

Photodynamic Therapy as an Adjunct to Scaling and Root Planing in Patients with Chronic Periodontitis: A Randomized Controlled Clinical Trial

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ABSTRACT

Background: Photodynamic therapy, which combines use of laser light along with a photosensitizing compound, may be a beneficial adjunct to mechanical periodontal therapy because of its bactericidal and detoxification effect.

Aim: To evaluate the effect of photodynamic therapy as an adjunct to scaling and root planing in patients with chronic periodontitis.

Materials and methods: Following non-surgical therapy, 40 patients with moderate chronic periodontitis were included in the randomized-controlled, split-mouth study. Treatment considered of 1% methylene blue application and irradiation with InGaAsP diode laser with 940 nm wavelength at the test site while only non surgical periodontal therapy at control site. Baseline and follow up measurements included Gingival index (GI), Probing pocket depth (PPD), Clinical attachment loss (CAL) and evaluation of microbial load of Aa, Pg and Pi (CFU/ml).

Results: The GI scores in the test group were statistically significant as compared to the control group. A statistically insignificant reduction was seen in Probing Pocket Depth (PPD) and Clinical attachment loss (CAL) in Group II patients at the end of 1 month and 3 months. In addition, there was insignificant reduction in the CFU counts of Aa, Pg and Pi in the test group as compared to control group.

Conclusion: Adjunctive use of PDT did not provide any additional benefit to those obtained with scaling and root planing alone. Hence, it was concluded that the application of PDT as an adjunct to scaling and root planing in patients with chronic periodontitis should be further evaluated.

Keywords: Periodontitis, Photodynamic therapy, Methylene blue.

INTRODUCTION

Periodontal disease is initiated by pathogenic plaque biofilm and characterized by bacterial induced destruction of tooth supporting structures and alveolar bone.¹

Non surgical treatment of periodontitis which includes scaling and root planing have shown to be an effective treatment approach. The purpose of

this is to eliminate pathogens, thus avoiding progression of the inflammation with continuous attachment loss.²

Despite the fact that non-surgical periodontal treatment may result in significant clinical improvements in the great majority of cases, none of the currently available instrumentation

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techniques are effective in completely eliminating subgingival bacteria and calculus.³ The limitations of scaling and root debridement have been shown in management of initially deep periodontal pockets.²

To overcome these problems adjunctive treatments have therefore been developed to improve the clinical effectiveness of scaling and root planing.²

In recent years there has been a growing interest in usage of diode lasers for periodontal treatment due to their antimicrobial and anti inflammatory properties. The use of laser in the form of photodynamic therapy, which combines use of laser light along with a photosensitizing compound, may be a beneficial adjunct to mechanical periodontal therapy because of its bactericidal and detoxification effect.⁴

Photodynamic therapy is based on the principle that a photosensitizer binds to the target cells and can be activated by a light of suitable wavelength. Following activation of the photosensitizer, reactive oxygen is produced that is extremely toxic to certain cells and bacteria.⁵ In vitro studies have demonstrated the effectiveness of photodynamic therapy against bacteria from subgingival plaque samples from patients with chronic periodontitis namely *Porphyromonas gingivalis* or *Fusobacterium nucleatum*.⁵

Thus photodynamic therapy provides with many advantages, such as non invasive nature, selective targeting, easy repeatability and great safety.⁶

The photosensitizer is a compound that is capable of absorbing light of a specific wavelength and transforming it into useful energy.⁵ Methylene blue is a very effective photosensitizing agent for the inactivation of both gram positive and gram negative periodontopathogenic bacteria.⁷ Therefore, in the present study we used methylene blue as the photosensitizer as it possesses high bactericidal effect on periodontal pathogens. Hence, the purpose of present study was to evaluate the beneficial effects of photodynamic therapy when used as an adjunct to non-surgical treatment of periodontal disease.

MATERIALS AND METHODS

SOURCE OF DATA:

The study was a *randomized controlled single-blind clinical trial*. It was conducted in the Department of Periodontics, KLE V.K. Institute of Dental Sciences, Belagavi. An ethical clearance (Annexure I) was obtained before conducting the study from the Ethical Committee, KLE V.K. Institute of Dental Sciences, Belagavi.

A total of 40 patients diagnosed as having *moderate chronic periodontitis* (1999 International workshop for a classification of periodontal diseases and condition)⁸, reporting to the outpatient unit, Department of Periodontics, KLE V.K. Institute of Dental Sciences, Belagavi, were selected for the study.

Patients who met the following inclusion and exclusion criteria were included in the study.

INCLUSION CRITERIA

- Non smoking adults > 18 years of age.
- Untreated chronic periodontitis with
 - Atleast 2 single/multi rooted teeth on each side of the mouth having probing depth $\geq$ 5mm.
 - Interproximal attachment loss $\geq$ 3mm.
 - Radiographic signs of bone loss.

EXCLUSION CRITERIA

- Pregnant or lactating women.
- Systemic disease affecting periodontal treatment outcome.
- Use of immunosuppressive agents.
- Patients on antibiotics or anti-inflammatory drugs in past 3 months.
- Periodontal treatment within past 6 months.

LASER UNIT: InGaAsP semiconductor 940 nm diode laser (BIOLASE EPIC)

- Peak power of 5.0 W
- Pulse length-0.05 ms
- Pulse interval-0.2 ms using a 300 micrometer fiber-optic tip.

PREPARATION OF METHYLENE BLUE SOLUTION

In the present study, 1% methylene blue was used as photosensitizer which was prepared in KLE University's Dr. Prabhakar Kore Basic Science

Research Center, Belagavi. To prepare 1% methylene blue 1gram of methylene blue was weighed and added to 100 ml of distilled water.

STUDY DESIGN

The study was a split-mouth design, wherein from each patient two sites were selected in contralateral quadrants and the sites were randomly (computer based software) divided into test group and control group.

1. Control Group (n = 40) – only scaling and root planing
2. Test Group (n = 40) – scaling and root planing along with photodynamic therapy.

Subjects who signed the informed consent were included in the study.

A special proforma (Annexure III) was designed for the study to have a systematic and methodological recording of all the observations and information. The relevant data comprising of personal details of the patient, chief complaint, past dental history were recorded in the special proforma. After recording of preliminary information, microbiological samples were collected and clinical examination was carried out. The clinical parameters were evaluated at baseline, 1 month and 3 months after treatment.

The following clinical parameters were recorded:

1. Gingival index
2. Probing Pocket Depth
3. Clinical Attachment Loss

PROCEDURE FOR PERIODONTAL THERAPY

All patients received a modified one – stage full mouth scaling and root planing under local anesthesia.

At the test site (Group 2), on completion of scaling and root planing and application of topical anesthetic gel, the periodontal pockets were filled with a 1% methylene blue (Photosensitizer) solution and left for 3 minutes. Excess was gently rinsed off. (Figure 3)

Photodynamic therapy was performed with an InGaAsP semiconductor 940 nm diode laser. The tip was initiated and introduced into the pocket with a

smooth stroking action, starting coronally and working towards the bottom of the pocket. This was followed by additional lateral movement combined with vertical movements in apical and coronal directions. No more than 30 seconds was allocated to each site.

Microbiological assessment

Subgingival plaque samples were taken at baseline from the site presenting with the deepest periodontal pocket for both the test as well as control group. The same sites were re-sampled at 1 and 3 months. (Figure 2) Each selected site was dried and isolated. Subsequently, a sterile paper point (4 paper points at each site) was inserted and left in place for 30 seconds.

The samples were collected in a sterilized microcentrifuge tube and transported to KLE University's Dr. Prabhakar Kore Basic Science Research Center, Belagavi. The samples were assessed for *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans* and *Prevotella intermedia* species by anaerobic culture method.

For *Porphyromonas gingivalis* and *Prevotella intermedia*, Kanamycin blood agar was prepared. For *Aggregatibacter actinomycetemcomitans*, Dentaid media was prepared. All plates were incubated at 37°C for 48 hours in anaerobic jar.⁹ Black pigmented bacteroids (*Porphyromonas gingivalis* and *Prevotella intermedia*) were identified as black pigmented colonies with β hemolysis on blood agar. *Aggregatibacter actinomycetemcomitans* (Aa) was identified as minute, white translucent colonies. The number of colonies of each type of microorganisms were counted and multiplied by the dilution factor and expressed as colony forming units per ml (CFU/ml).

Post-operative instructions:

Standardized post-operative instructions were given to each patient after the periodontal treatment procedure. All the patients were advised a standardized tooth brushing technique. The patients were also instructed not to use any mouthwashes or antibiotics during the study period.

Statistical analysis:

The mean and standard deviation was calculated for the clinical and microbiological parameters for both Group I and Group II. Inter-group comparison for clinical and biochemical parameters was done using *Mann-whitney u test*, while intra-group comparison was done using *Wilcoxon's signed rank test*. The level of significance was 0.0001. The SPSS v. 20.0, IBM, Chicago, IL. software was used for the statistical analyses.

RESULTS

When intra-group comparisons were made, it was observed that there was a significant reduction in the Gingival Index scores from baseline to 1 month and 3 months in both the test and control groups ($p = 0.0001$). When inter-group comparisons were made between group I and group II, the gingival index scores at 1 month and 3 months were significantly reduced ($p < 0.05$). However, when both groups were compared from baseline to 1 month and 3 months, the difference for gingival index scores was found to be insignificant.



Fig 1: Measurement of clinical parameters using William's periodontal probe at baseline.



Fig 2: Collection of plaque sample using paper points.



Fig 3: Application of methylene blue dye and laser.



Fig 4: 1month Postoperative



Fig 5: 3 Months Postoperative.

A statistically significant reduction in Probing Pocket Depths at 1 month (4.25 ± 0.54) and 3 months (4.23 ± 0.55) in the control group and in the test group reduced to (4.12 ± 0.66) at 1 month and at 3 months reduced to (4.10 ± 0.65) as compared to baseline. On inter-group comparison between group I and group II there was a statistically insignificant difference seen in Probing Pocket Depth (PPD). Though PPD reduction values were higher in test group, no statistical significance was found on comparison with control group.

Similarly, we found statistically significant reduction in Clinical attachment loss at 1 month (4.26 ± 0.56) and 3 months (4.25 ± 0.58) in the control group and in the test group reduced to (4.24 ± 0.54) at 1 month and at 3 months reduced to (4.23 ± 0.59) as compared to baseline. Nevertheless, on intergroup comparison between group I and group II there was a statistically insignificant difference seen in Clinical attachment loss (CAL). Though CAL reduction values were higher in test group, no statistical significance was found on comparison with control group.

The comparison of Colony forming units/ml showed that there was a significant reduction in both group I and group II at 1 month and 3 months. On intergroup comparison, the reduction of colony forming units in group II as compared to group I was found to be insignificant. However, it was found that the reduction in microbial colony forming units was more in group II as compared to group I but the difference between the two groups was not found to be significant.

Table 1: Comparison of control and Study groups with respect to gingival index scores at baseline, 1 month and 3 months by Mann-Whitney U test.

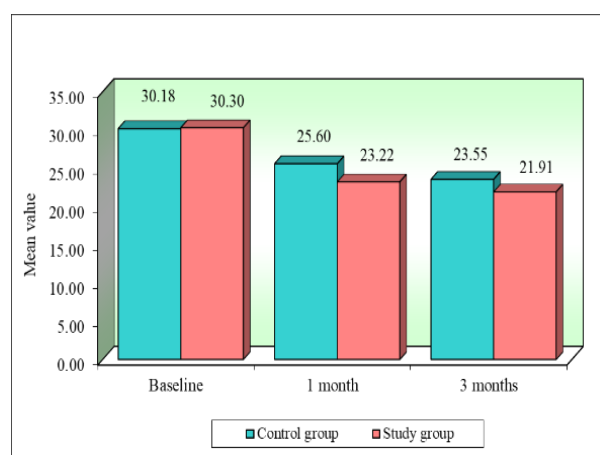
Variable	Group	Mean	SD	t-value	P-value
Baseline	Control group	1.82	0.21	1.51	
	Study group	1.76	0.20		0.13
1 month	Control group	1.48	0.26	2.03	
	Study group	1.41	0.18		0.046*
3 months	Control group	1.47	0.16	3.57	
	Study group	1.34	0.17		0.037*
Baseline-1 month	Control group	0.34	0.17	-0.19	
	Study group	0.36	0.19		0.85 NS
Baseline-3 months	Control group	0.35	0.17	-1.57	
	Study group	0.45	0.18		0.12 NS

Table 2: Comparison of control and Study groups with respect to PPD scores at baseline, 1 month and 3 months by independent t test.

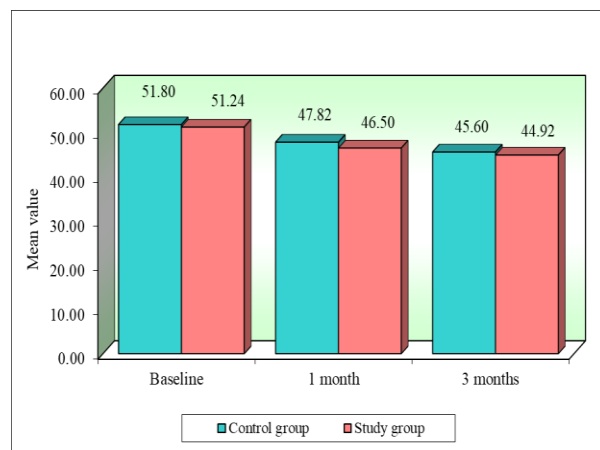
Variable	Group	Mean	SD	t-value	P-value
Baseline	Control group	5.14	0.36		
	Study group	5.21	0.42	-0.74	0.45 NS
1 month	Control group	4.25	0.54		
	Study group	4.12	0.66	0.97	0.33 NS
3 months	Control group	4.23	0.55		
	Study group	4.10	0.65	0.93	0.35 NS
Baseline-1 month	Control group	0.89	0.44		
	Study group	1.09	0.69	-1.52	0.13 NS
Baseline-3 months	Control group	1.60	0.78		
	Study group	2.86	0.67	-1.48	0.14 NS

Table 3: Comparison of control and Study groups with respect to CAL scores at baseline, 1 month and 3 months by independent t test.

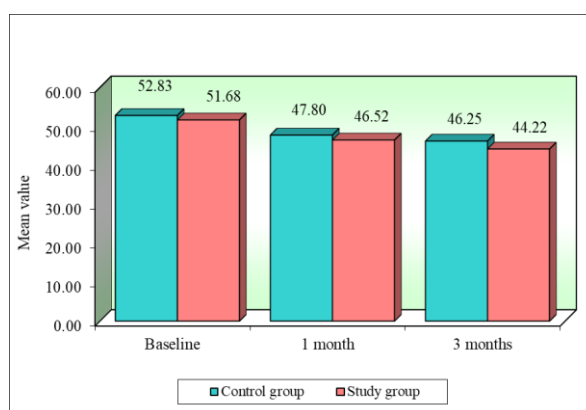
Variable	Group	Mean	SD	t-value	P-value
Baseline	Control group	5.21	0.44		
	Study group	5.24	0.48	-0.30	0.75
1 month	Control group	4.26	0.56		
	Study group	4.25	0.58	0.11	0.91
3 months	Control group	4.24	0.54		
	Study group	4.23	0.59	0.06	0.94
Baseline-1 month	Control group	0.95	0.43		
	Study group	0.99	0.72	-0.35	0.73
Baseline-3 months	Control group	0.97	0.47		
	Study group	1.01	0.74	-0.29	0.76



Graph 1: Comparison of control and study groups with respect to CFU counts of Aa organism at baseline, 1 month and 3 months time points.



Graph 2: Comparison of control and test groups with respect to CFU counts of Pg organism at baseline, 1 month and 3 months time points.



Graph 3: Comparison of control and test groups with respect to CFU counts of Pi organism at baseline, 1 month and 3 months time points.

DISCUSSION

Photodynamic therapy (PDT), because of its bactericidal and detoxification effect, has emerged in recent years as a non – invasive therapeutic modality for the treatment of various infections by bacteria, fungi, and viruses. It consists of three elements: harmless visible light, a non-toxic photosensitizer and oxygen. The photosensitizer binds to the targeted cells which is then activated by light of appropriate wavelength in presence of oxygen. This results in the generation of singlet oxygen and free radicals, which are extremely toxic to certain cells and bacteria.¹⁰

The results of studies investigating the effects of PDT on chronic periodontitis are conflicting and further studies are needed. Braun et al.⁵ reported

that the adjunctive application of PDT is appropriate to reduce periodontal inflammatory symptoms and may lead to significant improvement in clinical parameters. On the other hand, Christodoulides et al.³ reported that application of a single episode of PDT to scaling and root planing failed to result in an additional improvement in terms of PD reduction and CAL gain.

Therefore, the present study was conducted to assess the potential effect of photodynamic therapy when used as an adjunct to non-surgical periodontal treatment and to evaluate the clinical benefit using clinical and microbiological parameters.

In the present study, when inter-group comparisons were made between group I and group II, the gingival index scores at 1 month and 3 months were significantly reduced ($p < 0.05$). However, when both groups were compared from baseline to 1 month and 3 months, the difference for gingival index scores was found to be insignificant. The reduction in gingival inflammation in the test group could be attributed to the well-characterized anti-inflammatory effect of PDT, resulting in an improved gingival status. PDT results in increase of the anti-inflammatory cytokine levels, decreased production of pro-inflammatory mediators like, TNF- α and IL-1 β which may lead to reduction of inflammation in gingival tissues.¹⁰ This is in accordance with the study of Braun et al. (2009)¹¹, Theodoro et al. (2012)¹², Ravi et al. (2016)¹³ who demonstrated that a single episode of photodynamic therapy, as an adjunct to scaling and root planing, resulted in significant reduction of clinical parameters in terms of gingival index.

On inter-group comparison between group I and group II there was a statistically insignificant difference seen in Probing Pocket Depth (PPD). Though PPD reduction values were higher in test group, no statistical significance was found on comparison with control group. The reduction in pocket depth seen in test group could be attributed to the use of PDT as an adjunctive treatment. Similar results were seen in studies carried out by Polansky et al (2009)². They reported that repeated PDT adjunctive to debridement did not yield any additional improvement in clinical outcomes over a period of 3 months. Similarly, we found on inter-group comparison between group I and group II

there was a statistically insignificant difference seen in Clinical attachment loss (CAL) (Table 3 and 5). Though CAL reduction values were higher in test group, no statistical significance was found on comparison with control group. The reduction in CAL seen in test group could be attributed to the use of PDT as an adjunctive treatment which is in accordance to the studies carried out by Polansky et al (2000)², Ruhling et al (2010)¹⁴

The intergroup comparison of Colony forming units/ml showed that there was a reduction of colony forming units in group II as compared to group I was found to be insignificant. However, it was found that the reduction in microbial colony forming units was more in group II as compared to group I but the difference between the two groups was not found to be significant. The decrease in the number of colony forming units of Aa, Pg and Pi at 1 month and 3 months seen in group II may be explained by the antibacterial effect of the photosensitizer, methylene blue used in the study. Methylene blue, when activated by a light of appropriate wavelength, has been reported to penetrate into gram positive and gram negative bacteria which leads to localized damage resulting in increase in permeability.¹⁰ The frequency of the PDT application may be a possible explanation for the absence of clinical or microbiologic differences between the groups. In the study by Moreira et al. (2010)¹⁵, it is suggested that four sessions of PDT treatment should be provided to enhance the antimicrobial effect. However, in this study, a single episode of PDT was performed. Hence, future studies are needed to definitively elucidate to what extent multiple applications of PDT might enhance the outcome of therapy.

CONCLUSION

Thus within its limits, on the basis of the results of our study, adjunctive use of PDT did not provide any additional benefit to those obtained with scaling and root planing alone. Hence, it is concluded that the application of PDT as an adjunct to scaling and root planing in patients with chronic periodontitis should be further evaluated.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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