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Original Research Paper

Periodontology

ANTIMICROBIAL EFFICACY OF ANTIMICROBIAL PHOTODYNAMIC THERAPY (APDT) AS AN ADJUNCT TO NON-SURGICAL PERIODONTAL THERAPY: A RANDOMIZED CONTROLLED TRIAL

Dr. Shaswata Karmakar*

Post graduate student, Department of periodontics & Implantology, College of dental sciences, Davangere, Karnataka – 577004. *Corresponding Author

Dr. Shobha Prakash

Vice-Principal, Professor and Head 1,2- Department of periodontics & Implantology, College of dental sciences, Davangere, Karnataka – 577004.

ABSTRACT

Background: Antimicrobial photodynamic therapy (aPDT) has been introduced in periodontal therapy in an attempt to improve the efficacy of conventional root surface debridement. The aim of the present study was to microbiologically evaluate the efficacy of aPDT to non-surgical periodontal treatment in chronic periodontitis patients.

Methods: Twenty subjects with Chronic Periodontitis were randomly treated with scaling and root planning (SRP) (control) and SRP with aPDT (test). Sites of the control group and test group were treated by SRP and SRP+aPDT,respectively. Subgingival plaque samples were collected from both the sites and sent for microbiological analysis. Microbial profiles from the samples were assessed at baseline and after 3 months.

Results: Intra-group analysis after 3 months showed significant reduction in all the periopathogens in both the groups whereas inter-group analysis showed non-significant results.

Conclusion: present study suggests that application of aPDT could be a beneficial adjunct to non-surgical periodontal therapy.

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KEYWORDS : Antimicrobial Photodynamic therapy, Chronic Generalized Periodontitis, Indocyanine Green, periodontopathogens,

INTRODUCTION

The main objective of periodontal therapy is to eliminate bacterial niches by removing the supra and subgingival biofilm. Plaque removal with eradication of niches of causative pathogens is currently performed using mechanical methods, such as nonsurgical therapy, which results in significant clinical improvements. However, it has been demonstrated that conventional mechanical therapy cannot completely remove all periodontal pathogens because of the anatomical complexity of the tooth roots, which may contain furcation areas , concavities and the bacteria invading the surrounding soft tissues.[1]

Several adjunctive modes like use of antimicrobial agents, local or systemic antibiotics in conjunction with mechanical debridement are current approaches to decrease the bacterial loads and improve the outcomes of nonsurgical periodontal therapy. The drawbacks in using the above mentioned are i)the development of resistance to antibiotics by organisms, ii)to achieve and maintain a stable therapeutic concentrations of the drug for a sufficient length of time to eradicate the organisms present in the biofilm.[2]

Antimicrobial photodynamic therapy (aPDT) has been used in the treatment of skin cancers in medical field since 1960's and its use is increasing rapidly in the field of dentistry.[3] The concept of antimicrobial photodynamic therapy implies use of a low intensity visible light at specific wavelength along with a specific non-toxic photosensitizer. The combined effect of photosensitizer and low intensity visible light, causes photo destruction of target cells due to cytotoxic effect in the presence of oxygen. This light induced effect is due to the conversion of the excited photosensitizer from the ground state to the triplet state resulting in production of singlet oxygen and other reactive agents, which are very toxic to certain cells or bacteria.[4] Indocyanine green (ICG), a new photosensitizer dye, had been proven to be effective against *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, when activated at 810 nm wavelength by a diode laser. ICG, a tri-carbocyanine that belongs to family of cyanine dyes is approved by FDA for various cardiovascular uses. It has high absorption in the infrared spectrum with an absorption peak near 810 nm which is close to the emission of diode lasers. It has low toxicity, rapid elimination and is a ideal photosensitizer.[5]

Studies have suggested the killing of key periodontopathogens like *P.gingivalis, A.actinomycetemcomitans* by diode laser activated ICG.[6]. Recently, in a review it was also demonstrated that ICG when activated by a diode laser (810 nm) provides bactericidal effect and can be used as an adjunct in the reduction of bacterial loads.[7] However, currently there is lack of an established literature and protocol for adjunctive laser treatment with scaling and root planing.Therefore the purpose of the present study was to evaluate the effects of aPDT as an adjunct to non-surgical periodontal therapy for the treatment of chronic periodontitis using ICG as a photosensitizer.

MATERIALS AND METHODS

Subject selection

A total of 40 sites from 20 patients (age range 35 to 55 years; mean age 38.2 ± 9.8 years) diagnosed with chronic generalized periodontitis (as defined by AAP 1999), referred for periodontal treatment to the department of Periodontics, College of Dental Sciences, Davangere, Karnataka, were included in the study after having signed an informed consent. The inclusion criterias were 1) Patients with more than 50% of sites involved with pocket formation and bone loss. 2) Patients with more than 50% of sites with clinical attachment loss of ≥ 4 mm. with the radiographic evidence of bone loss. 3) Patients who had more than 20 teeth with at least 2 or more

sites with the pocket depth of ≥ 6 mm in at least 2 quadrants of the mouth. 4) Patients who had not been treated for periodontitis in previous 6 months and 5) Patients who had not received antibiotics within past 2 weeks. The exclusion criterias were 1) Pregnant and lactating patients. 2) Patients with history of allergy. 3) Patients who showed evidence of systemic diseases and 4) Patients with the history of smoking and alcohol consumption. The microbiological parameters were detection and quantitative comparison of the periodontopathogens ***Porphyromonas gingivalis, Tanerella forsythia*** and ***Treponema denticola (Red complex)*** by using Multiplex Polymeric Chain Reaction (PCR) method.

Study design

The study was a randomized controlled, double blinded clinical trial with a split-mouth design, intended for comparison of 2 treatment modalities: Scaling and Root Planing (SRP) only and Scaling and Root Planing+ Photodynamic Therapy (SRP+aPDT) using Indocyanine Green (ICG) photosensitizer (ELEXXION AG PERIOGREEN, GERMANY) (Figure 1) in chronic generalized periodontitis patients. In each patient 2 quadrants were randomly assigned as **group 1 (control group)** where 20 Selected sites were treated only by SRP and group **2 (test group)** where 20 Selected sites were treated by SRP + aPDT.

Treatment protocol

By randomization, the sites were assigned as control and experimental groups. First all patients received a professional scaling four weeks prior to the treatment. On the baseline day microbiological samples from deepest site from each quadrant were collected for microbial analysis. Later the sites in the control group were subjected to SRP and test group were subjected to SRP+aPDT.

Intrapocket application of periogreen

Three to four drops of freshly prepared ICG dye was applied to each pocket and overfilled and left over for 3 minutes for proper tissue exposure.Then the excess agent was removed by flushing with sterile water. Activation was done with a laser unit **(PICASSO, DIODE LASER, 400µ** tip)internally to the pocket for 40 seconds on each location **(300 mW power, 810nm wavelength)**. 6 locations on each tooth were exposed to aPDT.[8]

Microbiological assessment

All subgingival plaque samples were obtained by the same operator to standardize the sampling procedure. Samples were collected from the deepest site of each quadrant. The selected sites were cleaned, isolated and air dried using sterile cotton rolls. The sample was taken using a sterile paper points ISO (International Organization for Standardization) #40 , and sent for microbial analysis.[9] Paper points contaminated with blood and saliva were discarded.

Statistical analysis

A site-specific intra and inter-group comparison of Bacterial Quantification levels was performed. The results were subjected to statistical analysis, which are expressed as mean ± SD and proportions as percentages. Descriptive and inferential statistics were used in the present study. Wilcoxon signed ranked test and Mann-whitney U test were used for intra and inter group comparison of microbiological parameters. A *P*-value of $\leq$0.05 was considered statistically significant and *P*-value of $\leq$0.001 was considered as highly significant.

RESULTS

All subjects completed the 3-month re-evaluation period. Healing was uneventful in all cases. No adverse effects were reported by any of the subjects. The microbial levels of all 3 periodontopathogens, ***Porphyromonas gingivalis(P.g), Tanerella forsythia(T.f)*** and ***Treponema denticola(T.d),*** in this study showed reduction in both the groups (Test and Control) from baseline to 3 months post-operative. However, on comparison between the groups the reduction was found to be non-significant. **(Figure 2,3)**

FIGURE 1: PERIOGREEN (PHOTOSENSITIZER DYE)

Parameters		Baseline	3 Months	Mean difference	P value
T.d	Test group	$2.05X10^4$	0	$2.05X10^4$	0.013
	Control group	$2.45X10^4$	0	$2.45X10^4$	0.002
	P value	0.989 (NS)	0.124 (NS)		
P.g	Test group	$61.5X10^4$	$0.53X10^4$	$60.90X10^4$	0.001
	Control group	$335X10^4$	$4.1X10^4$	$330.9X10^4$	0.001
	P value	0.465 (NS)	0.172 (NS)		
T.f	Test group	$0.2550X10^4$	0	$0.2550X10^4$	0.058
	Control group	0	0	0	0.001
	P value	0.102 (NS)	0.671 (NS)		

S= SIGNIFICANT (P< 0.05), HS=HIGHLY SIGNIFICANT (P< 0.001), NS= NON SIGNIFICANT (P> 0.05)

FIGURE 2: DIFFERENCES BETWEEN MICROBIOLOGICAL PARAMETERS (GRAPH)

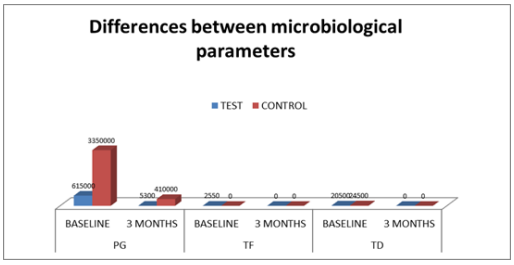

FIGURE 3: DIFFERENCES BETWEEN MICROBIOLOGICAL PARAMETERS (GRAPH)

DISCUSSION

Periodontitis is a multifactorial disease that is associated with loss of the supporting tissues (i.e., periodontal ligament and alveolar bone) of the tooth. A major objective of periodontal therapy is to remove microbial deposits from the root surface to stop disease progression. Numerous studies reported significant improvements in clinical and microbial parameters following non-surgical periodontal therapy. 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 instrume ntation techniques are effective in completely eliminating subgingival deposits. These limitations could be attributed to several factors, such as the complex anatomy of teeth and mechanical limitations related to the size of instruments or invasion of periodontal pathogens into the surrounding soft tissues or possible recolonization of periodontal pockets from other diseased sites or intraoral niches.[10]

Mechanical debridement can create significant changes in the microbiological environment of periodontal pockets by shifting the pathogenic biofilm to a beneficial one. This leads to a decrease in microbial loading and concentration of its products, such as lipopolysaccharide, thereby resulting in a better control of host immuno-inflammatory responses, reduction in gingival crevicular fluid flow and a more neutral subgingival environment compatible

with periodontal health. Nonsurgical subgingival debridement significantly decreases the population of bacteria associated with chronic periodontitis, including *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Prevotella intermedia, Tannerella forsythia and Treponema denticola.* However, certain pathogens, such as *A. actinomycetemcomitans and P. gingivalis,* are particularly resistant to the effects of subgingival debridement. This has been linked with their ability to invade the pocket epithelium and underlying connective tissues.

Clinicians who recognize the impact of specific bacteria on periodontal conditions have incorporated antimicrobials as a part of periodontal therapy. Systematic reviews have shown that systemic and local delivery of antimicrobials can significantly improve the microbiological and clinical outcomes of periodontal therapy, especially when it is timed correctly with thorough subgingival debridement. However, frequent use of antimicrobials may lead to antimicrobial resistance, development of opportunistic infections, and unwanted systemic effects, which limits their clinical usage. Clinicians are therefore in search of alternative adjunctive therapies that might provide similar benefits to antimicrobial therapy with fewer side-effects.[11]

Antimicrobial Photodynamic therapy (aPDT), also called photoradiation therapy, phototherapy, or photochemotherapy, was introduced in medical therapy in 1904 as the light-induced inactivation of cells, microorganisms, or molecules. aPDT involves the combination of visible light, usually through the use of a diode laser and a photosensitizer. The photosensitizer is a compound that is capable of absorbing light of a specific wavelength and transforming it into useful energy. Each factor is harmless by itself, but when combined they can produce lethal cytotoxic agents that can selectively destroy cells. Thus, aPDT may represent a promising alternative for reducing the bacterial load or even for eradicating certain periodontal pathogens.[12]

The present clinical trial was performed to investigate PDT as an adjunct to non surgical periodontal therapy for treatment of chronic generalized periodontitis. Indocyanine green is a photosensitizer used in the study. Nagahara et al (2013)[5] and Parker. S (2013)[7] showed that the maximum absorption wavelength of ICG is approximately 810 nm, a tissue penetrating wavelength and they proposed that an 810 nm wavelength diode laser with ICG might enable a bactericidal effect by external irradiation without causing damages to the host tissues.In the present study, the split mouth design was used because it excludes the influence of patient's specific characteristics and facilitates the interpretation of trials by minimizing the effects of inter-patient variability .

The microbial levels of all 3 periodontopathogens in this study showed reduction in both the groups from baseline to 3 months post-operative which was similar to the study by Nicos Christdoulides (2008)[10]. However, on comparison between the groups the reduction of periodontopathogens was found to be non-significant. This indicates that both the treatment protocols have almost similar efficiency on Periodontopathogens in treatment of Chronic Generalized Periodontitis.

Studies suggest that PDT treatment should be performed repeatedly during the first weeks of healing to enhance the antimicrobial effect. However, in this study, a single episode of PDT was performed to avoid an additional confounding factor (i.e., frequency of applied treatment), which could influence the microbiological outcome. Future studies are needed to elucidate the effects of multiple applications of PDT on the outcome of therapy.[10]

CONCLUSION

Within its limits, the present study showed that the addition of a single episode of PDT to SRP could be a beneficial adjunct to non-surgical treatment of chronic generalized periodontitis on a short term basis. The benefits were seen in terms of reduction of potent periodontopathogens. Thus, we can analyze that by adding antimicrobial Photodynamic therapy (aPDT) procedure to conventional treatment it might be possible to improve non-surgical periodontal therapy. Further longitudinal trials are needed to investigate the PDT on microbiological parameters.

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