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Effectiveness of photodynamic therapy as an adjunct to periodontal scaling for treating periodontitis in geriatric patients

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Abstract. – OBJECTIVE: The present study aimed to explore the efficacy of photodynamic therapy (PDT) as an adjunct to scaling and root planning (SRP) in the treatment of chronic periodontitis among geriatric patients.

PATIENTS AND METHODS: This clinical trial assessed 60 geriatric patients having severe periodontitis (Stage III/Grade C). Participants were randomized in two groups: Group A – SRP + PDT (test group) and Group B – SRP alone. The assessment of clinical periodontal parameters included plaque scores (PS), bleeding on probing (BOP), probing depth (PD) and clinical attachment level (CAL). Crevicular fluid interleukin (IL)-1β and IL-6 were assessed using Enzyme Linked Immunosorbent Assay (ELISA). All measurements were performed at baseline, 3 months, and 6 months, respectively. Mann-Whitney test was employed to analyze the mean values and establish inter-group comparisons. The *p*-value of <0.05 was considered to be statistically significant.

RESULTS: The mean age of the included patients ranged from 65.4 to 67.1 years. On inter-group comparison, a statistically significant reduction in PS and BOP was seen for Group A patients compared to Group B patients at 3 months follow-up ($p<0.001$). Probing depth and CAL were reduced in both groups. However, at 3 months and 6 months follow-up, the inter-group comparison showed reduced PD ($p<0.01$) and gain in CAL ($p<0.001$) for Group A in comparison to Group B. At each follow-up re-evaluation, there was no significant difference in the IL-1β levels between both the groups ($p>0.05$). The same trend was followed by IL-6 at 3 months. However, the reduction in the IL-6 was maintained until 6 months of re-evaluation.

CONCLUSIONS: PDT helped to reduce the clinical and pro-inflammatory load within the diseased periodontal pockets in geriatric patients.

Key Words:
Photodynamic therapy, Geriatrics, Periodontitis, Dental scaling.

Introduction

Periodontitis is termed as a multifactorial, inflammatory disease that is characterized by an increase in the periodontal probing depth (PD) and loss of clinical attachment levels (CAL) that could lead to tooth loss if sufficient treatment is not provided timely[1]. The microbial plaque and the host immune responses are considered to be important causative factors that are highly responsible for the progression of this disease[1]. Some of the modifying factors of chronic periodontitis include systemic diseases, such as type 2 diabetes mellitus, obesity, tobacco smoking and advancing age[2-4]. In geriatric subjects, the immune system undergoes ageing, resulting in impaired immune-defensive capacities (immune senescence). Elderly people display a decline of T-cells in peripheral blood and lymphoid tissues, whereas their proportions of highly differentiated effector and memory T-cells increase[5].

The basic concept behind the strategy for disease control is to introduce different treatment methods that can help in the removal or alteration of the causative factors. The gold standard treatment modality for periodontal disease is scaling and root planning (SRP)[6]. The use of SRP has proven to be beneficial in treating periodontitis as it reduces PD, improves CAL and the associated inflammatory conditions[7]. However, SRP has limitations too. SRP may not be a viable treatment option in inaccessible deep pockets and root furcation and concavities[8]. To improve the outcomes, health care professionals and researchers have been working together to come up with treatment strategies that are easy to perform and accessible to the general population. One such treatment strategy is the use of photodynamic therapy (PDT) in medical and dental practice.

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Photodynamic therapy (PDT) is one of the disinfection methods that is being readily used to treat dental diseases. These diseases involve white lesions, gingival, periodontal, and peri-implant diseases[9-16]. The mechanism of PDT is dependent upon the use of a diode laser, freely present oxygen, and a photosensitizing agent. The photosensitizer (PS) or the dye molecule is applied to the site on which the diode laser is to be applied. The application of diode laser allows the dye molecules to get activated from a dormant singlet state to an active triplet state. The highly active molecules react with the nascent oxygen to allow the formation of reactive oxygen species (ROS). Because of their toxic nature, these molecules are responsible for initiating wanted cellular death[17,18].

There is dearth of studies that assessed the efficacy of various periodontal therapies in individuals ≥ 65 years of age. According to the authors, a comprehensive search of the literature revealed that Shanbhag et al[19] gave forward the conclusion that non-surgical periodontal treatment in the form of SRP moderately improved the periodontal parameters in older adults. On the contrary, Tonetti et al[20] concluded that periodontal tooth loss is inevitable in old-age patients even after long supportive periodontal therapy. With this concept, we proposed the use of PDT to improve the oral health in geriatric patients with periodontal disease. Therefore, the present study aimed to explore the efficacy of PDT as an adjunct to SRP in the treatment of chronic periodontitis among geriatric patients.

Patients and Methods

The current randomized controlled clinical trial was executed according to the guidelines described in the Declaration of Helsinki. Each participant was requested to read the consent form and provide their approval in the form of a signature. They were also permitted to leave the study at any point of the time without facing any consequences.

Inclusion and Exclusion Criteria

All the patients in the present study were diagnosed with Stage III (severe)/Grade C periodontitis per the diagnostic criteria reported in the new classification of periodontal disease proposed in the '2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions'[21]. The criterion for inclusion included: i) age ≥65, ii) patients with diagnosed Stage III/Grade C periodontitis, iii) PD >5 mm, iv) presence of bleeding, v) clinical attachment loss >5 mm, and vi) >10 occluding pairs. The exclusion criteria involved: i) any history of periodontal therapy in the last six months, ii) intake of any antimicrobial medication in the past six months, iii) systemic conditions that can alter the progression of the disease, such as HIV, diabetes mellitus, renal disease, cardiovascular problems, iv) use of any probiotics.

Group Stratification

Based on the mode of treatment the study participants were stratified into two groups. The patients in Group A underwent full-mouth disinfection (SRP) followed by adjunctive photodynamic therapy (SRP + PDT). Group B (control group) included patients who underwent full mouth SRP alone. A single session was planned for each participant in the study. Randomization was performed by using the coin-toss method, whereas the allocation concealment was accomplished with the help of non-sealed envelopes. These envelopes were opened before commencing the treatment to the study participants.

Intervention Protocol

Full Mouth Disinfection (SRP)

Each participant from both the study groups was rendered ultrasonic scaling before the start of the treatment. SRP was conducted by one trained periodontist who was not informed about the treatment allocation. A single session of SRP was completed using both the hand instruments and a sterilized ultrasonic piezoelectric scaler (Cavitron Select SPC, DENTSPLY Professional York, PA, USA) which was followed by a polishing session. A session of dental education was then initiated to educate the participants about the tooth brushing techniques and oral hygiene maintenance. They were advised to brush their teeth twice daily, use dental floss (Oral B Superfloss™, Saudi Arabia), and chlorhexidine mouth wash (Clorasept, Riyadh, Saudi Arabia) once daily, respectively. The use of anti-inflammatory medications was strictly prohibited during the study.

Photodynamic Therapy (PDT)

After full mouth disinfection, individuals from Group I were subjected to treatment with PDT

with the help of a diode laser HELBO® TheraLite – Bredent Medical, Germany). Each participant underwent a single session of PDT. The laser parameters, such as wavelength, spot area, density, power output, and laser energy were set at 670 nm, 0.028 cm^2, 1.1 W/cm^2, 100 mW, and 150 mW, respectively. A concentration of 0.005% methylene blue was used as a photosensitizer. Methylene blue was applied inside in the gingival sulcus with the help of a blunt needle.

Periodontal Parameters

The evaluated clinical parameters included bleeding on probing (BOP), plaque scores (PS), CAL gain, and PD. PS and BOP were estimated using dichotomous scoring criteria (0 – indicated absence of plaque/bleeding, 1 – indicated presence of plaque/bleeding). The readings for PD and CAL were measured with the help of a periodontal probe (UNC-15, Hu Friedy). The values were noted by measuring the distance from the periodontal pocket base to the gingival crest margin. Moreover, CAL was calculated by adding the value of clinical recession and PD. The clinical scores were observed at baseline, 3 months, and 6 months, respectively. All assessments were done under the guidelines reported in the document of the Eleventh European Workshop in Periodontology[22].

Gingival Crevicular Fluid (GCF) Collection

Gingival crevicular fluid (GCF) was sampled from the deepest part of the periodontal pocket from all the individuals. The surroundings of the periodontal pockets were dried using an air syringe and the isolation was maintained by using cotton rolls. The supragingival plaque was removed using appropriate scalers. Paper points (Periopaper, Pro Flow, Amityville, NY, USA) were inserted for 30 s in the periodontal pocket until the resistance was felt. Blood or salivary contaminated paper points were discarded. The measurement of the fluid samples was done with the help of a calibrated electronic gingival fluid device (Periotron 6000, Amityville, NY, USA). The samples were collected at baseline, 3 months, and 6 months, respectively.

Evaluation of Biomarkers

The estimation of c-reactive protein from the blood and interleukin-6 (IL-6) and interleukin-1-beta (IL-1β) was carried out by using the Enzyme-Linked Immunosorbent Assay (ELISA) method. The GCF taken from the patient's oral cavity was diluted with sample diluent. The reagents were thawed at room temperature. 100 µL volume of standard solution and diluted GCF samples were subjected to their respective labeled wells. The plate was covered and was allowed to incubate at 25°C for an hour. Each well was then washed (three times) by incorporating 300 µL of wash solution. This was followed by introducing 100 µL of biomarker-specific polyclonal antibodies into each well. The plates were then incubated at room temperature for 2 hours. The reaction was stopped by adding a stop solution to each well. The optical density (OD) of the samples was evaluated with a calibrated well plate reader (ELISA Processor II, Boehring, Germany). The calculations were expressed as concentration of biomarker (pg)/GCF volume (mL).

Statistical Analysis

SPSS Software (SPSS Version, Chicago, IL, USA) was used to perform the statistical analysis for the observed data. All the reported values were noted in means and standard deviation (mean ± SD). The normality of the observed data was checked with the Shapiro-Wilk test. Bonferroni's post-hoc test was employed by the researchers to establish multiple comparisons with the present data. On the other hand, the Mann-Whitney test was employed to compute the *p*-value for the inter-group comparisons. Regarding the intra-group comparisons, the *p*-value was calculated with the help of the Wilcoxon signed ranked test.

Results

A total of 60 patients completed the clinical trial without any withdrawals. The baseline characteristics were explained in Table I. For Group A (PDT + SRP), the females were found to be slightly higher than males, whereas an equal distribution of both genders was seen in Group B (SRP only). The mean age for patients in Group A and Group B was calculated as 68 years and 66 years respectively. A majority of patients reported once daily tooth brushing for maintaining oral hygiene.

Table II describes the clinical periodontal parameters. No statistically significant difference in any of the assessed periodontal parameters

Table I. General characteristics of the study group.

Variables	Group-A (PDT + SRP)	Group B (SRP only)
Number of patients	30	30
Gender (male/females)	13/17	15/15
Mean age (in year ± SD)	68.4 ± 2.8	66.1 ± 3.3
CRP in mg/dl	0.89 ± 0.03	0.92 ± 0.05
Brushing frequency (%)		
Once daily	85	81
Twice daily	15	19

was observed in between both the study groups at baseline. A statistically significant reduction was seen for both PS and BOP in both the groups. On inter-group comparison, a statistically significant reduction in PS and BOP was seen for Group A patients compared to Group B patients at 3 months follow-up ($p<0.001$). There was no statistically significant difference in both PS and BOP parameters between both the groups measured at 6 months follow-up ($p>0.05$). Probing depth and CAL was observed to reduce in both the groups. However, at 3 months and 6 months follow-up, the inter-group comparison showed reduced PD ($p<0.01$) and gain in CAL ($p<0.001$) for Group A in comparison to Group B (SRP only).

The changes in the pro-inflammatory cytokines achieved before and after the treatment are demonstrated in Table III. A statistically significant reduction was noted for both IL-1β and IL-6 in both groups ($p<0.01$). At each follow-up re-evaluation, there was no significant difference in the IL-1β levels between both the groups ($p>0.05$). The same trend was followed by IL-6 at 3 months. However, the reduction in the IL-6 was maintained until 6 months of reevaluation.

Discussion

The present clinical trial was conducted to evaluate the efficacy of PDT as adjunctive therapy to non-surgical periodontal therapy on the periodontal and pro-inflammatory parameters in geriatric patients having chronic periodontal disease. The study concluded that PDT plays a significant role in reducing the values of clinical parameters and biochemical biomarkers in old age patients having periodontal disease.

According to the results obtained, the use of PDT has proven to be effective in the treatment of periodontal disease in geriatric patients. During the evaluation at the first follow-up (3 months), a significant decrease in the clinical parameters and pro-inflammatory cytokines indicated positive results. The use of different agents used in PDT plays a crucial role in making it a potent therapeutic option in periodontal disease. The application of PS in deep periodontal pockets is considered a very important step. The interaction of PS with the light of a specific wavelength allows its activation which results in the formation of free oxygen species. The transmission of photon energy from PS to the nascent oxygen molecules permits the formation

Table II. Clinical inflammatory parameters in the study groups at baseline, 3 months, and 6 months.

Clinical parameters (mean ± SD)	Baseline		3 months		6 months	
	Group-A (PDT + SRP)	Group-B (SRP only)	Group-A (PDT + SRP)	Group-B (SRP only)	Group-A (PDT + SRP)	Group-B (SRP only)
Plaque scores (% on sites)	48.4 ± 15.6^{A}	50.1 ± 13.6^{A}	27.6 ± 4.8^{B}	38.5 ± 5.2^{C}	17.4 ± 3.3^{D}	22.9 ± 10.2^{D}
Bleeding on probing (% on sites)	38.7 ± 13.2^{A}	36.9 ± 10.6^{A}	21.2 ± 6.1^{B}	29.4 ± 8.1^{C}	19.7 ± 3.4^{D}	22.4 ± 7.6^{D}
Probing depth (in mm)	6.5 ± 1.7^{A}	6.7 ± 1.6^{A}	5.1 ± 0.12^{B}	5.8 ± 0.12^{C}	4.3 ± 0.6^{D}	5.1 ± 0.10^{E}
Clinical attachment level gain (in mm)	7.4 ± 0.92^{A}	8.2 ± 0.97^{A}	6.3 ± 1.07^{B}	7.2 ± 1.6^{C}	5.7 ± 0.98^{D}	6.5 ± 1.2^{E}

Dissimilar uppercase letters indicate statistical significance at $p < 0.05$ along rows.

Table III. Proinflammatory cytokine levels in the study groups at baseline, 3 months, and 6 months.

Laboratory parameters (mean ± SD)	Baseline		3 months		6 months	
	Group-A (PDT + SRP)	Group-B (SRP only)	Group-A (PDT + SRP)	Group-B (SRP only)	Group-A (PDT + SRP)	Group-B (SRP only)
IL-1β	161.5 ± 97.6^{A}	176.1 ± 94.5^{A}	125.3 ± 89.2^{B}	158.1 ± 96.3^{B}	132.8 ± 88.1^{B}	141.6 ± 86.2^{B}
1L-6	175.3 ± 92.5^{A}	182.6 ± 98.3^{A}	119.8 ± 82.6^{B}	160.2 ± 89.7^{B}	147.1 ± 67.3^{C}	167.3 ± 65.2^{A}

Dissimilar uppercase letters indicate statistical significance at $p < 0.05$ along rows.

of singlet oxygen species and free radicals, also called reactive oxygen species (ROS)[23-25]. These species are responsible for cellular death. Therefore, the combination of photosensitizer, laser light, and ROS is responsible for reduced biofilm levels in periodontal disease. The Hawthorne effect can also be taken into consideration for the improvement of plaque levels in the test group which involves both SRP and PDT[26]. The effect signifies the fact that patients receiving laser treatment and perceiving it as a special treatment may have maintained high levels of oral hygiene as compared to the group that did not receive any laser treatment.

A positive outcome for BOP at both intervals was seen but a significant reduction was seen at the 3-month interval. The reason for the improvement can be supported by the application of laser light as this light can penetrate the gingival blood circulation which elicits the immune-modulatory response, hence improving the tissue conditions[10].

The pro-inflammatory cytokines, interleukin 6 (IL-6), and interleukin 1-beta (IL-1β) were assessed during this clinical trial. Statistically significant changes for IL-6 were observed in Group A participants in comparison to Group B. IL-6 is commonly found around the synovial joint and it plays a crucial role in the activation of IL-1 and IL-8 which are responsible for bone destruction[27]. According to the observed results, PDT in conjunction with SRP helped in decreasing the IL-6 levels from baseline to 3 months, followed by an increase at 6 months. These results were obtained as PDT allows a significant increase in the immune-modulating cells. The immune-modulating cells express chemical reactions which decrease the stimuli for pro-inflammatory cells (B-cells, T-cells). By decreasing their activity, an improvement in the pro-inflammatory cytokines is achieved (IL-6, IL-1β)[28]. But on the contrary, the increase in IL-6 levels at 6 months interval can be associated with the lack of interest from the old age patients towards their general oral hygiene. The deficiency of motivation, decreased use of tools for oral hygiene maintenance are two factors that can be linked with the increase in IL-6 levels which result in worsening the periodontal conditions.

A few limitations of the present trial include a small sample size. An increased amount of patient recruitment as samples would have allowed us to project improved results regarding the use of PDT as adjunctive therapy in periodontal disease and other diseases[29-33]. Moreover, the evaluation of other biomarkers, such as matrix metalloproteinases and other cytokines were not evaluated in the present clinical study. The use of lasers with a variety of wavelengths preferably lesser should also be taken into consideration in future trials. Use of different photosensitizers should also be employed with the same technique to gain more knowledge regarding their effect on periodontal disease in geriatric patients. The inclusion of microbiological analysis should also be considered in future studies.

Conclusions

PDT helped to reduce the clinical and pro-inflammatory load within the diseased periodontal pockets in geriatric patients.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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