Original Article

PHOTODYNAMIC THERAPY IN TREATMENT OF CHRONIC PERIODONTITIS IN COMPARISON WITH SRP: A SPLIT-MOUTH STUDY

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ABSTRACT

Chronic periodontitis is a multifactorial disease with proven bacterial etiology. Mechanical debridement is the mainstay treatment in non-surgical periodontal therapy. However, limited accessibility in various inaccessible areas leads to an exploration of other adjunctive modalities to augment the effects of conventional scaling and root planning. Systemic and local antibiotics, probiotics, ozone therapy and photodynamic therapy have been tried as other alternative modalities in the management of periodontal diseases. As antibiotics are associated with systemic side effects and the chance of developing bacterial resistance their use has limits. Photodynamic therapy (PDT) has evolved as a modern, non-invasive, non-toxic, and potent antimicrobial treatment discipline for treating various diseases & conditions. PDT utilizes photosensitizer dye which upon irradiation with a suitable low-level laser of 660-680nm at 100mW, gets excited and produces a very potent antibacterial compound, i.e., singlet oxygen having strong oxidative action to kill bacteria. The aim of this split-mouth study is to evaluate the efficacy of photodynamic therapy as an adjunct to SRP in comparison with SRP alone in patients with chronic periodontitis. Clinical parameters were assessed at baseline and 90 days post-application of photodynamic therapy. The present study has shown statistically superior results for clinical parameters in the SRP+ PDT group. PDT when used as an adjunct with SRP, has shown improved periodontal parameters when compared to SRP alone, thus having a beneficial effect in chronic periodontitis patients.

Key words: Chronic periodontitis, Photodynamic therapy, Photosensitizers, Singlet oxygen, SRP.

Introduction

American Academy of Periodontology defined Chronic periodontitis as "an infectious disease resulting in inflammation within the supporting tissues of the teeth, progressive attachment and bone loss characterized by pocket formation and recession of the gingiva" [1]. Its clinical manifestation results from the loss of attachment apparatus around teeth, resulting in subsequent tooth loss. Bacterial biofilm and host inflammatory mediators such as pro-inflammatory cytokines play a major role in the etiology of periodontitis [2, 3].

The main goal of periodontal therapy is to arrest the inflammatory disease process, slow or arrest disease progression and allow the regeneration of the lost periodontium [4]. This will result in improved periodontal comfort and function. Treatment objectives focuses on removing the dental plaque and calculus and thus reduction of overall bacterial load. The therapeutic modalities can be surgical or nonsurgical periodontal therapy based on severity of disease [5].

Nonsurgical therapy includes mechanical and chemotherapeutic methods to minimize or eliminate microbial biofilm. Conventional non-surgical treatment includes mechanical debridement, hand instrumentation and ultrasonic instrumentation of the diseased root surfaces [6]. However comprehensive mechanical debridement of sites with deep periodontal pockets is difficult to accomplish with non-surgical periodontal therapy such as SRP. This necessitates the need for an alternative modality to improve the therapeutic outcome of non-surgical treatment of chronic periodontitis. Some therapeutic adjunctives, such as systemic and local antibiotics, have been used in cases not responding to conventional therapies. However, the use of systemic antimicrobials brings undesirable side effects like the development of resistant microorganisms and other associated side effects on prolonged usage, which again limits their utilization as a treatment adjunct [7].

Considering the problems and complications related to the local and systemic use of antibiotics, continuous attempts have been made to develop new approaches to managing chronic periodontitis. Recently, a novel but powerful non-invasive approach named Photodynamic therapy (PDT) has emerged in the field of clinical dentistry [8].

PDT is based on the triad of a photosensitizer, a low-level laser for activating photosensitizer and oxygen. These three altogether lead to the generation of cytolethal reactive oxygen species (ROS) with singlet oxygen in predominance, having toxic effects on the microorganisms imparting the antimicrobial action [9]. Though Oscar Raab made the accidental discovery of phototherapeutics in 1900 but antibacterial PDT (aPDT) was first introduced in 1960 when Macmillan used toluidine blue (TBO) against microorganisms. PDT's major advantages are its specificity to the targeted cells, with no collateral damage, initiation of activity only on light exposure, and lack of resistance development among bacterial species, which is seen frequently in cases of indiscriminate use of antibiotics [10].

Current literature has varied views regarding the efficacy of photodynamic therapy. In view of this same, the present study was conducted to add to the existing scientific data and strengthen the current evidence on the efficacy of photodynamic therapy.

Materials and Methods

Study design and population

This prospective interventional split-mouth study was conducted at the Dept of Periodontology in a tertiary care facility in accordance with the applicable ethical principles, including the World Medical Association Declaration of Helsinki. Twelve subjects (seven men and five women) were recruited from the OPD, with the age group from 18 to 65 years. All the study subjects gave informed consent after they were given detailed information about the trial.

Sample size calculation

The sample size was calculated regarding the primary outcome carriable as pocket probing depth, with a 5% level of significance and 80% power sample size as per statistics in this split-mouth study was 12 subjects.

Inclusion and exclusion criteria

The patient included in the study are as follows: 1) with good general health 2) minimum 20 number of teeth 3) generalized moderate to severe chronic periodontitis with probing depth ≥4mm in at least 2 posterior and 2 anterior teeth in each quadrant. However, patients excluded who were 1) smokers 2) who have received treatment for periodontitis in the last 6 months 3) those requiring antibiotic coverage for routine dental therapy 4) pregnant and lactating women 5) patients who are allergic to photosensitizer dye.

Clinical parameters

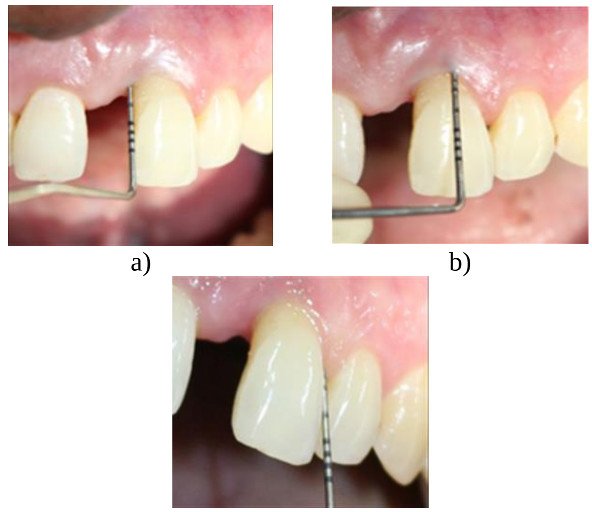
The following parameters i.e., plaque index (PI), gingival index (GI), bleeding on probing (BOP), and pocket probing depth (PPD) were recorded at baseline, after one month and after 3 months. Clinical parameters were measured at 6 sites per tooth, using Williams periodontal probe (Hu-Friedy Mfg. Co., Chicago, IL).

Patient allocation

As it is the Split mouth study, the patient's mouth was divided into two halves. One half comprised the right side upper and lower quadrants & the other half comprised the left side upper and lower quadrants. The halves of the patient's mouth were randomly assigned into either of the groups i.e., Group A (Test Group) and Group B (Control Group), by the coin toss method.

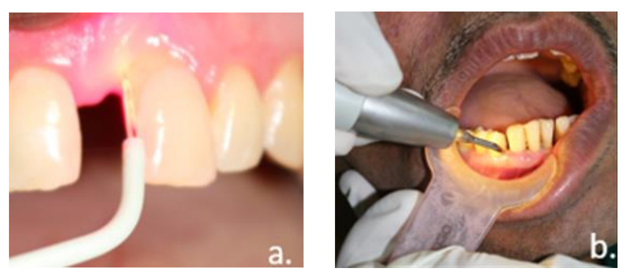
Treatment procedure

All Chronic Periodontitis patients included in the study as per the inclusion and exclusion criteria were treated with conventional non-surgical periodontal therapy, i.e., scaling and root planning with ultrasonic scalers and periodontal hand instruments, i.e., Gracey curettes.



a) b) c)

Figure 1. Group A (SRP+PDT) PRE-OP pocket probing depth (PPD) baseline. a) 4mm at Mesiofacial, b) 2mm at Midfacial, c) Distofacial 3mm surface of 12



a) b)

Figure 2. a) Group A with PDT in addition to SRP, b) Group B sites for SRP

In GROUP A (Test Group) - Patient mouth halves received photodynamic therapy following scaling and root planing. Photodynamic therapy was carried out using HELBO TheraLite (Bredent medical™) diode laser (660 nm) with a power output of 100mW and HELBO®3D Pocket Probe delivering a power density of 60 mW/cm^2. Within an irradiation time of 10 seconds, an energy fluence of 3.53 J/cm2 is applied on each of the six surfaces of the treated tooth. HELBO blue photosensitizer (concentration 10 mg/mL, i.e., 1% with absorbance peak at 670 nm) containing methylene blue was used as photosensitizer dye imparting the antibacterial action upon laser activation. The photosensitizer was applied into the pocket using a viscoelastic cannula and kept in-situ for 60 secs allowing the dye to get adsorbed to bacteria. The pocket was subsequently rinsed thoroughly removing any excess dye, as it may act as an optical shield during laser irradiation. After rinsing, the pocket surface was exposed to HELBO Theralite diode laser for 1 minute per tooth (10 seconds for each site). Singlet oxygen so released locally, will cause the selective killing of dyed cells of bacteria.

GROUP B (Control Group) - Patient mouth halves received scaling and root planing alone; no additional therapy would be given.

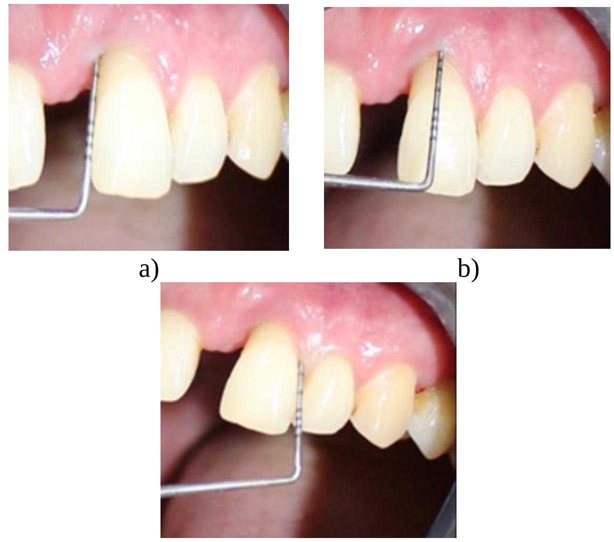
Statistical analyses

Data was collected in an excel sheet. Analysis of collected data of clinical parameters was done using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 26. Differences between the two populations were considered significant when $p < 0.05$. The intra-group and inter-group comparisons of means of continuous variables were made using paired t-tests as the dependent variable was normally distributed and was a split-mouth trial, so the groups were related. Then, the mean of each of the two groups were compared to get the t value. Categorical variables of the data were depicted as n (% of cases) and continuous variables of the data were presented as Mean and Standard deviation (SD) across two study groups.

Results and Discussion

Baseline and 90 days post-intervention parameters for all the study patients for the control group (Group B) and test group (Group A) were tabulated in **Table 1** to 8. At baseline, the comparison of all clinical parameters i.e., % of BOP, PPD, and CAL, was statistically insignificant.

There is an overall reduction of plaque index from 2.02±0.122 at baseline to 0.87±.214 at 90 days post-intervention. Bleeding sites percentage at baseline, SRP (Group B) was 79.47±65.41 and decreased to 23.15±4.49 at 90 days following SRP (mean of difference 56.13±1.92). In SRP+ aPDT (Group A), the baseline value was 78.71±55.16 and decreased to 18.52±34.15 at 90 days post-therapy (mean of difference 60.19±2.01). There was a statistically significant decrease in the mean percentage of bleeding sites after 90 days post-therapy in both groups ($p<0.05$) **(Table 1 and Figure 5)**. Mean difference in the pocket probing depth at 90 days after the intervention was 2.9±0.17 for Group A and 2.18±0.24 for Group B **(Table 1)** Reduction in mean probing pocket depth in SRP + aPDT (Group A) was better than SRP alone (Group B).



a) b) c)

Figure 3. Group A (SRP+PDT) POST-OP pocket probing depth (PPD) after 3 months. a) 2mm at Mesiofacial, b) 1mm at Midfacial, c) 2mm at Distofacial surface of 12

The mean difference in the clinical attachment level at 90 days after intervention reduced to 2.58±0.63 for Group A and 1.89±0.57 for Group B **(Table 1)**. There was a significant ($p<0.05$) gain in mean clinical attachment level in SRP + aPDT (Group A) post-treatment as compared to SRP alone, i.e., Group B **(Table 1 and Figure 6)**. Also 3 months after intervention there is an overall improvement in the patient clinical outcomes as chronic periodontitis responded well towards the non-surgical periodontal therapy including both SRP and in combination with photodynamic therapy.

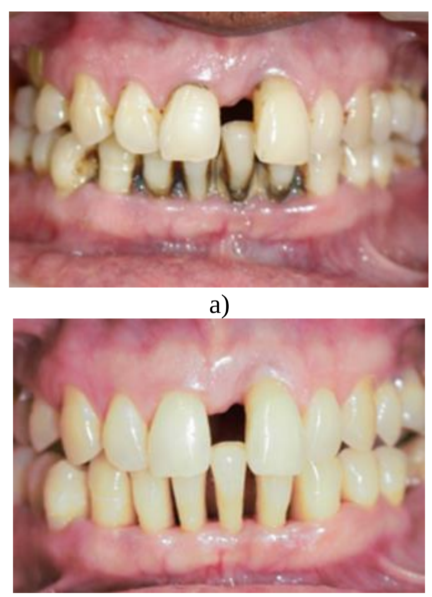


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Figure 4. Pre-Op and 3 months post op comparison with overall improvement in clinical presentation

Table 1. Inter-group comparison of Mean of Differences of clinical parameters at 90 days Post the interventions between the Control and Test group

	Group A (SRP+ PDT) Difference between before & after intervention (Mean ± SD	Group B (SRP) Difference between before & after intervention (Mean ± SD	Remarks
% of Bleeding Sites	60.19±2.01	56.13±1.92	Significant
PPD (in mm)	2.9±0.17	2.18±0.24	Significant
CAL (in mm)	2.58±0.63	1.89±0.57	Significant

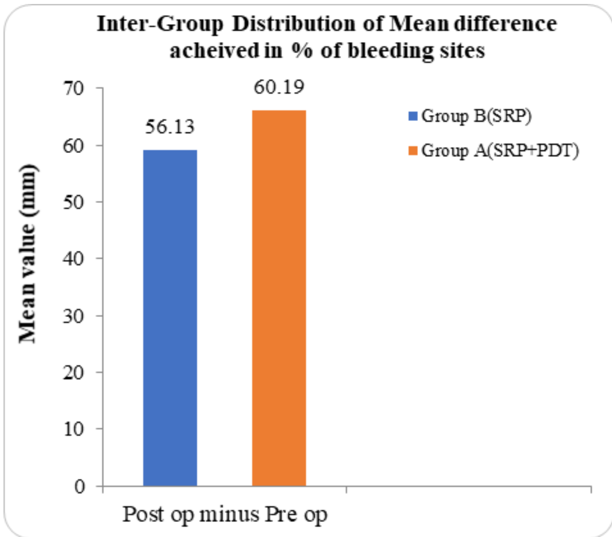

Figure 5. Inter-Group Comparison of Mean of differences % of bleeding sites

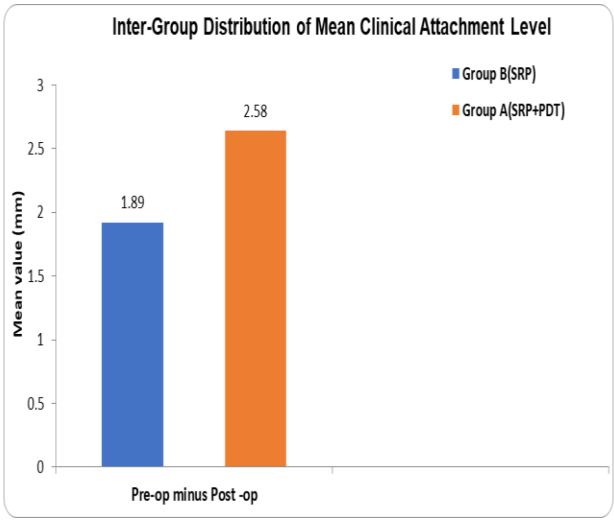

Figure 6. Inter-Group Comparison of Mean of differences Clinical Attachment Level

The main objective of non-surgical periodontal therapy is reducing microbial load in periodontal disease sites, thereby decreasing the cause of inflammation. The non-surgical periodontal treatment involves supragingival scaling, subgingival scaling, and root planing. But there are limitations in terms of accessibility, especially in furcation areas, deep pockets and root concavities which necessitated the need to explore adjunctive modalities like locally administered antibiotics, probiotics, ozone therapy, and photodynamic therapy [11]. Antibiotics are associated with bacterial resistance and systemic side effects whereas probiotics and ozone therapy have been tried in periodontitis cases with inconclusive clinical trials. Though in infancy, Photodynamic therapy (PDT) emerged as a revolutionary treatment modality in various fields of medicine and dentistry.

Photodynamic therapy works by two mechanisms, type I reaction, where laser irradiation to photosensitizer leads to the generation of reactive oxygen species (ROS). Polysaccharides, enzymes and other proteins in the extracellular matrix of the bacterial biofilm are sensitive to ROS, which causes photodamage to them. In Type II reaction, cell injury of the pathogens occurs due to the cytolethal effect of the singlet oxygen. The photosensitizer in the excited state transmits energy to the oxygen molecule (present in their basic triplet state), producing singlet oxygen with very high oxidative potential. In periodontology, singlet oxygen is useful in managing chronic periodontitis and peri-implantitis cases due to its antibacterial action when used in the form of aPDT (antibacterial photodynamic therapy) [12].

The study duration selected was 3 months, in accordance with many other studies where adjunctive modalities were clinically compared with standard SRP keeping a similar study duration [13-17]. Statistical data obtained in our study demonstrated significant improvement in the clinical parameters, i.e., percentage bleeding on probing, pocket depths, and clinical attachment levels in chronic periodontitis cases after the application of PDT. There was an overall reduction in the plaque index values from 2.02±0.122 at baseline to 0.87±.214 after 3 months post-intervention, suggestive of good oral hygiene maintenance by the patients. As it's a split-mouth study, the groups could not be compared to each other as the plaque index was calculated for the full mouth to know the status of oral hygiene practice. As per Lang *et al.* (1986), gingival bleeding on probing is the initial sign of gingival inflammation and acts as a very good diagnostic criterion to predict progressive attachment loss [18]. In the present study, also 3 months after PDT intervention, a clinically significant reduction in bleeding percentage was evident, which is under similar observations reported in a systematic review and network meta-analysis by Ramanauskaite *et al*. (2021) [19]. After SRP alone, there was a significant reduction in PPD and CAL levels, but the intergroup comparison showed greater improvement in these clinical outcomes for the SRP+ aPDT group leading us to conclude the clinical effectivity of the PDT; this was in concurrence with observations reported, by Dalvi *et al*. (2021) in their systematic review and meta-analysis [20]. Also, recent systematic review of the literature by Sales *et al*. (2022), did in-vitro evaluation of effectiveness of photodynamic therapy in reduction of microorganisms associated with periodontal disease and in 25 studies (78.12%) showed a reduction greater than or equal to 3 logs CFU/mL of species associated with periodontal disease [21]. Contrary to our finding, Christodoulides *et al*. (2008) [22], Polansky *et al*. (2009) [23] and Balata *et al*. (2013) [24] reported that aPDT provided no additional benefits in PPD reduction and CAL adjunct to SRP in the non-surgical treatment and management of chronic periodontitis. These controversial reports in the literature regarding the success of PDT as an adjunct to NSPT might be due to variations in the technique used, photosensitizer, and their concentration and time duration of exposure to the desired wavelength.

The limited sample size and assessment of only clinical parameters could be a few limitations in the current study. But despite controversial reports pertaining to the efficacy of PDT, the present study has shown statistically superior results for clinical parameters in SRP+ aPDT (Group A) when compared with SRP alone/Group B. Considering the existing advantages of short treatment time, selective action of dyes on microbes, prevention of chances of bacterial resistance, multiple easy repeatable treatment options, and relatively safer modality makes this a futuristic approach in the field of periodontology.

Conclusion

Based on the findings obtained from the present study, it was concluded that applying a single episode of aPDT to SRP showed significant improvement in clinical parameters (i.e., PPD reduction, CAL gain, and a greater reduction in the percentage of bleeding sites). Smaller sample sizes, assessment of only clinical parameters and shorter follow-up duration may be a few shortcomings in concluding the beneficial holistic role of PDT. Hence, it is proposed to carry out future studies with larger sample sizes, varied parameters, and long-term follow-up.

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Conflict of interest: None

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Ethics statement: All the treatment performed was following the principles embodied in the Declaration of Helsinki and in accordance with local statutory requirements as per department protocol and approved by the ethical committee vide letter no DYPV/EC/571/2020 and written consent was obtained from each patient.

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