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Evaluation of combined efficacy of photodynamic therapy and non-surgical periodontal therapy (SRP) in management of chronic periodontitis - A randomized split-mouth pilot study

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Abstract

Background

AIM: The aim of this study was to evaluate the clinical efficacy of multiple applications of PDT as an adjunct to scaling and root planning in the management of chronic periodontitis patients.

Materials and Method: 30 patients with bilateral periodontal destruction were randomly treated with either test (SRP + PDT) or control (SRP) intervention. PDT was employed with a diode laser (940 nm) and Indocyanine green (ICG) dye at baseline, 1st, 2nd, and 4th-week post-SRP. Probing pocket depth (PPD), clinical attachment level (CAL), and gingival bleeding index (GBI) were recorded at baseline, 28 days, and 3 months follow-up.

Results: Statistically significant improvement was noted in all clinical parameters in both groups from baseline to three months. The mean PPD and CAL decreased in control sites from 5.93±0.80 and 6.27±0.96 at baseline to 2.67±0.62 and 2.93±0.80 at 3 months and in test sites from 6.0±0.76 and 6.33±0.82 to 2.27±0.46 and 2.60±0.63 at 3 months ($P \leq 0.05$).

Conclusion: The clinical outcomes suggested that adjunctive applications of PDT to SRP significantly reduce all the clinical parameters over SRP alone.

Keywords: Photodynamic Therapy, Indocyanine Green, Diode Laser, Scaling and Root Planing.

Introduction

Periodontitis is an oral disease that is known to cause inflammation of tooth-supporting structures due to the

presence of plaque (dental biofilm). It results in a progressive breakdown of the periodontal ligament and its supporting tissues.[1] Untreated periodontitis can lead to the formation of deep periodontal pockets and progressive loss of alveolar bone which causes tooth loosening eventually leading to tooth loss. Epidemiological studies have determined a high prevalence of this multifactorial, polymicrobial infection amongst the Indian population. [2] It is the disconcerting presence of the disease that drove researchers into finding an efficient treatment protocol that restores the periodontium to a healthy state.

The frontline treatment for periodontitis includes scaling and root planning (SRP). Although SRP is an indispensable phase of periodontal therapy, it single-handedly is unable to eliminate the tissue-invading pathogens completely indicating the need for adjuvant therapy. So, the adjunctive use of lasers in nonsurgical therapyhas been becoming a part of treatment planning in the field of dentistry.

In both surgical and non-surgical periodontal therapy, many lasers have been used for treatment and research is still going on various forms of lasers. Among many lasers, the most frequent laser used in treating periodontal infection is the Diode laser. This laser is mostly applied because of its high absorption properties by pathogenic microbes that cause periodontal infections. But it also has some disadvantages like some unexpected detrimental effects seen in surrounding healthy tissues.

The anti-bactericidal effect of laser is even enhanced by impregnating the photosensitizer dye known as Photodynamic therapy (PDT). The working principle of PDT is that it undergoes a transition from the ground state to an excited state (triple state), releasing reactive oxygen species. This excited state photosensitizer interacts with biomolecules in two different reactions. They are type I and type II. In type I, an electron transfer reaction takes place that results in the production of free radicals. Type II mainly involves interaction between triple state photosensitizer and oxygen that results in singlet oxygen formation that causes oxidative damage by interacting with biological substrate resulting in damaging the bacterial cell by their toxic effects. [3,4]

Antimicrobial photodynamic therapy (aPDT) is now been developing rapidly in treating periodontal diseases. Indocyanine green (ICG) belongs to the family of cyanine dyes with a peak absorption rate. It has both hydrophilic and lipophilic properties. The mechanism of action of ICG is different from other photosensitizers, it exhibits a 20% photodynamic effect and the main action is through the photothermal effect (PTT), which induces cell damage by increasing intracellular temperature [5].This mechanism represents mainly for reducing bleeding and it has limited destruction of pocket epithelium when ICG is used as a photosensitizer.

Some other commercial photosensitizers, toluidine blue (TBO) & methylene blue (MB) also showed effective results, but they had some limitations such as staining of the teeth due to their prolonged adhesive property. Further, the subgingival environment lacks oxygen, which may not provide favorable conditions for better action of these traditional photosensitizers. Whereas, ICG, works even in the absence of oxygen.

In a systematic review and meta-analysis by Jervoe-storm PM et al in 2015,[6] the authors suggested that multiple application of PDT is more efficient in reducing periodontal pathogens compared to a single application.Moreover, current clinical trials [7,8,9-13] substantiated that adjunctive photodynamic therapy provides propitious outcomes and has been considered as a versatile antimicrobial approach to which microbes

don't elicit resistance. To my knowledge, only limited clinical trials [14,15] had reported the efficacy of multiple applications of PDT employing ICG and diode lasers as an adjunct to SRP in the management of chronic periodontitis subjects. Further, the long-term efficacy of this combination treatment needs to be investigated.

Therefore, the purpose of this research was to evaluate the changes in clinical parameters following multiple applications of PDT using ICG and diode laser as an adjunct to scaling and root planing in treating moderate periodontal pockets of chronic periodontitis patients over a 3 month follow-up period.

Materials and Methods

The split-mouth randomized controlled clinical trial was approved by the institutional ethical committee and scientific research board of KAHER KLE university and was conducted in the department of periodontics, from September 2021- May 2022 in KAHER KLE VK Institute of dental science, Belagavi.

The sample size was calculated based on the previous study results obtained by Moreira et al, 2014 [13]. To obtain a study power of 90% with an alpha error set at 5%, a total number of 30 participants had to be included in this study. Owing to the 10 % dropouts which may occur during the follow-up, a total number of 34 systemically healthy subjects presenting with chronic periodontitis were recruited. Verbal and written consent forms were obtained duly from all the participants.

Inclusion criteria consisted of patients presenting bilateral periodontal destruction in the posterior segments involving a minimum number of 2 permanent teeth in each segment. Moderate periodontal pockets with probing pocket depth of 4-6 mm and clinical attachment loss, were included. Sites with pseudo pockets or gingival recession, having advanced periodontal destruction with intra-bony defects and mobility were excluded. Additionally, teeth with restorations or endodontic lesions and patients with a history of antibiotic therapy or periodontal treatment in the previous 3 months, and individuals who are known hypersensitive to PDT dye, smokers, pregnant women or individuals having systemic condition/disease/ any medication influencing the course of periodontal disease and therapy were also excluded.

Clinical Parameters

Clinical parameters such as plaque Index (PI), gingival Index (GI), gingival bleeding index (GBI), probing pocket depth (PPD), and clinical attachment level (CAL) were recorded by a single experienced periodontist who was blinded to the treatment being performed.

To perform intra-examiner calibration, five nonstudy subjects were recruited. The investigator measured both PPD and CAL twice, 72 hrs apart. Calibration was accepted if the outcomes were similar at baseline and at 72 hours in > 90% of cases.

Gingival bleeding was considered positive if, bleeding occurs within 10 seconds after gentle probing of the sulcus. PPD was measured as the distance from gingival margin to base of the gingival sulcus and CAL was calculated as the distance from the cementoenamel junction to the base of the gingival sulcus. Three sites with moderate periodontal pockets fulfilling the study criteria were identified in each segment and considered for clinical analysis. After the documentation of clinical parameters, randomization was performed using the numbering system. Control sites treated with SRP alone and test sites treated with SRP + multiple PDT.

Treatment Protocol

By using ultrasonic scalers and area-specific curettes, Scaling and root planing were performed until smooth root surface was achieved followed by photodynamic therapy was performed in the test sites. PDT was

performed using 1 mg/ml of ICG photosensitizer (PS) solution as suggested by Parker, 2013 [16] (AUROGREEN®). The solution was delivered subgingivally using a syringe with blunt cannula needle in an apico-coronal direction into the periodontal pockets till the pocket entrance. Irradiation with 940 nm diode laser was executed for 30 seconds with a power output of 0.1 W in a non-contact mode at the entrance of the pocket (Fig. 2). Excess dye was removed using sterile saline irrigation. The procedure was repeated at 1st, 2nd and 4th week.

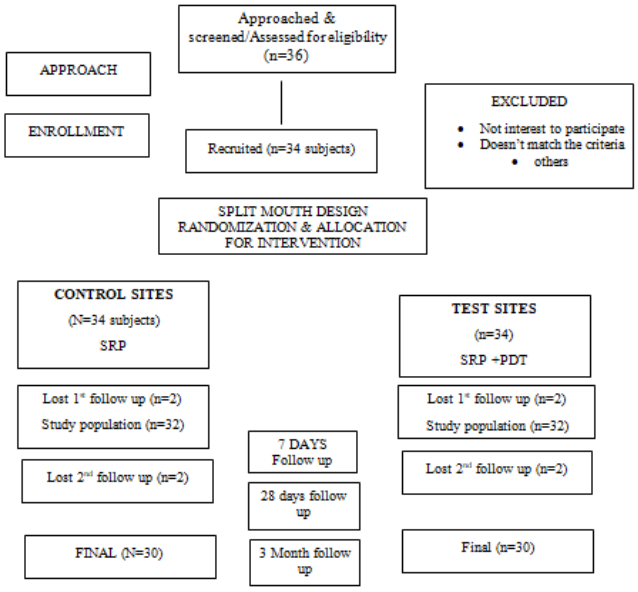

Fig.1: Consort flowchart showing the study design.

Table 1: Demographic details of the study participants.

Total number of study subjects (N = 30)		
AGE (Years)		Mean ± S.D 38.60 ± 6.75
Gender	Male Female	n (%) 22 (73.3%) 8 (26.7%)

Statistical Analysis

Statistical analysis was performed using SPSS version 17 software. Kolmogorov-Smirnov test showed that the data followed a non-normal distribution and accordingly non-parametric tests were applied for data analysis. Intergroup comparison was performed using the independent t-test. An intragroup comparison was performed using Repeated measures ANOVA. Groups with different letters in superscript show statistically significant differences (^{a,b,c,} Test Applied: Dunn's Post-Hoc test- pairwise comparison to baseline within the group). $P \leq 0.05$ was considered statistically significant.

Result

A total of 34 systemically healthy patients presenting bilateral periodontal destruction in mandibular posterior segments were included in the current study. During the course of the study period, four patients dropped out and at the end of the study, result analysis was performed on 30 patients. None of the subjects presented with any adverse reactions or hypersensitivity reactions.

Clinical Outcome

In the current study, the assessment of clinical parameters were analyzed at baseline, 28^{thday},and 3-monthfollow-up. The intergroup and intra-groupcomparisons were assessed on both control and test sites for mean scores of PPD,CAL, and Bleeding index at baseline, 28th day and 3 months follow-up were shown in Table 2.

At baseline, no statistically significant differences were noted between test and control sites. The mean PI and GI scores in Test sites at baseline were 2.10 ± 0.00, ± 0.00 ; were significantly reduced to 1.00 ± 0.00, 0.93 ± 0.27 at 28th days and 0.15 ± 0.34, 0.15 ± 0.37 at 3 months. In control sites at baseline were 2.10 ± 0.00, 2.10 ± 0.00 which reduced significantly to 1.11 ± 0.17, 1.06 ± 0.23 at 28th months, and 0.56 ± 0.40, 0.60 ± 0.35 at 3 months. By intergroup analysis, it tells that test sites showed a superior overall reduction in mean PI and GI compared

to control sites during follow-up visits for 28th days and 3 months.

Table 2: Comparison of clinical parameters in the Control group and Test group (Photodynamic therapy) for mean score of BOP,PPD and CAL at baseline , 28th day and 3 months.

Severity	Group	Mean ± SD			Statistics
		Baseline	28th day	3 month	P-value##
BOP	Group I	2.27 ± 0.46[a]	0.40 ± 0.51[b]	0.08 ± 0.05[c]	<0.001**
	Group II	2.27±0.46[a]	0.47±0.52[b]	0.05 ± 0.04[c]	<0.001**
	P-value#	0.065	0.065	0.064	
PPD	Group I	5.93± 0.80[a]	3.33±0.72[b]	2.67±0.62[c]	<0.001**
	Group II	6.0 ± 0.76[a]	3.0 ±0.76[b]	2.27±0.46[c]	<0.001**
	P-value#	0.077	0.162	0.007*	
CAL	Group I	6.27±0.96[a]	3.60±0.74[b]	2.93±0.80[c]	<0.001**
	Group II	6.33±0.82[a]	3.27±0.70[b]	2.60±0.63[c]	<0.001**
	P-value#	0.077	0.162	0.007*	

BOP, bleeding on probing; PPD, pocket probing depth; CAL, clinical attachment loss.

Group I- Control, Group II- Photodynamic therapy group. The values are presented as Mean ± Standard deviation (SD).

*P-value ≤ 0.05- Statistically significant, **P-value ≤ 0.001- Highly statistically significant; 95 % CI. #Test Applied: Independent t-test (Intergroup comparison); ##Test Applied: Repeated measures ANOVA (Intragroup comparison); Groups with different letters in superscript show statistically significant differences ([a,b,c,] Test Applied: Dunn's Post-Hoc test- pairwise comparison to baseline within the group).

Discussion

In the medical field, for many years, Indocyanine green has been commonly used for clinical diagnosis. In dentistry, the impact of ICG as a photosensitizer for PDT against periodontal pathogens is limited. So the present study aimed to evaluate the clinical efficacy of multiple applications of PDT (0, 1st, 2nd, and 4th week) using ICG photosensitizer and diode laser 940nm as an adjunct to SRP in treating chronic periodontitis patients over 3 months follow-up. The primary objectives of the study were to evaluate and compare the changes in Bleeding on probing, probing pocket depth, and clinical attachment level, at test and control sites before and after therapy. The secondary objective was to compare the changes in mean GI and PI in the test and control groups before and after therapy.

There is various factor that includes radicular anatomy, location of teeth, and depth of periodontal pockets that influence the accessibility and efficacy of instrumentation. significant overcome these difficulties, in the current study only mandibular posterior segments were included manifesting with moderate periodontal destruction (PPD 4-6 mm with CAL).In the present study, the mean PPD and CAL values for both groups showed significant improvement, and also showed significantly superior outcomes in test sites at both 28th days&3-monthfollow-up visits (P ≤ 0.05).

Birang et al 2015 [17] and Monzavi et al 2016 [18], in their studies, reported significant changes in PPD alone (P ≤ 0.05). The percentage of sites positive for bleeding on probing reduced significantly from baseline to 3 months

post-therapy ($P \leq 0.05$). On comparing the current study outcomes with previously published studies, Birang et al 2015 [17], reported a significant reduction in bleeding scores accompanied with insignificant changes in mean plaque scores in both groups at 3 months. Furthermore, at the end of the study, there were no significant differences in mean plaque and bleeding scores between the groups. Monzavi et al 2016 [18], observed significantly superior outcomes in test sites with regard to changes in mean BoP scores at 1 months and mean PI scores at 1 month follow-up visit. But in our present study showed significant changes in BOP, PPD, and CAL from baseline to 3 months period.

As there was no exclusive meta-analysis available stating the efficacy of multiple applications of PDT as an adjunct to SRP in treating periodontitis patients, the outcomes of the current study were compared with result of the meta-analysis which included clinical trials employing both sigle and multiple application of PDT.

Dong Xue et al 2017 [19] reported that SRP + PDT treated sites had a significant additional benefit in reduction of probing depth (0.40 mm) but not in gain of clinical attachment, based on the analysis from 11 RCTs. On contrary, Leandro Chambrone et al 2018, [20] stated that SRP + PDT protocol presented with a modest additional PPD reduction of 0.43 mm and CAL gain in the treatment of moderate periodontal pockets (5-6 mm). In the current study, there were a significant reduction in all clinical parameter mentioned as primary outcomes.

Within the limitation of the study, we infer that both test and control group show statistically significant results in a reduction in all clinical parameters at baseline to 3 months. By comparing both the test and control group; values were shows similar result but the test group was a little superior tothe control group. Hence, PDT can be adjunct to conventional treatment for long-term benefits in the management of periodontal pockets because PDT is applied in multiple times. The difference in the current study outcome with previous literature was the application of PDT protocol and patient characteristics. Moreover, the addition of a group-like single application of PDT would have enhanced the design of the study.

Conclusion

Within the limitation of the study, multiple applications of PDT as an adjunct to SRP resulted in superior outcomes, in terms of clinical parameters when compared with conventional therapy at 3 months follow-up. In forthcoming studies with long-term investigations in the wider population, the number of applications and time intervals for repeated PDT performance need to be considered in order to establish this as a standard protocol. Additionally, new photosensitizers and an improved delivery system need to be outlined in the future to attain enhanced outcomes

Declaration of Competing interest

No conflict of interest related to this study. All procedures followed were in accordance with the institutional ethical committee and informed consent was obtained from all the patient for being included in the study. No funding has been received for the conduct of this study and/or preparation of this manuscript.

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