Journal of Oral Biology and Craniofacial Research 15 (2025) 525–533

Contents lists available at ScienceDirect

Journal of Oral Biology and Craniofacial Research

journal homepage: www.elsevier.com/locate/jobcr

Indocyanine green mediated antimicrobial photodynamic therapy: A non-invasive treatment approach for chronic periodontitis with type 2 diabetes mellitus: A randomized controlled clinical trial

Priyanka Agarwal, Pratibha Shashikumar *, Rakshitha S

Dept of Periodontology, JSS Dental College and Hospital, Mysuru, Karnataka, 570015, India

ARTICLE INFO

Keywords:
Antimicrobial photodynamic therapy
Chronic periodontitis
Type 2 diabetes mellitus
Nonsurgical periodontal therapy
Glycemic control

ABSTRACT

Background: Periodontitis is a destructive chronic inflammatory disorder of the periodontium and is a major cause of loss of teeth. Uncontrolled diabetes affects periodontal status and chronic periodontitis affects the glycemic status. Nonsurgical periodontal therapy is often not sufficient in completely eliminating the pathogens. Hence antimicrobial photodynamic therapy (aPDT), is being used in medically compromised patients as it does not cause adverse effects that are seen with other adjunctive treatments. This study aimed to evaluate the efficacy of antimicrobial photodynamic therapy using Indocyanine green as an adjunct to scaling and root planing in the treatment of periodontitis in controlled Type 2 Diabetes Mellitus (DM) patients with chronic generalized periodontitis. The objective to see improvements in clinical parameters and microbiological parameters along with its effect on glycemic levels.

Materials and methods: In this randomized controlled clinical trial a total of 40 chronic periodontitis patients with Type 2 DM were randomly assigned into test and control groups of 18 participants each. The test group received. Scaling and root planing (SRP) + aPDT) while the control group received only SRP. In SRP + aPDT group, pockets were irradiated with a diode laser after irrigation with Indocyanine green. Assessment of clinical parameters like plaque index (PI), gingival index (GI), probing depth, (PD), clinical attachment level (CAL), and glycated haemoglobin (HbA1c), as well as microbiological analysis for *Porphyromonas gingivalis (Pg)* and *Aggregatibacter actinomycetem comitans (Aa)* was done at baseline & 3 months post-therapy and data were statistically analysed.

Results: aPDT as an adjunct to SRP improved clinical and microbiological parameters. A statistically significant difference ($p < 0.001$) was noted on intergroup comparison with respect to PD, CAL, and colony forming units (CFU/ml) of Pg and Aa. There was an improvement in HbA1c levels from baseline to 3 months in both the groups however, there was no significant difference between the groups at 3 months.

Conclusion: The use of Indocyanine green mediated aPDT as adjuvant therapy in treatment of chronic periodontitis in Type 2 diabetes mellitus patients resulted in significant reduction in microbial counts as well as rendered additional clinical benefits.

Clinical significance: aPDT as adjunctive therapy to SRP can be a non-invasive treatment of choice for chronic periodontitis in medically compromised patients like Type 2 Diabetes mellitus patients.

1. Introduction

Periodontitis is a destructive chronic inflammatory disorder of the periodontium and is one of the major causes of loss of teeth globally. The prevalence of diabetes in India has been rising.[1] Diabetes mellitus is a modifying factor for periodontal disease progression. There is enough scientific evidence showing a bidirectional relationship between these two entities. Uncontrolled diabetes affects periodontal status and chronic periodontitis affects the glycaemic status, increasing the risk of complications in patients with diabetes. Periodontitis is known to be the sixth complication of diabetes. More than 90 % of patients with diabetes are found to have various degrees of periodontal tissue damage, that can be attributed to increased inflammatory response, effects of advanced glycosylation end products (AGEs) and increased oxidative stress as a

* Corresponding author.
E-mail addresses: priyuagarwal.31@gmail.com (P. Agarwal), dr.pratibhashashikumar@jssuni.edu.in (P. Shashikumar), rakshitha074@gmail.com (R. S).

https://doi.org/10.1016/j.jobcr.2025.03.004
Received 9 November 2024; Received in revised form 3 March 2025; Accepted 4 March 2025

primary connecting link between chronic periodontitis and diabetes.[2,3]

Various studies have shown that patients with poor control of DM have an increased risk of periodontitis, and the reverse is also true. Periodontal therapy has been reported to show a reduction in glycemic levels of around 0.4 %.[4] Hence it is important to eliminate the dysbiotic plaque mediated inflammatory response that can worsen either of the two chronic diseases.

The primary goal of periodontal therapy is to preserve the natural dentition by reducing the microbial load and inflammation, thus, achieving a healthy functional periodontium. Nonsurgical periodontal therapy is the gold standard in the treatment of periodontitis which comprises oral hygiene instructions, plaque and calculus removal and mechanical debridement of root surfaces. However, SRP is often not effective in completely eliminating the pathogens, due to anatomical complexity of the tooth and deep periodontal pockets rendering these areas inaccessible.[5] Hence many adjunctive treatments such as systemic and local administration of antimicrobials were introduced in addition to SRP. However, these treatment choices have their own disadvantages namely bacterial resistance, poor patient compliance among others. So, a newer treatment option i.e., antimicrobial photodynamic therapy, is being used in medically compromised patients without causing any adverse effects, drug reactions, or bacterial resistance.[6] Antimicrobial PDT has been suggested as an adjuvant to non-surgical periodontal therapy which results in photo-oxidative destruction of bacterial tissues with no damage to healthy tissues or cells.[7] The mechanism behind aPDT is that when a photosensitizer (PS) is exposed to laser light of a specific wavelength, it undergoes photo-activation and excitation of the PS in the presence of oxygen, releasing free radicals (Type 1 reaction) or singlet oxygen (Type 2 reaction) or both. These reactions are responsible for the oxidation and destruction of the cytoplasm and DNA thus facilitating a reduction in bacterial load.[8]

Indocyanine green (ICG) is a photosensitizer that received FDA approval in 1959 and was employed for the diagnostic purposes like measuring cardiac output, ophthalmic angiography, hepatic blood flow, and burn depth assessment. It has a quick clearance rate of 18 %–24 % per minute by the liver. It is also used in PDT because of its ability to absorb light, with peak absorption and emission at 800–830 nm wavelength.[9] Though, there are studies evaluating the efficacy of ICG-mediated aPDT for the treatment of chronic periodontitis,[10,11] there are not many studies that have evaluated the efficacy of aPDT using Indocyanine green in the treatment of chronic periodontitis patients with Type 2 DM.

This study is aimed to evaluate the efficacy of aPDT using Indocyanine green as an adjunct to SRP in Type 2 Diabetes Mellitus patients with chronic generalized periodontitis. The primary outcome was to evaluate the changes in probing depth, clinical attachment level, and colony count of Aa, and Pg, while the secondary outcome was to evaluate PI, GI, and HbA1c levels.

2. Materials and methods

2.1. Study design

This randomized controlled parallel design trial was carried out from March 2021 to March 2022 at JSS Dental College and Hospital, Mysuru, India. The ethical clearance was given by the ethical review board of JSS Dental College and Hospital, Mysuru (JSSDCH/IEC Research Protocol no. 50/2020). The trial is registered under clinical trials.gov with CTRI number “CTRI/2022/08/044,884”.

2.2. Calculation of sample size

The sample size was calculated considering a mean difference of at least 1.5 and a standard deviation of 2 between groups. In view of this, it was determined that a number of 18 patients per group was needed to obtain a study power of 90 % with a significance level of $p < 0.001$. Considering a possible loss of 10 % of the patients, the number of 20 patients per group was determined, totalling to 40.

The formula used to calculate the sample size as follows:

$$n = \frac{2\left(Z_{\alpha/2} + Z_{\beta}\right)^2 S^2}{\left(\bar{d}\right)^2}$$

Where $z\alpha 2/ = 1.96$, $z\beta = 1.28$.

2.3. Inclusion and exclusion criteria

Patients between ages 30–60 years, with controlled Type 2 Diabetes mellitus and diagnosed with chronic generalized periodontitis with at least 20 teeth in the dentition and a PD of 4–7 mm in at least 6 sites and a clinical attachment loss of ≥2 mm were included in the study. Pregnant and lactating patients, patients having any other immunocompromising conditions, patients who were on antibiotic therapy, those undergoing any kind of periodontal therapy in the last 6 months, and smokers were excluded.

2.4. Randomization

The randomization of 40 patients was done as follows. The selected patients with Type 2 DM and chronic periodontitis reported to the investigator (PS) of the study. The investigator then randomly assigned 40 patients into test and control group by sequentially numbered sealed opaque envelopes. The operator (PA) then according to the treatment assigned in the sealed envelope treated the patients either by SRP alone or SRP + aPDT and then recalled the patients after 3 months for follow-up. The CONSORT guidelines were followed as illustrated in Fig. 1.

2.5. Parameters assessed

Variables such as plaque index (PI) (Silness and Loe, 1964),[12] gingival index (GI) (Loe and Silness 1967),[13] Clinical attachment level (CAL) and probing pocket depth (PD)[14] were recorded. The clinical examination was performed by a single investigator (PS) at baseline and 3 months post-treatment (Fig. 2). For intraexaminer reliability an interclass correlation coefficient (ICC) of 0.4–0.75 was deemed acceptable All the clinical parameters were recorded with a millimeter-gauged periodontal probe (PCPUNC15, Hu-Friedy). The glycemic levels of the patients were assessed by HbA1c test using high performance liquid chromatography method. HbA1c was recorded to assess effect of periodontal therapy using PDT on the glycemic control in diabetic patients. The CFU count for Pg and Aa were recorded at baseline and 3 months as photodynamic therapy is essentially bacteriocidal in mechanism of action. These microorganisms were assessed as these are specific to periodontal disease.

3. Methodology

On the first visit, the patients were given oral hygiene instructions and were advised to get a blood investigation for HbA1c levels and recalled for intervention. On the second visit, full mouth scores of clinical parameters were recorded and subgingival plaque samples were collected. Full mouth scaling and root planing was performed in all the patients. In test group additionally, aPDT was performed. All the procedures were performed under local anaesthesia by single operator (PA), different from the investigator (PS).

All the patients were recalled one week after the intervention and the periodontal tissues were examined during this visit in order to verify the presence of periodontal abscesses, erythema, edema, or discomfort due to aPDT. The patients were under observation and recalled every month to evaluate their periodontal condition and oral hygiene instructions were reinforced. After a period of 3 months post-treatment, a

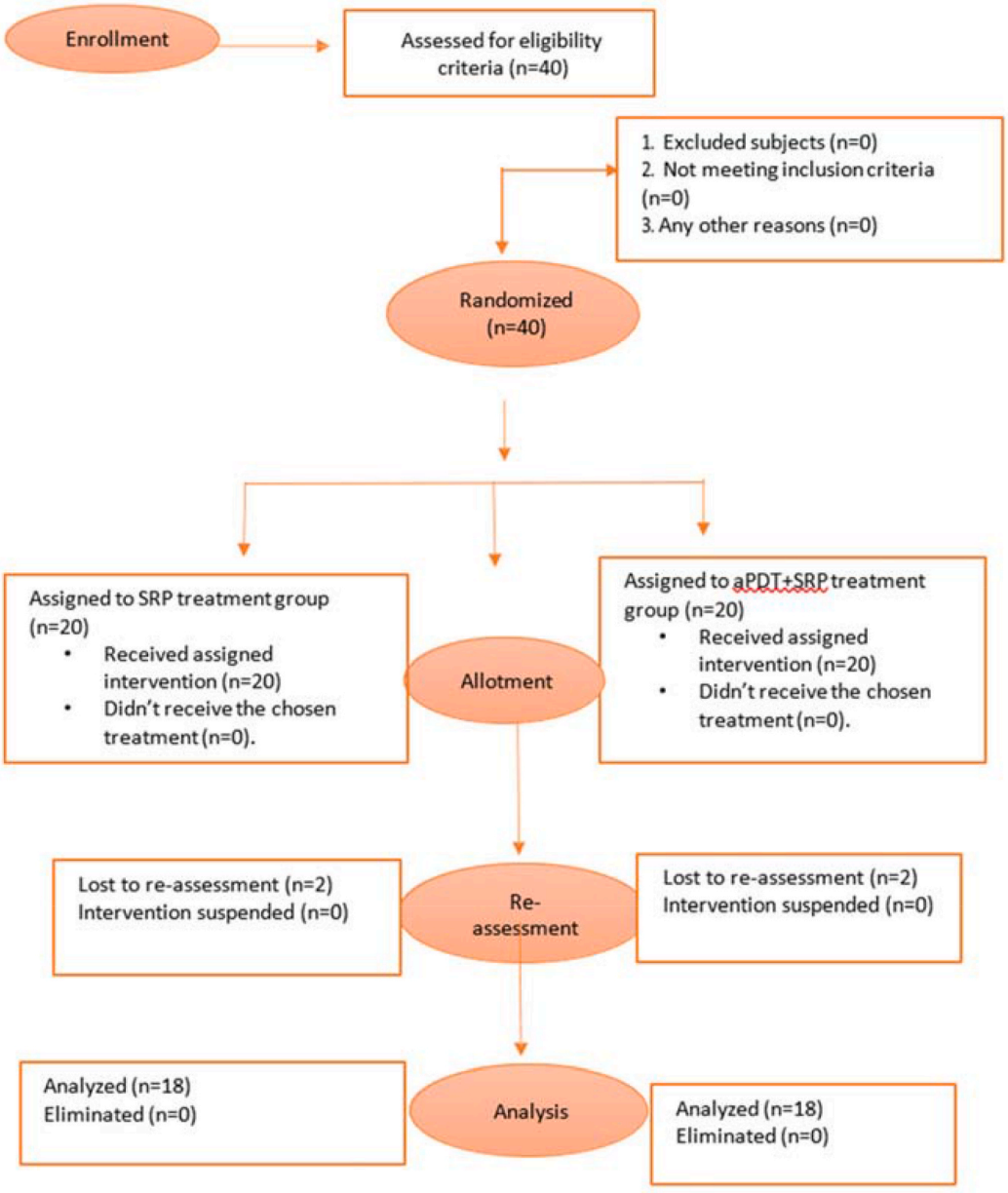


Fig. 1. Consort Flow chart.

periodontal clinical examination along with microbiological sample collection was done by the investigator (PS). The participants were advised to get a blood investigation report of HbA1c test at 3 months. The participants were followed up for further periodontal therapy as required after 3 months post-therapy.

3.1. Antimicrobial photodynamic therapy (aPDT)

In the test group all sites with PD $\geq$ 4 mm, were irrigated using 1 mg/ml of Indocyanine green (ICG) (Aurogreen, Aurolab, Madurai, Fig. 2) using a disposable syringe and blunt cannula until the pocket was completely flooded with the photosensitizer (Fig. 3) after 1 min the pocket was thoroughly irrigated with normal saline to remove excess dye from the pocket and was photoactivated using a diode laser of 808 nm wavelength (Mikro® Sunny 808 nm diode laser) at 0.8W power in continuous contact mode with a flexible 320 nm thin fibre optic cable. The cable was inserted in the periodontal pocket and slowly moved in an apical-coronal direction for 60s to activate the photosensitizer.[15] All the patients including the operator wore the protective eyewear during the entire irradiation period following the OSHA guidelines. The participants were asked to report back to the operator immediately if any discomfort or adverse reaction was encountered. Fig. 3 shows preoperative and postoperative probing depth.

3.2. Microbiological analysis

The association between Pg, Aa and chronic periodontitis is well established.[16] Hence microbiological analysis included assessment of CFU/ml of Pg and Aa. Subgingival samples were collected in three deepest pockets from each patient at baseline, and 3 months post-treatment. To perform the microbiological collection at the experimental sites, the supragingival biofilm was removed, followed by light irrigation, drying and isolation was done using sterile gauze or cotton rolls. A sterile curette (Gracey, Hu-Fridey) was introduced into the periodontal pocket, and subgingival plaque was collected. Plaque samples contaminated with blood and saliva were discarded. The collected

Fig. 2. Indocyanine green – Photosensitizer (Aurogreen, Aurolab, Madurai, India). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

plaque was pooled in sodium thioglycolate broth,[17] the transport medium. The samples were immediately sent for microbial analysis of *P. gingivalis* and *A. actinomycetemcomitans* (Aa), which were then separately vortexed, inoculated and incubated in an anaerobic jar for culturing and quantification of anaerobic bacteria. Fig. 4 shows the microscopic view of cultured microorganisms.

3.3. Statistical analysis

The data obtained from the clinical, microbiological, and haematological assessment were tabulated and subjected to statistical analysis using statistical software (SPSS version 29 for Windows). The demographic data like the age and gender of the patients were subjected to Descriptive statistics and a mean and standard deviation were obtained. Independent sample *t*-test helped compare average scores of the variables in both the groups. Paired *t*-test helped compare average scores between the various time points. A p-value <0.001 was deemed statistically significant.

4. Results

All 40 recruited patients were subjected to the treatment protocol in the assigned group and were assessed for clinical, microbiological parameters and HbA1c levels at baseline and 3 months post-therapy. During the 3 months follow-up, 2 patients in the test group and 2 patients in the control group were lost to follow-up. A total of 36 patients, 18 males and 18 females in 30–60 years age range with a mean age of 46.5 were analysed.

4.1. Clinical findings

There was no statistically significant difference between the two groups at baseline in all the parameters ($p > 0.001$) (Table 1).

4.2. Plaque index

Intragroup comparison of PI from baseline to 3 months in test and

Fig. 3. a. Baseline Probing depth b. Application of ICG using blunt cannula c. Activation of ICG with diode laser d. PD 3 months post-aPDT.

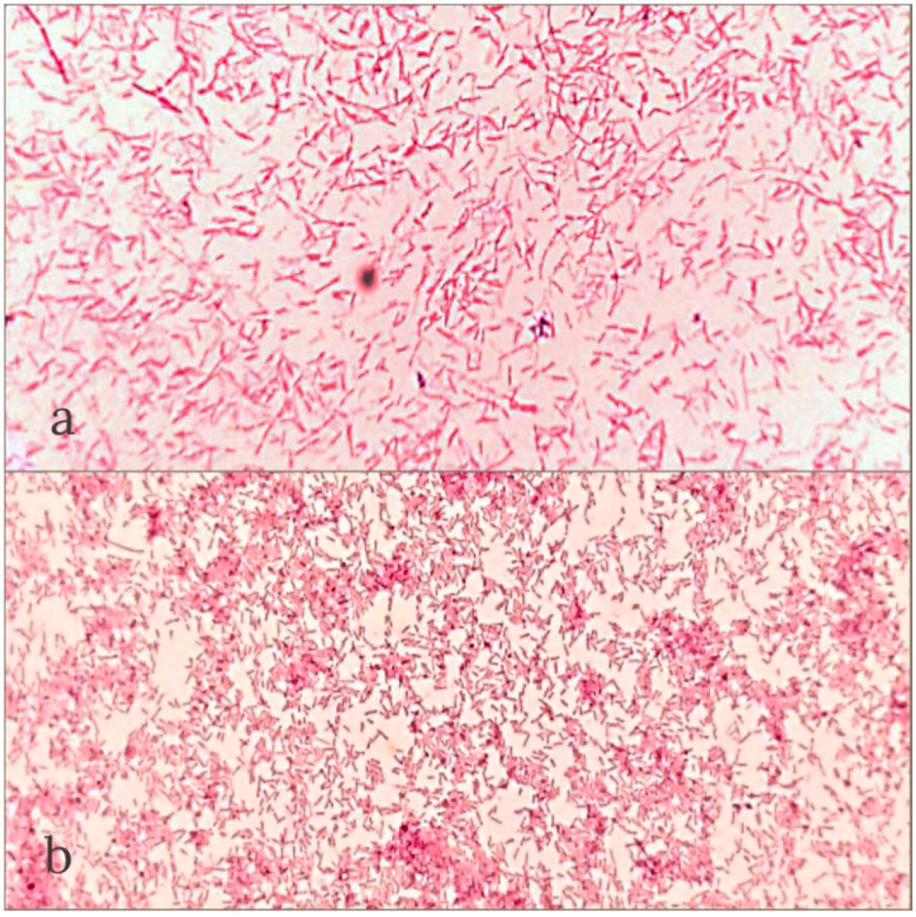


Fig. 4. Microscopic view of a. Aggregatibacter actinomycetemcomitans and b. Porphyromonas gingivalis.

Table 1
Demographic statistics, mean and standard deviation(M±SD) of glycated hemoglobin, and clinical parameters (PI, GI, CAL) at baseline.

Parameters	Control group	Test group
Age	46.1 ± 6.49	47 ± 6.2
Male/Female	8/10	9/9
PI	2.24 ± 0.35	2.35 ± 0.28
GI	2.34 ± 0.41	2.20 ± 0.26
PD (mm)	3.55 ± 0.38	3.70 ± 0.46
CAL (mm)	6.72 ± 1.92	6.76 ± 1.62
HbA1c mean (%)	8.0 ± 1.24	7.9 ± 1.18

Table 2
Clinical Parameters Assessment at baseline and 3 months in the Test and Control Groups.

Clinical Parameter	Evaluation Point	Control Group	Test Group	P value
PI	Baseline	2.24 ± 0.35	2.35 ± 0.28	0.010
	3 months	1.55 ± 0.10	1.32 ± 0.22	
	P value	<0.001	<0.001	
GI	Baseline	2.34 ± 0.41	2.20 ± 0.26	0.052
	3 months	1.31 ± 0.30	1.02 ± 0.17	
	P value	<0.001	<0.001	
PD	Baseline	3.55 ± 0.38	3.70 ± 0.46	<0.001
	3 months	2.78 ± 0.84	1.24 ± 0.10	
	P value	<0.001	<0.001	
CAL	Baseline	6.72 ± 1.92	6.76 ± 1.62	<0.001
	3 months	6.01 ± 1.85	2.81 ± 1.11	
	P value	<0.001	<0.001	

control groups showed a notable difference ($p < 0.001$). A decrease in scores of PI from 2.3 to 1.3, in the test group was noted. Similarly, in the control group, a reduction was noted from 2.2 to 1.5. However, on intergroup comparison, there was no statistical significance ($p = 0.010$) (Table 2).

4.2.1. Gingival index

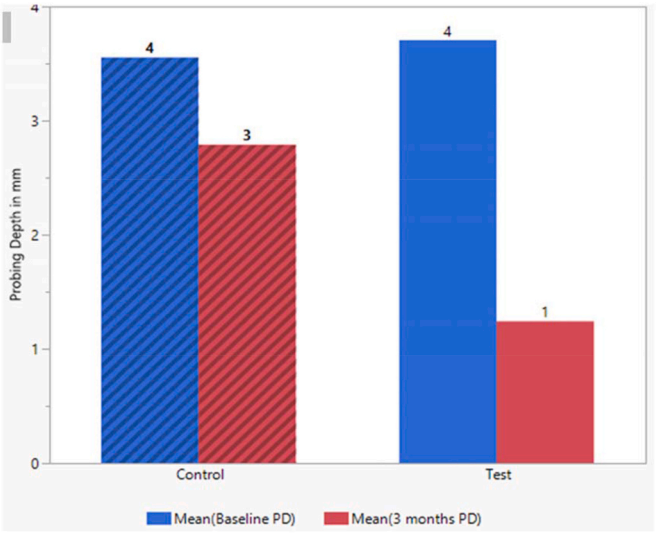
On intragroup comparison, a statistically significant reduction in gingival index from baseline to 3 months was noted in both groups ($p < 0.001$). On intergroup comparison, it was found that the group treated with indocyanine green showed a greater reduction in GI scores when compared to the SRP group, however, the difference between the groups ($p = 0.052$) was not statistically significant (Table 2).

4.3. Probing depth (PD) and clinical attachment level (CAL)

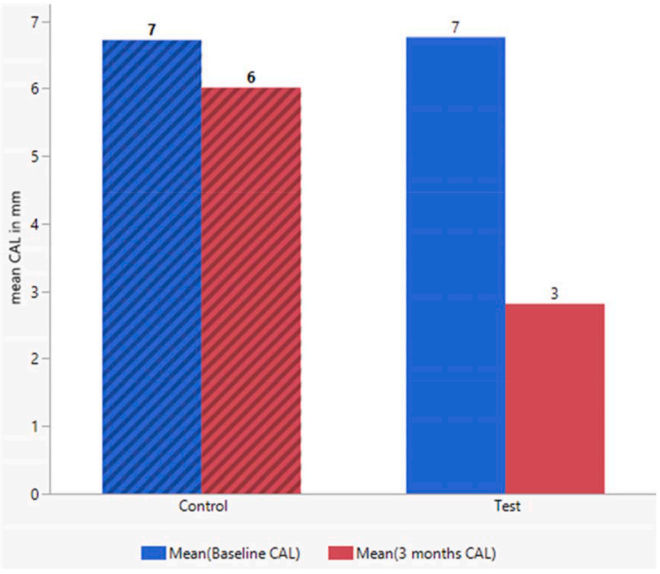
Full mouth probing depth reduced from 3.7 to 1.24 in the test group and from 3.5 to 2.7 in the control group post-operatively at 3 months follow up. CAL score reduced from 6.76 to 2.8 in the test group and from 6.72 to 6.0 in the control group from baseline to 3 months post-treatment. A statistically significant reduction in mean probing depth and gain in clinical attachment level after 3 months post-treatment was noted ($p < 0.001$) on the intergroup comparison at different time points. (Table 2, Graph 1, 2). Test group showed significant improvement in terms of pocket depth and attachment gain.

4.4. HbA1c levels

On intragroup comparison, the levels of HbA1c significantly improved from baseline to 3 months in both groups ($p < 0.001$).



Graph 1. Comparison of mean probing depths in test and control groups at baseline and 3 months.



Graph 2. Comparison of mean clinical attachment level at baseline and 3 months between test and control groups.

However, on intergroup comparison, no statistically significant difference was noted between test group and control group ($p = 0.85$) at 3 months follow-up (Table 3).

4.5. Microbiological findings

On intragroup comparison in both test and control groups, a statistically significant difference was noted in colony counts of Pg and Aa from baseline to 3 months follow-up ($p < 0.001$). The colony counts of Pg and Aa showed a statistically significant difference ($p < 0.001$) on the intergroup comparison at 3 months follow-up (Table 4, Graph 3,4).

Table 3
Glycemic Levels (HbA1c in %) of Control Group and Test Group at baseline and 3 months.

Parameter	Evaluation Point	Control Group	Test Group	P value
HbA1c (%)	Baseline	8.01 ± 1.24	7.98 ± 1.18	0.085
	3 months	7.40 ± 1.18	7.1 ± 0.81	
	P value	<0.001	<0.001	

5. Discussion

Diabetes mellitus and Periodontitis have a well-established bidirectional relationship and hence it is important to treat both entities.[2] Often, conventional non-surgical periodontal therapy fails to eliminate the dysbiotic biofilms and hence various adjunctive methods have been used along with SRP. PDT is an effective adjunctive therapy that can eliminate pathogens without the emergence of resistance. It has become a useful addition to the treatment plan of medically compromised patients. Hence in this study,the efficacy of aPDT using ICG in the treatment of chronic periodontitis patients with Type 2 Diabetes mellitus was assessed.

Antimicrobial PDT comprises three main components, i.e., light source, photosensitizer (PS), and singlet oxygen. When a photosensitizer is exposed to a light source of a suitable wavelength, it changes from a ground state to an excited state. This produces oxygen free radicals and a singlet oxygen, which are known to cause bacterial destruction. There is enough evidence, suggesting that aPDT does not lead to bacterial resistance. Therefore, photodynamic therapy can be an effective treatment of choice in the treatment of chronic generalized periodontitis.[18,19]

The destruction of bacterial cells by PDT is by either of the two mechanisms: (i) cytoplasmic membrane destruction, leading to leakage of cellular constituents or inactivation of the membrane to enzymes and transport systems or (ii) DNA damage.

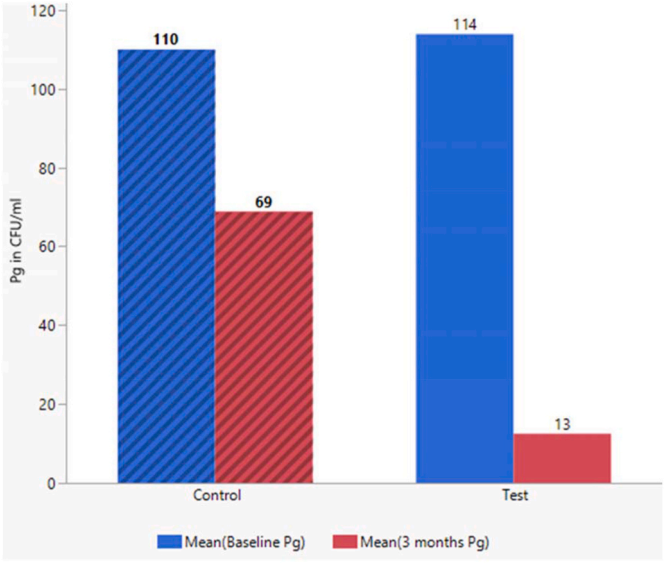
Unlike blue dyes (methylene blue and toludene blue), ICG causes selective coupling to bacterial cells alone which not just avoids staining of the healthy human tissues but also helps prevent any collateral damage rendering it safer for use. ICG dye does not require a separate laser unit, as the commercially available 810 nm GaAlAs diode laser is compatible with it, rendering it an economic edge over the other dyes.[10]

Karmakar S et al. reported that ICG and diode laser light 808 nm is effective for both killing the periodontal pathogenic species, *Treponema denticola*, *Porphyromonas gingivalis*, and *Tannerella forsythia* and significantly improving the clinical parameters after 3 months of therapy.[20] There are very few randomized controlled trials that have been conducted in chronic periodontitis patients with Type 2 DM.[21–23]

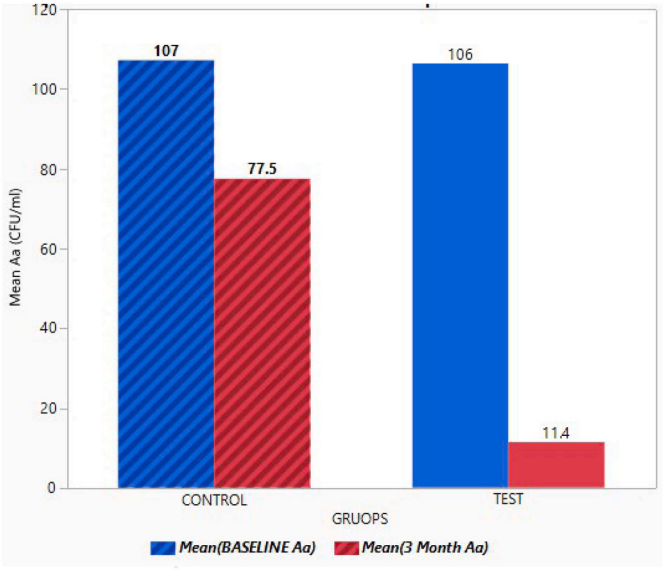
Results of the present study show that there was a statistically significant improvement in the scores of PD, CAL, and CFU/ml of Pg and Aa, in the SRP + aPDT group when compared to the SRP group at 3 months post-therapy. PI and GI and glycemic levels showed a significant improvement in both the groups however there was no significant difference between the groups 3 months post-therapy.There was a significant reduction in PI from baseline to 3 months in both groups. However, on intergroup comparison there was no statistical significance found($p = 0.010$), i.e., a reduction in PI score was seen irrespective of the treatment provided. PI was used to assess the oral hygiene status of the

Table 4
Microbiological parameters in CFU/ml of Control Group and Test Group at baseline and 3 months.

Microbiological Parameter	Evaluation Point	Control Group	Test Group	P value
Pg (CFU/ml)	Baseline	110.0 ± 32.31	113.88 ± 39.39	<0.001
	3 months	68.88 ± 17.95	12.5 ± 9.27	
	P value	<0.001	<0.001	
Aa (CFU/ml)	Baseline	107.22 ± 16.73	106.38 ± 26.16	0.001
	3 months	77.50 ± 15.64	11.38 ± 5.89	
	P value	<0.001	<0.001	



Graph 3. Comparison of mean colony forming units of Pg level at baseline and 3 months between test and control groups.



Graph 4. Comparison of mean colony forming units of Aa level at baseline and 3 months between test and control groups.

participants. These observations are in agreement with the research conducted by Theodoro et al. and Christodoulides et al..[24,25]

The gingival index is used to assess the severity of gingival inflammation. However, there is enough evidence stating that gingival inflammation usually subsides after SRP alone.[26,27] On intergroup comparison, it was found that the group treated with indocyanine green showed an increased reduction in GI scores when compared to the SRP group, however, there was no statistically significant difference($p = 0.052$) between the groups. This result is in accordance with Shingnapurkar S et al.,[28] who reported similar trends in GI scores on the intergroup comparison.

A statistically significant reduction in mean probing depth (PD) and gain in clinical attachment level (CAL) after 90 days post-treatment was noted ($p < 0.001$) on intergroup comparison at different time points. These results were in accordance with various other randomized clinical trials conducted to compare the adjunctive effect of aPDT to SRP in chronic periodontitis patients.[28–32]

A recent systematic review by Oktawati S et al.[33] showed a reduction of clinical parameters namely PD, CAL, and BOP after photodynamic therapy.

Chitsazi et al. in their clinical trial reported that the adjunctive use of aPDT to SRP did not show a significant improvement in the analysed clinical parameters in aggressive periodontitis patients.[34] While some studies failed to demonstrate "statistically significant" improvements in clinical outcomes, several studies have shown that aPDT as an adjunct to SRP was more effective than SRP alone in improving clinical parameters in the treatment of periodontal disease.[11,23,24,27,31–35]

The subgingival plaque samples were collected from the patients and transferred to thioglycolate transport media and immediately transported to the microbiological lab on the same day to eliminate any error or delay. The subgingival plaque samples were cultured by using selective culture media in anaerobic conditions.

In the present study,a significant reduction was noted in colony counts of Pg and Aa in both SRP + aPDT group and SRP group from baseline to 3 months follow-up. Both intragroup comparison at different time points and intergroup comparison showed, a significant reduction in the levels of Pg and Aa in the SRP + aPDT group when compared to the SRP group ($p < 0.001$). These results are in accordance with research conducted by Wadhwa et al.,[35] where a statistically significant reduction in CFU of Pg, and Aa, was reported.

Similarly, Srikanth et al., in their pilot study reported a considerable reduction in the percentage of viable bacteria at the end of 1 week following aPDT using ICG.[36] This is because ICG along with the diode laser has antibacterial efficacy. The diode laser alone kills bacterial cells at commensurate potency but the presence of the green dye aids the killing effect at low power in a short time period and the liquid also helps in reducing the unwanted heat generation within the pockets, avoiding thermal damage to the tissues. ICG and diode lasers are both known for their ability to penetrate inaccessible tooth sites or deep periodontal pockets.[11]

Kranz et al.[37] conducted an in vitro study in which they studied the antibacterial efficacy of ICG on perio-pathogens and reported that ICG was more efficacious in the suppression of *P.gingivalis* and *F.nucleatum* than compared to *A. actinomycetemcomitans*. This can be attributed to less susceptibility of Aa to PDT compared to other species tested. This behaviour is most likely explained by the bacterial cell surface's strong negative charge, which repels anionic and neutral photosensitizers.

In the present study, there was no statistically significant difference in the glycated haemoglobin levels between the two groups. The intragroup comparison showed statistical significance within the groups at different time points. Similar results were seen by various researchers, where they noted no statistical significance on HbA1c levels on the intergroup comparison.[38–40] This could be due to the non-control of variables that could influence glycated haemoglobin levels. These include changes in the patient's lifestyle, use of antidiabetic drugs, and regulating stress levels which influences glycaemic control. Meta-analyses of the effect of periodontal treatment on glycemic control in diabetic patients are contradictory. Some studies have found a beneficial effect in improving HbA1c level control after SRP,[38–41] whereas others did not.[42,43]

Limited number of studies are done, where ICG is used as a photosensitizer and its efficacy in antimicrobial photodynamic therapy. The results of present study agree with these studies, wherein significant improvement in clinical parameters[44,45] and a reduction of bacterial count were noted.[34,36]

However, it is important to note that the results of the present study are difficult to compare with previous studies as there is a lack of standardization regarding the use of PDT in the treatment of chronic periodontitis. This could be because of the different wavelengths of lasers, with different power settings, and irradiation time and different types of photosensitizers used. Meta-analyses have suggested that aPDT could be used in conjunction with scaling and root planing to treat shallow and moderate pockets in chronic periodontitis patients..[46,47] In

a recent systematic review it was stated that antimicrobial photodynamic therapy adjunct to periodontal therapy contributes to the improvement of periodontal clinical parameter bleeding on probing and probing depth in individuals with type 2 diabetes mellitus.[48]

The limitations of the study were short-term follow-up and small-scale population. Only one concentration of ICG was tested. Thus, there is a need for further randomized trials with standardized treatment protocols for aPDT and to incorporate its use for an added benefit to SRP. Furthermore, additional studies involving a comprehensive follow-up of diabetic patients are required in order to establish protocols that benefit in the treatment of periodontitis in DM2 patients. Long-term clinical trials with larger sample sizes and multiple sessions of aPDT using different concentrations of ICG could be conducted. Trials investigating the effectiveness of this novel photosensitizer in patients with periodontal maintenance, aggressive periodontitis, and peri-implant infections are possible.

6. Conclusion

The results of the study led to the conclusion that when ICG-mediated aPDT when used as an adjunct to SRP in the treatment of chronic periodontitis patients with Type 2 DM can render improvements in clinical as well as microbiological parameters. ICG can be considered as an alternative to conventional photosensitizers used in aPDT for the treatment of mild to moderate chronic periodontitis.

No separate acknowledements to be included

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Borgnakke WS, Genco RJ. Periodontal disease and diabetes mellitus. In: *International Textbook of Diabetes Mellitus*. Chichester, UK: John Wiley & Sons, Ltd; 2015: 988–1004.
2. Chee B, Park B, Bartold MP. Periodontitis and type II diabetes: a two-way relationship. *Int J Evid Base Healthc*. 2013 Dec;11(4):317–329.
3. Preshaw PM, Taylor JJ, Jaedicke KM, et al. Treatment of periodontitis reduces systemic inflammation in type 2 diabetes. *J Clin Periodontol*. 2020 Jun 12;47(6): 737–746.
4. Belstrøm D, Grande MA, Sembler-Møller ML, et al. Influence of periodontal treatment on subgingival and salivary microbiotas. *J Periodontol*. 2018 May;89(5): 531–539.
5. Sculean A, Romanos GE. Photodynamic therapy in periodontal and peri- implant treatment. In: *Advanced Laser Surgery in Dentistry*. Wiley; 2021:209–214.
6. Soukos NS, Goodson JM. Photodynamic therapy in the control of oral biofilms. *Periodontol*. 2000. 2011 Feb;55(1):143–166.
7. Herrera D. Photodynamic therapy for chronic periodontitis. *Evid Base Dent*. 2011 Sep 7;12(3):78–79.
8. Reinhart MB, Huntington CR, Blair LJ, Heniford BT, Augenstein VA. Indocyanine green. *Surg Innov*. 2016 Apr 10;23(2):166–175.
9. Shingnapurkar S, Mitra D, Kadav M, Shah R, Rodrigues S, Prithyani S. The effect of indocyanine green-mediated photodynamic therapy as an adjunct to scaling and root planing in the treatment of chronic periodontitis: a comparative split-mouth randomized clinical trial. *Indian J Dent Res*. 2016;27(6):609.
10. Parker S. The use of diffuse laser photonic energy and indocyanine green photosensitiser as an adjunct to periodontal therapy. *Br Dent J*. 2013 Aug 23;215(4): 167–171.
11. Sufaru IG, Martu MA, Luchian I, et al. The effects of 810 nm diode laser and indocyanine green on periodontal parameters and HbA1c in patients with periodontitis and type II diabetes mellitus: a randomized controlled study. *Diagnostics*. 2022 Jul 2;12(7):1614.
12. Silness J, Löe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand*. 1964 Jan 2;22(1):121–135.
13. Löe H. The gingival index, the plaque index and the retention index systems. *J Periodontol*. 1967 Nov;38(6):610–616.
14. Measurement of Attachment Level in Clinical Trials: Probing Methods. *Pihlstrom B L. J Periodontol*. 1992 Dec;63(Suppl 12S):1072–1077.
15. Betsy J, Prasanth CS, Baiju KV, Prasanthila J, Subhash N. Efficacy of antimicrobial photodynamic therapy in the management of chronic periodontitis: a randomized controlled clinical trial. *J Clin Periodontol*. 2014;14(6):573–581.
16. Socransky SS, Haffajee AD. Periodontal microbial ecology. *J Periodontol*. 2000;38 (2005):135–187.
17. Survival in transport media of Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis and Prevotella intermedia in human subgingival samples, van Steenbergen TJ, Petit MD, Tijhof CJ, van Winkelhoff AJ, van der Velden U, de Graaff J. *Oral Microbiol Immunol*. 1993 Dec;8(6):370–374.
18. Boehm TK, Ciancio SG. Diode laser activated indocyanine green selectively kills bacteria. *J Int Acad Periodontol*. 2011 Jul;13(2):58–63.
19. Topaloglu N, Gulsoy M, Yuksel S. Antimicrobial photodynamic therapy of resistant bacterial strains by indocyanine green and 809-nm diode laser. *Photomed Laser Surg*. 2013 Apr;31(4):155–162.
20. Karmakar S, Prakash S, Jagadeson M, Namachivayam A, Das D, Sarkar S. Clinico-microbiological efficacy of indocyanine green as a novel photosensitizer for photodynamic therapy among patients with chronic periodontitis: a split-mouth randomized controlled clinical trial. *J Pharm BioAllied Sci*. 2021;13(5):143.
21. Mirza S, Khan AA, Al-Kheraif AA, Khan SZ, Shafqat SS. Efficacy of adjunctive photodynamic therapy on the clinical periodontal, HbA1c and advanced glycation end product levels among mild to moderate chronic periodontal disease patients with type 2 diabetes mellitus: a randomized controlled clinical trial. *Photodiagnosis Photodyn Ther*. 2019 Dec;28:177–182.
22. Ramos UD, Ayub LG, Reino DM, et al. Antimicrobial photodynamic therapy as an alternative to systemic antibiotics: results from a double-blind, randomized, placebo-controlled, clinical study on type 2 diabetics. *J Clin Periodontol*. 2016 Feb;43 (2):147–155.
23. Theodoro LH, Silva SP, Pires JR, et al. Clinical and microbiological effects of photodynamic therapy associated with nonsurgical periodontal treatment. A 6-month follow-up. *Laser Med Sci*. 2012 Jul 18;27(4):687–693.
24. Christodoulides N, Nikolidakis D, Chondros P, et al. Photodynamic therapy as an adjunct to non-surgical periodontal treatment: a randomized, controlled clinical trial. *J Periodontol*. 2008 Sep;79(9):1638–1644.
25. Konopka Ł, Pietrzak A, Brzezińska-Błaszczyk E. Effect of scaling and root planing on interleukin-1β, interleukin-8 and MMP-8 levels in gingival crevicular fluid from chronic periodontitis patients. *J Periodontal Res*. 2012 Dec;47(6):681–688.
26. Thomas P Hughes, Caffesse Rau LG. Gingival changes following scaling, root planing and oral hygiene A biometric evaluation. *J Periodontol*. 1978 May;49(5):245–252.
27. Lang NP, Adler R, Joss A, Nyman S. Absence of bleeding on probing an indicator of periodontal stability. *J Clin Periodontol*. 1990 Nov;17(10):714–721.
28. Braun A, Dehn C, Krause F, Jepsen S. Short-term clinical effects of adjunctive antimicrobial photodynamic therapy in periodontal treatment: a randomized clinical trial. *J Clin Periodontol*. 2008 Oct;35(10):877–884.
29. Betsy J, Prasanth CS, Baiju Kv, Prasanthila J, Subhash N. Efficacy of antimicrobial photodynamic therapy in the management of chronic periodontitis: a randomized controlled clinical trial. *J Clin Periodontol*. 2014 Jun;41(6):573–581.
30. Mauri-Obradors E, Merlos A, Estrugo-Devesa A, Jané-Salas E, López-López J, Viñas M. Benefits of non-surgical periodontal treatment in patients with type 2 diabetes mellitus and chronic periodontitis: a randomized controlled trial. *J Clin Periodontol*. 2018 Mar;45(3):345–353.
31. Birang R, Shahaboui M, Kiani S, Shadmehr E, Naghsh N. Effect of nonsurgical periodontal treatment combined with diode laser or photodynamic therapy on chronic periodontitis: a randomized controlled split-mouth clinical trial. *J Lasers Med Sci [Internet]*. 2015 Jun;6(3):112–119. Available from: https://journals.sbmu.ac.ir/jlms/article/view/6045.
32. Joshi K, Baiju CS, Khashu H, Bansal S. Clinical effectiveness of indocyanine green mediated antimicrobial photodynamic therapy as an adjunct to scaling root planing in treatment of chronic periodontitis- A randomized controlled clinical trial. *Photodiagnosis Photodyn Ther*. 2020 Mar;29, 101591.
33. Oktawati S, Rukmana A, Patimah Wahab RF, Syafar IF, Wahab W. Photodynamic therapy as adjunctive treatment of chronic periodontitis: a systematic review. *Sys Rev Pharm*. 2020;11(6):492–498.
34. Chitsazi MT, Shirmohammadi A, Pourabbas R, et al. Clinical and microbiological effects of photodynamic therapy associated with non-surgical treatment in aggressive periodontitis. *J Dent Res Dent Clin Dent Prospects*. 2014;8(3):153–159.
35. Wadhwa A, Mallapragada S, Sharma P. Novel indocyanine green mediated antimicrobial photodynamic therapy in the management of chronic periodontitis - a randomized controlled clinico-microbiological pilot study. *J Oral Biol Craniofac Res*. 2021 Jan;11(1):57–62.
36. Srikanth K, Chandra RV, Reddy AA, Reddy BH, Reddy C, Naveen A. Effect of a single session of antimicrobial photodynamic therapy using indocyanine green in the treatment of chronic periodontitis: a randomized controlled pilot trial. *Quintessence Int*. 2015 May;46(5):391–400.
37. Kranz S, Huebsch M, Guellmar A, Voelpel A, Tonndorf-Martini S, Sigusch BW. Antibacterial photodynamic treatment of periodontopathogenic bacteria with indocyanine green and near-infrared laser light enhanced by Trolox TM. *Laser Surg Med*. 2015 Apr;47(4):350–360.
38. Jain A, Gupta J, Bansal D, Sood S, Gupta S, Jain A. Effect of scaling and root planing as monotherapy on glycemic control in patients of Type 2 diabetes with chronic periodontitis: a systematic review and meta-analysis. *J Indian Soc Periodontol*. 2019; 23(4):303.
39. Corbella S, Francetti L, Taschieri S, de Siena F, Fabbro M del. Effect of periodontal treatment on glycemic control of patients with diabetes: a systematic review and meta-analysis. *J Diabetes Investig*. 2013 Sep;4(5):502–509.
40. Teshome A, Yitayeh A. The effect of periodontal therapy on glycemic control and fasting plasma glucose level in type 2 diabetic patients: systematic review and meta-analysis. *BMC Oral Health [Internet]*. 2016;17(1):31. https://doi.org/10.1186/s12903-016-0249-1.

41. Abduljabbar T, Vohra F, Javed F, Akram Z. Antimicrobial photodynamic therapy adjuvant to non-surgical periodontal therapy in patients with diabetes mellitus: a meta-analysis. *Photodiagnosis Photodyn Ther*. 2017 Mar;17:138–146.
42. Correa FOB, GonÃ§alves D, Figueredo CMS, Bastos AS, Gustafsson A, Orrico SRP. Effect of periodontal treatment on metabolic control, systemic inflammation and cytokines in patients with type 2 diabetes. *J Clin Periodontol*. 2010 Jan;37(1):53–58.
43. Janket SJ, Wightman A, Baird AE, van Dyke TE, Jones JA. Does periodontal treatment improve glycemic control in diabetic patients? A meta-analysis of intervention studies. *J Dent Res*. 2005 Dec 15;84(12):1154–1159.
44. Monzavi A, Chinipardaz Z, Mousavi M, et al. Antimicrobial photodynamic therapy using diode laser activated indocyanine green as an adjunct in the treatment of chronic periodontitis: a randomized clinical trial. *Photodiagnosis Photodyn Ther*. 2016 Jun;14:93–97.
45. Bhat M, Acharya S, Prasad KV, Kulkarni R, Bhat A, Bhat D. Effectiveness of erythrosine-mediated photodynamic antimicrobial chemotherapy on dental plaque aerobic microorganisms: a randomized controlled trial. *J Indian Soc Periodontol*. 2017;21(3):210.
46. Ai R, Nie M, Yang J, Deng D. Effects of antibiotics versus repeated applications of photodynamic therapy as an adjunctive treatment for periodontitis: a systematic review and meta-analysis. *Photobiomodul Photomed Laser Surg*. 2021 Mar 1;39(3):211–220.
47. Sgolastra F, Petrucci A, Gatto R, Marzo G, Monaco A. Photodynamic therapy in the treatment of chronic periodontitis: a systematic review and meta-analysis. *Laser Med Sci*. 2013 Feb 16;28(2):669–682.
48. da Silva-Junior PGB, Abreu LG, Costa FO, Cota LOM, Esteves-Lima RP. The effect of antimicrobial photodynamic therapy adjunct to non-surgical periodontal therapy on the treatment of periodontitis in individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. *Photodiagnosis Photodyn Ther*. 2023 Jun;42,103573.