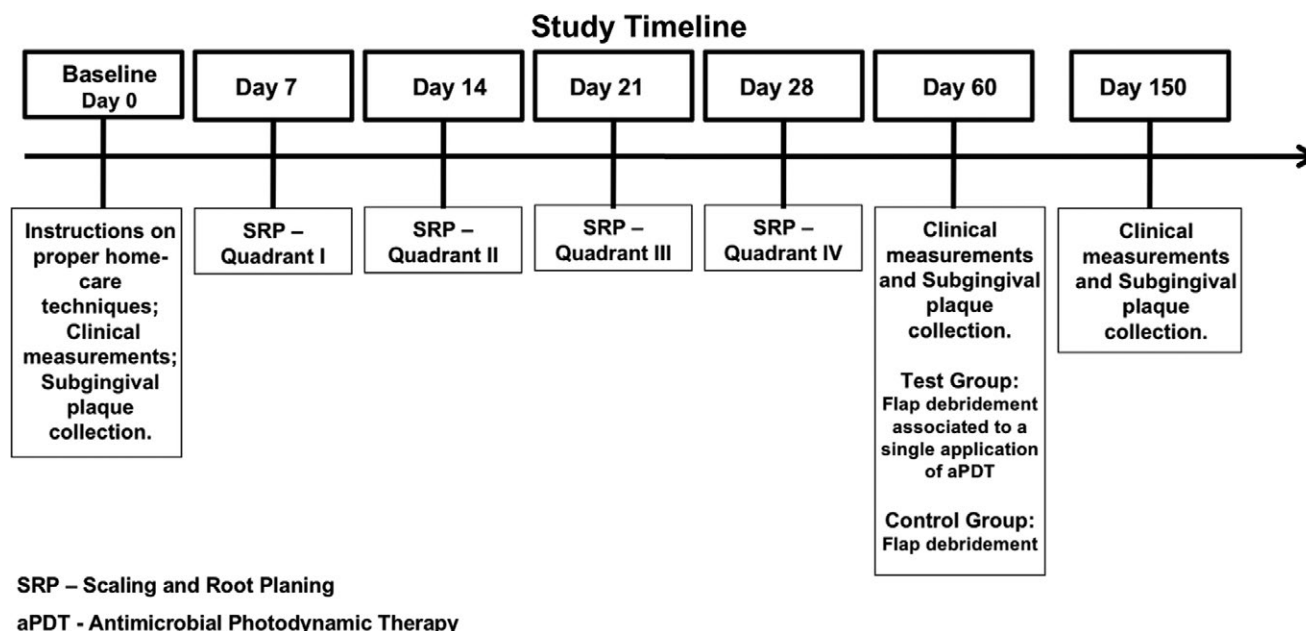


FIGURE 2 Surgical Therapy - Control Group: (a) First molar; (b) Preoperative probing showing PPD ≥ 5 mm; (c) Intra-sulcular incision; (d) Mucoperiosteal flap (e) Scaling and root planing; (f) Nylon 5.0 sutures

**FIGURE 3** Study Timeline

2.9 | Statistical analysis

Data were analyzed using statistical software (SPSS Inc.). The primary outcome measures were the differences within each group for changes in PPD. Secondary outcome measures included CAL, GR, percentage of positive clinical endpoint (pockets with final PPD < 4 mm) and counts and proportions of the 40 bacterial species analyzed. The significance level was set at 5%.

The Lilliefors normality test was applied for all variables studied and the results showed necessity of non-parametric tests. The inter-group analysis for bleeding on probing, plaque index, and desired clinical endpoint (pockets that reached 3 mm PPD, or less, after treatment) were performed using Friedman test. Mann–Whitney test was used for intergroup analysis of stratified periodontal pockets, reductions above 2 mm, clinical attachment level and gingival recessions.

Microbiological data were presented as mean counts of individual bacterial species in both groups. Bacterial species were also grouped into complexes, according to (Socransky, Haffajee, Cugini, Smith, & Kent, 1998). Wilcoxon Test was used to detect significant differences within each group for mean counts of individual bacterial species. Analyses were performed after adjustments for multiple comparisons (Socransky, Haffajee, Smith, & Dibart, 1991). Significance of differences between groups as well as changes within each group for mean proportions of microbial complexes were determined using Paired *t* Test.

2.10 | Surgical procedures

The surgical procedures were performed 4 weeks after last session of scaling and root planing. Patients were clinically monitored, and sites with PPD ≥ 5 mm and presence of BP were submitted to Flap debridement (Control Group) or Flap debridement associated to a single application of aPDT (Test Group). The surgical procedures were

performed by the same experienced periodontist. Initially the patients received extra-oral antiseptics with 2% chlorhexidine solution. After infiltrative local anesthesia with 2% lidocaine and adrenaline solution (1: 100,000), an intrasulcular incision with 15C scalpel blade was performed, encompassing the site with PPD ≥ 5 mm and both (mesial and distal) adjacent teeth, preserving gingival papillae. A mucoperiosteal flap was then raised until bone crest exposure and subgingival calculus and/or granulation tissue deposits were removed by SRP with conventional Gracey and Mini-Five curettes, numbers 5/6, 7/8, 11/12, and 13/14 (Hu-Friedy, Chicago, IL, USA) and ultrasonic devices. Shortly after completion of SRP, aPDT was applied in Test Group and Sham procedure was performed in Control Group, as previously described. After that, the flap was replaced and sutured with 5-0 nylon sutures. Paracetamol 750 mg, 6/6 hr for 2 days was prescribed for pain. The sutures were removed 7 days after surgery.

3 | RESULTS

Figure 4 presents the flow chart of the study design. All subjects successfully completed the study. The postoperative healing was uneventful in all cases.

3.1 | Clinical monitoring

Medians and standard deviations of PPD, CAL and GR are presented in Table 1. Absolute and relative frequencies of BOP and PI are presented in Table 2. No significant differences were observed between groups at baseline. All therapies led to a decrease in median values of CAL, PI and BOP (Table 1 and Table 2). All therapies led to an increase in median values of GR (Table 1). Analyzing deep periodontal pockets (PD ≥ 5 mm), Test Group presented a statistically significantly

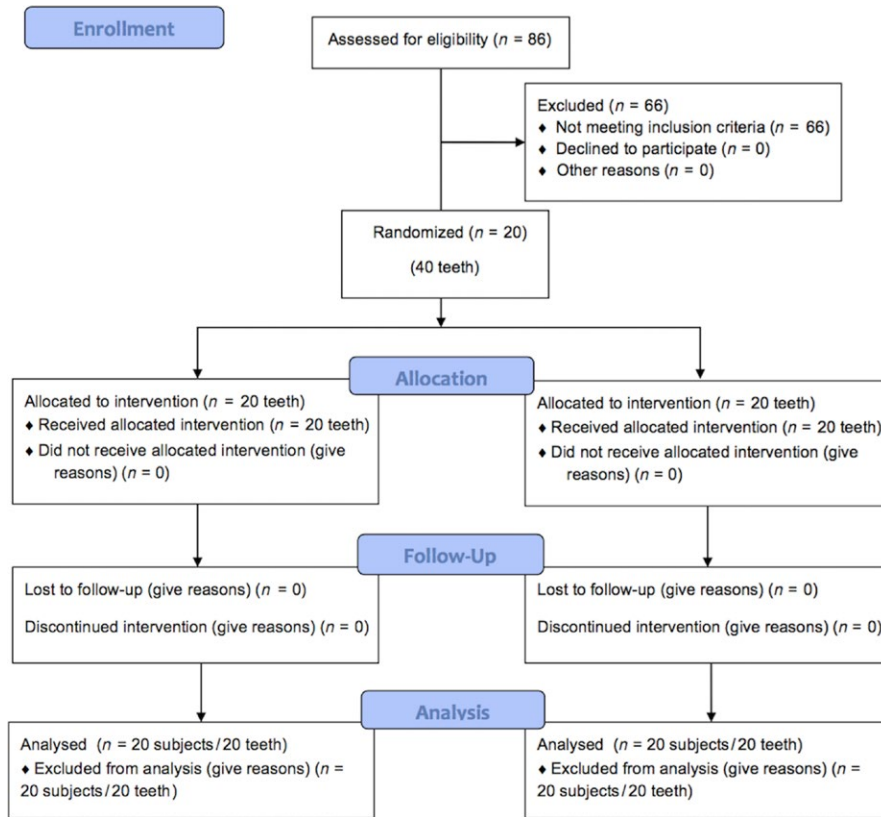


FIGURE 4 Study flowchart diagram explaining the clinical trial

TABLE 1 Medians and standard deviations of PPD, CAL and GR in Test and Control groups at baseline, 60 and 150 days, and the results of intra and intergroup comparisons

Variable	Periods	Experimental Groups		Intergroup comparisons (Paired t Test)			
		Control (N = 20)	Test (N = 20)	Mean difference	Median (IQR)	CI 95%	p value
PPD (mm)	Baseline	5.70 ± 0.53	5.63 ± 0.45	0.075	5.5 (5, 6)	−0.2942 to 0.4442	NS
	+60	5.70 ± 0.50	5.60 ± 0.5	0.075	5.5 (5, 6)	−0.2942 to 0.4442	NS
	+150	3.40 ± 0.50 ^a	2.70 ± 0.3 ^a	0.7	2.5 (2.5, 3)	0.3884 to 1.0116	<.0001
CAL (mm)	Baseline	6.18 ± 0.74	6.05 ± 0.82	0.125	6 (5.5, 6.88)	−0.4946 to 0.7446	NS
	+60	6.30 ± 0.69	6.30 ± 0.7 ^a	0	6 (5.5, 6.9)	−0.5486 to 0.5486	NS
	+150	4.18 ± 0.66 ^{a,b}	3.70 ± 0.8 ^{a,b}	0.475	3.8 (2.5, 4.5)	−0.1201 to 1.0701	.0572
GR (mm)	Baseline	0.48 ± 0.53	0.43 ± 0.73	0.05	0.25 (0, 1)	−0.4732 to 0.5732	NS
	+60	0.60 ± 0.51 ^a	0.68 ± 0.61 ^a	−0.075	0.5 (0, 1)	−0.4961 to 0.3461	NS
	+150	0.78 ± 0.49 ^{a,b}	1.00 ± 0.60 ^{a,b}	−0.225	1 (0.1, 1.9)	−0.6624 to 0.2124	NS

CAL, clinical attachment level; CI, Confidence interval; GR, Gingival recession; IQR, interquartile range; NS, no significant difference; PPD, probing pocket depth; SD, Standard deviation; SRP, Scaling and root planing.

^aDifferent from baseline, $p < .05$, ^bDifferent +60, $p < .05$ (Friedman Test, $p < .05$).

higher reduction in PPD ($p < .05$) when compared to Control Group at 90 days after surgical therapy (Table 1). Gingival recession and Clinical Attachment Level showed no difference between groups on intergroup and intragroup analysis.

3.2 | Microbiological monitoring

In general, subjects presented high counts of species of orange and red complexes bacteria at baseline. No significant differences were

observed between groups in the mean counts and proportions of any of the tested species at baseline. Figure 5 and Figure 6 demonstrates mean total counts of the 40 subgingival species evaluated in Control Group and Test Group, respectively. More species of orange and red complexes decreased in Test Group when compared to Control Group. Microbial profiles were affected by treatments, and the most beneficial changes were observed in subjects who received flap debridement associated with single application of aPDT: Test group showed a significant reduction in periodontal pathogens of the red

TABLE 2 Absolute and relative frequencies for PI and BOP in Test and Control groups, and results of intra and intergroup comparisons

Variable	Periods	Control (N = 20)		Test (N = 20)		Chi-Square Test	
		Number	(%)	Number	(%)	Relative risk	p value
PI	Baseline	35	87.5	31	77.5	1.00	NS
	+60	30	75	25	62.5	1.17	NS
	+150	19	47.5	13	32.5	0.87	NS
Hight Risk for PD progression	Baseline	40	100	40	100	NS	NS
	+60	34	85	35	87.5	0.745	NS
	+150	1	2.5	0	0	0.314	NS
BOP	Baseline	33	82.5	33	82.5	1.13	NS
	+60	28	70	24	60	1.20	NS
	+150	13	32.5	25	50	1.46	NS

BOP, Bleeding on probing; NS, no significant difference; PD, Periodontitis; PI, Plaque index; Hight Risk for PD progression = ≥ 9 sites with PPD ≥ 5 mm (Lang & Tonetti, 2003)

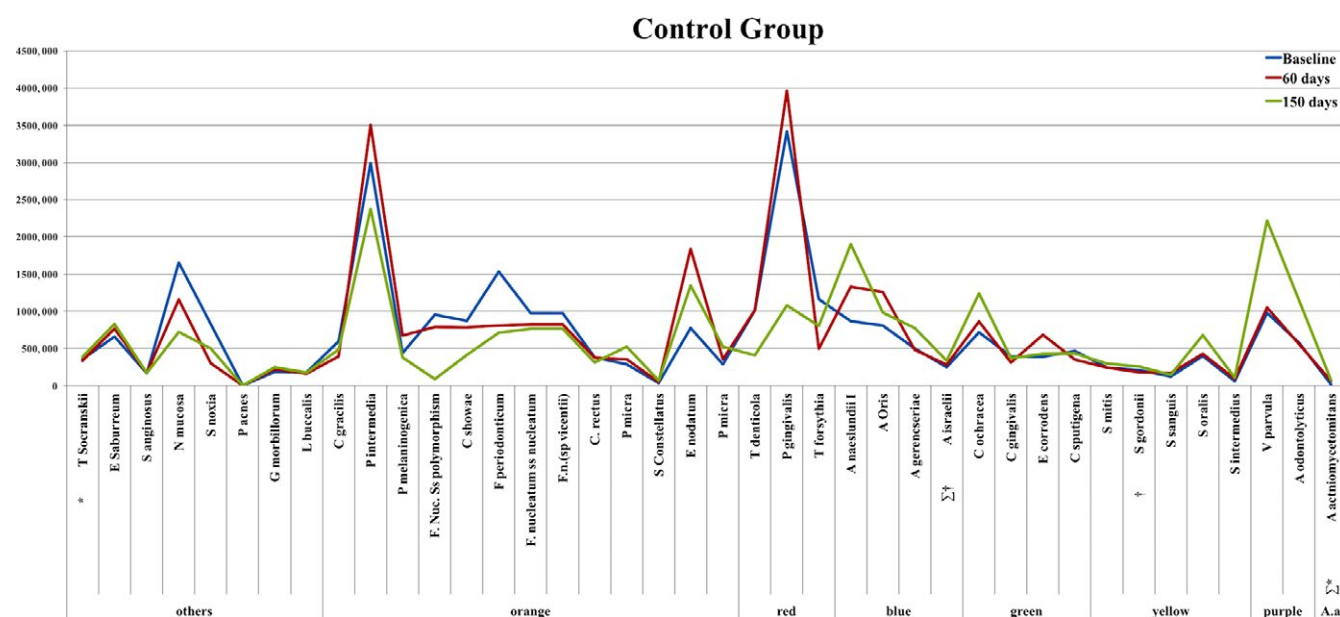


FIGURE 5 Mean counts of 40 bacterial species in Control Group at baseline, 60 and 150 days, and results of intragroup comparisons. The species were ordered according to the microbial complexes described by Socransky et al. (1998). The results were adjusted for multiple comparisons. Statistically significant differences when compared to baseline: (*) 60 days; (Σ) 150 days. (†) Statistically significant differences when compared to 60 days

complex (*T. denticola*) ($p = .0221$), yellow complex (*S. mitis*) ($p = .0178$), orange complex (*C. gracilis*) ($p = .0324$) and significant increase in periodontal pathogens of the blue complex (*A. oris* [$p = .0427$] and *A. gerencseriae* [$p = .0039$]). Figure 7 shows changes in the proportions of microbial complexes at baseline, 60 and 150 days.

4 | DISCUSSION

Complete calculus removal is extremely difficult to perform, especially with the closed approach of scaling and root planing (Deas et al., 2016). In sites deeper than 5 mm, complete calculus removal was achieved only 11% of the time (Waerhaug, 1978): so, if the pocket depth is

more than 5 mm after non-surgical treatment, the chances of failure are so great that there is an indication for surgical pocket elimination or reduction. Residual periodontal pockets are frequently observed in chronic periodontitis patients having received the initial periodontal therapy, and they represent a predictive risk factor for disease progression and increased attachment loss. Residual periodontal pockets were defined as periodontal sites presenting PD ≥ 5 mm with bleeding on probing (Xue & Zhao, 2016).

Data from the present study indicated that aPDT in combination with flap debridement led to significant improvements in PPD over flap debridement alone. The improvement of adjunctive aPDT in PPD parameter is in line with outcomes of previous clinical studies (Chondros et al., 2009; Christodoulides et al., 2008).

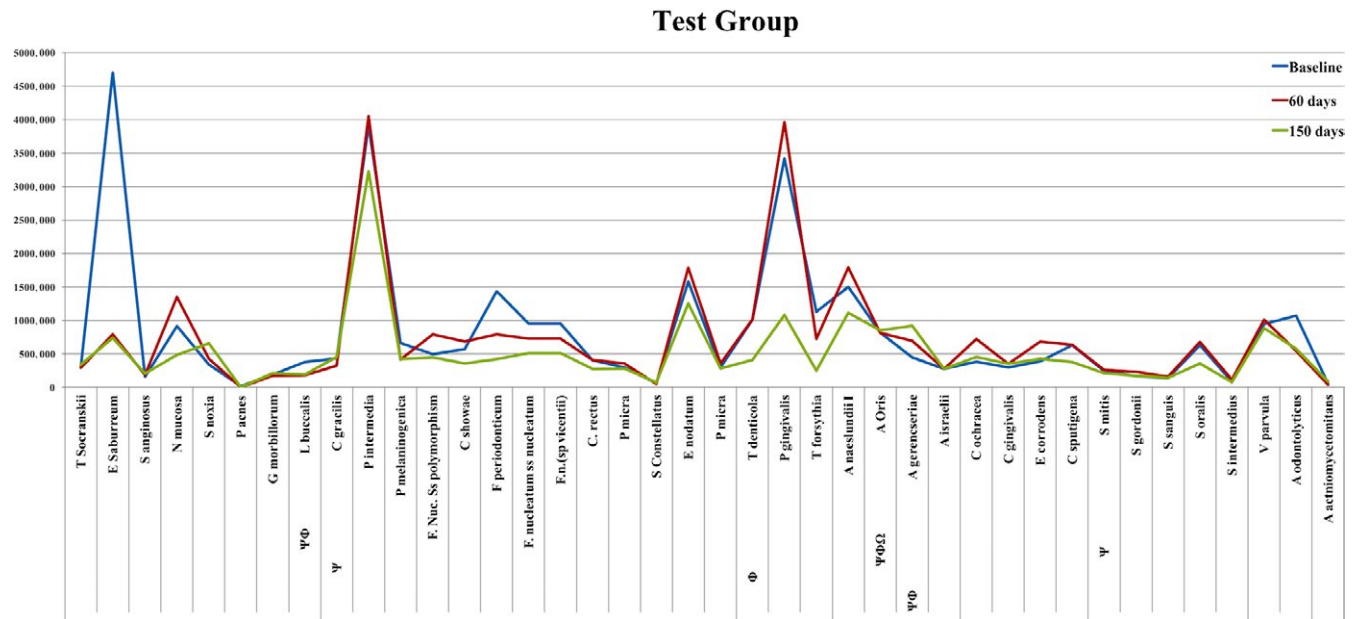


FIGURE 6 Mean counts of 40 bacterial species in Test group at baseline, 60 and 150 days, and results of intragroup comparisons. The species were ordered according to the microbial complexes described by Socransky et al. (1998). The results were adjusted for multiple comparisons. Statistically significant differences when compared to baseline: (Ψ) 60 days; (Φ) 150 days. (Ω) Statistically significant differences when compared to 60 days

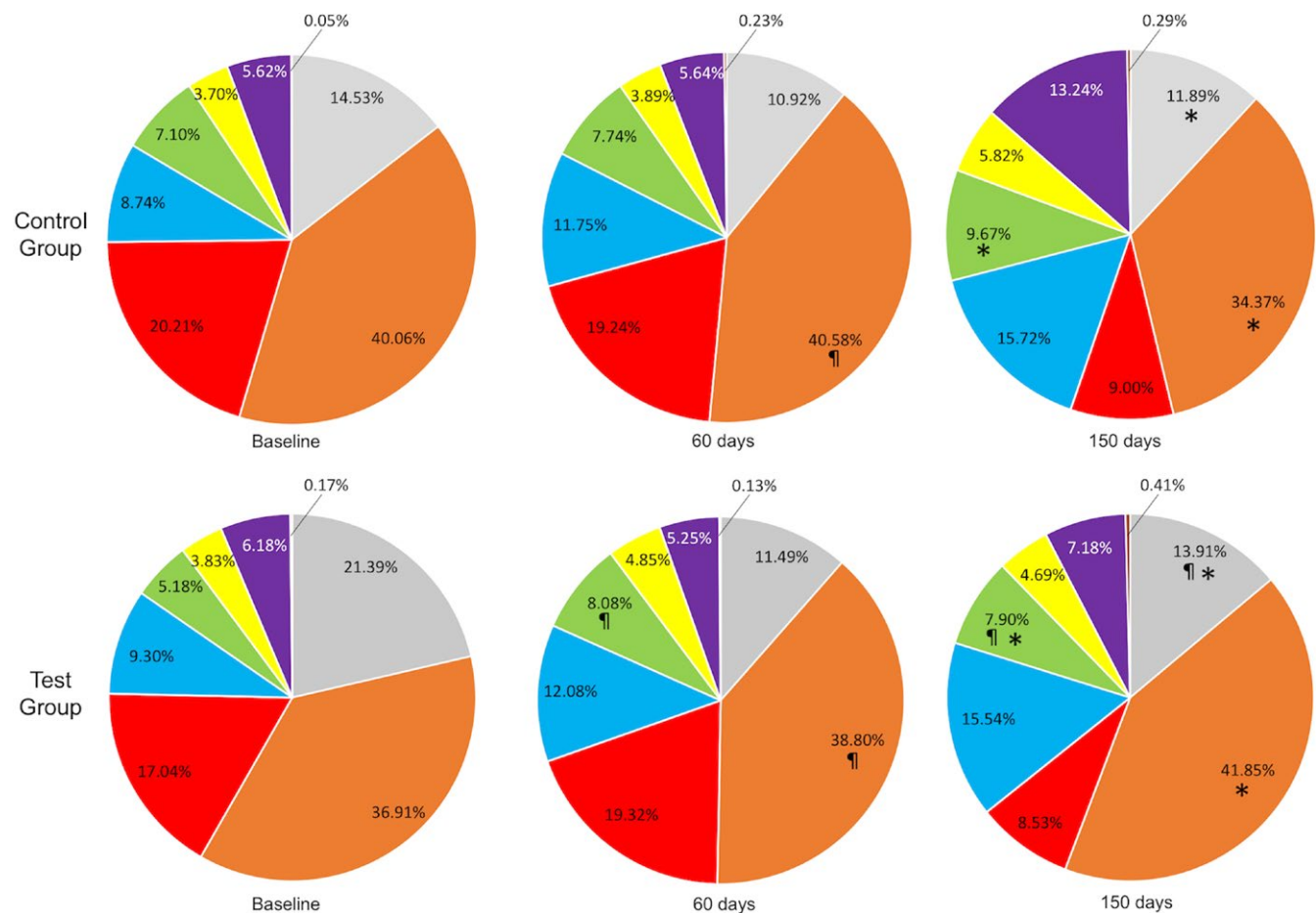


FIGURE 7 Pie charts of the mean proportions of each microbial complex at baseline, +60 and +150 days in Test and Control groups. The colors represent different microbial complexes (Socransky et al., 1998). ¶Significant difference when compared to baseline; *Significant difference between groups in the same period of analysis. Paired *t* test ($p < .05$)

Braun et al. (2008) showed superior results in favor of aPDT in all evaluated parameters. On the other hand, other clinical studies have found that adjunctive aPDT may not significantly improve the clinical outcomes of non-surgical treatment of chronic periodontitis (Bassir et al., 2013; Ge et al., 2011; Polansky et al., 2009; Ruhling et al., 2010). Cappuyns, Cionca, Wick, Giannopoulou, and Mombelli (2012), in a split-mouth randomized clinical trial, showed that the same improvement in the median of PPD and BOP was achieved in three treatment modalities (SRP, aPDT and diode soft laser therapy) for treating patients affected by chronic periodontitis. Similarly, Monzavi et al. (2016), in one full-mouth double-blind randomized controlled clinical study, concluded that aPDT, as an adjunctive approach, yielded complete resolution of inflammation and significant reduction in periodontal pocket depth. However, such an association did not have any additional advantage in terms of clinical attachment gain and plaque score over conventional SRP. However, it must be emphasized that the previous studies reported on the non-surgical therapy of chronic periodontitis.

The findings of the present study showed that flap debridement alone or flap debridement associated with a single application of aPDT resulted in clinical differences in PPD values, and that there was a similar gain in CAL, GR, PI and BOP, with no significant differences between groups. This observation is in agreement with the results of other clinical studies, which did not confirm statistically significant difference in CAL, GR, PI or BOP gain between SRP + aPDT and SRP alone for non-surgical treatment of periodontitis (Bassir et al., 2013; Chondros et al., 2009; Ge et al., 2011; Polansky et al., 2009; Ramos et al., 2016; Ruhling et al., 2010; Theodoro et al., 2012). In contrast, some clinical studies have supported the efficacy of aPDT in CAL, GR, PI or BOP (Alwaeli, Al-Khateeb, & Al-Sadi, 2015; Berakdar et al., 2012; Carvalho et al., 2015; Giannelli, Formigli, Lorenzini, & Bani, 2012; Moreira et al., 2015; Muller Campanile, Giannopoulou, Campanile, Cancela, & Mombelli, 2015; Queiroz et al., 2013). It is important to notice that differences in PPD should have been caused by differences in GR; however, the results showed that there was not any difference in GR between the two study groups.

The benefits of aPDT are more evident in cases of advanced periodontitis. Furcations, deep invaginations and root concavities are difficult to access with hand instruments (Waerhaug, 1978; Wasserman & Hirschfeld, 1988). The use of aPDT, however, is not affected by this problem, as it can easily irradiate those inaccessible places. Another problem with conventional therapy is the increase of bacterial resistance to antibiotics, whereas aPDT, using reactive oxygen species to kill bacteria in a short time, is highly unlikely to cause bacterial resistance (Crispino et al., 2015; Wilson, 2004).

The aforementioned studies had used the same photosensitizer that was used in the present study (phenothiazine chloride 10 mg/ml) and the protocols consisted on irrigation of the pocket and a pre-irradiation time ranging 1 to 3 min, followed by irrigation with saline solution and red laser application for 10 s per site. On the present study, a pre irradiation time of 5 min was used, in accordance to a previous publication that considered it the optimal preirradiation time (Qin, Luan, Bi, He, et al., 2008).

The clinical results observed in the present study may be supported by microbiological findings. Although the values for standard deviation were high, the statistical analysis (Wilcoxon Test) showed that Test Group presented significant reduced proportions of the *T. denticola* (150 days) when compared to Control Group, and there was also a reduction of the red complex in both groups from baseline to post-operative periods. Periodontal sites that present elevated counts of red-complex bacteria have a higher risk for attachment loss (Hamlet et al., 2004) and a greater severity and progression of PD (Chen et al., 2005; Silva-Senem et al., 2013).

The percentage of host-compatible species was also affected by aPDT in the present study. Besides the reduction of periodontal pathogens, an increase of beneficial species is important for successful periodontal treatment (Teles et al., 2012). In the present study, the increase in the proportion of blue complex species observed in the Test Group and Control Group after 150 days was similar to that obtained by (Mestnik et al., 2012), when systemic antimicrobials were associated with SRP.

An important point to be discussed is the influence of supragingival biofilm control for maintaining periodontal health. Previous studies indicated that the performance of periodontal supportive therapy every 3 months would be sufficient to maintain the results of periodontal therapy. Patients in the present study were controlled weekly and monthly until completion of the revaluation period (Axelsson, Nystrom, & Lindhe, 2004; Lindhe & Nyman, 1987; Ramfjord, 1987, 1993). Thus, control of supragingival biofilm was certainly important to the stability of the results in all groups during the postoperative period. Supportive therapy, which encompasses professional mechanical plaque removal (PMPR), may limit the incidence and yearly rate of tooth loss as well as the loss in clinical attachment in patients treated for periodontitis (Sanz et al., 2015; Trombelli, Franceschetti, & Farina, 2015; Xue & Zhao, 2016).

Until now, the present study is the first to evaluate the clinical and microbiological effects of aPDT as an adjunct to periodontal surgical treatment of Severe Chronic Periodontitis. A limitation of this study is the impossibility of carrying out microbiological collection at 30 days after surgery, because it would be detrimental to periodontal healing. It would be interesting in future studies a longer follow up of patients in order to ascertain whether combination therapy can sustain the changes obtained in clinical and microbiological parameters in the long term, thus verifying how long it generates beneficial effect. Furthermore, a model with multiple applications aPDT before, during and after surgery may improve clinical and microbiological outcomes achieved in this study.

5 | CONCLUSION

The single application of aPDT as adjunctive to flap debridement in patients with SCP was able to significantly reduce PPD 90 days after surgery. Adjunctive aPDT was also able to significantly reduce levels of bacteria in subgingival plaque samples analyzed 90 days after treatment. The use of aPDT adjunct to surgical periodontal treatment in sites with deep pockets is a clinical option to be considered.

CONFLICT OF INTEREST

The authors declare to have no conflicts of interest in this study.

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How to cite this article: Martins SHL, Novaes Jr AB, Taba Jr M, et al. Effect of surgical periodontal treatment associated to antimicrobial photodynamic therapy on chronic periodontitis: A randomized controlled clinical trial. *J Clin Periodontol*. 2017;44:717–728. <https://doi.org/10.1111/jcpe.12744>