



Photodynamic Periodontal Therapy vs. Diode laser as an Adjunctive to Conventional periodontal treatment in Management of Chronic Periodontitis

Marwa Younis Mohammed^{1*}, Osama S. El-Shall², Nora Abdelgawad Mohammed³

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azhardentj@azhar.edu.eg

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ABSTRACT

Purpose: This study was made to evaluate and compare the efficacy of photodynamic periodontal therapy and diode laser as an adjunctive approach to conventional periodontal therapy in management of chronic periodontitis. **Subjects and methods:** 30 patients with chronic periodontitis and age range from 30-40 years old were divided randomly into three groups. **Group I (control group)** 10 patients received conventional periodontal therapy alone. **Group II (laser group):** patients received SRP + additional application of a 940-nm diode laser. **Group III (photodynamic group):** patients received SRP + antimicrobial photodynamic therapy by using low level 670 nm diode laser application in addition to application of 1% toluidine blue as photosensitizer. **Results:** there were a significant difference of PD, CAL, IL-1 β , IL6, NO, NO2 between three groups with superior result found in photodynamic group, but there were no significant differences between three groups in the term of NO3. **Conclusion:** Diode laser and photodynamic therapies add a beneficial effect in clinical and biochemical parameters when used as adjunctive to scaling and root planning but there was no significant difference between them.

KEYWORDS

Photodynamic Therapy,
Diode Laser, Chronic
Periodontitis.

INTRODUCTION

Periodontitis is an inflammatory disease affecting the supporting tissues of the teeth. In the presence of risk factors, it is a multi-factorial and multi-etiological infectious disease process induced by periodontal

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1. Dentist at Egyptian Ministry of Health, Egypt.
2. Professor of Oral Medicine, Periodontology, Oral Diagnosis and Radiology Department, Faculty of Dental Medicine for Girls, Al-Azhar University, Cairo, Egypt.
3. Lecturer at Oral Medicine, Periodontology, Oral Diagnosis and Radiology Department, Faculty of Dental Medicine for Girls, Al-Azhar University, Cairo, Egypt.

* Corresponding author email: marwasleim94@gmail.com

bacteria and the host immunological response ⁽¹⁾. It is characterized by apical drifting of the junctional epithelium along the root surface, loss of attachment, deepening of pockets, and alveolar bone loss ⁽²⁾. This drifting is caused directly by microorganisms and indirectly by the immunological response of the host ⁽³⁾.

The disease's pathogenicity was triggered by bacterial colonization, which changed the microbiota's composition and total numbers, disrupting tissue homeostasis. The immune response is over-activated in these circumstances, resulting in immune cell infiltration and inflammatory mediator activation such as cytokines and prostaglandins that stimulate osteoclastic activity, and eventually lead to bone resorption ⁽⁴⁾.

Periodontal tissue degeneration can be reduced by removing pathogenic biofilms and suppressing inflammation. However, the ability to restore lost tissues is dependent on a multiple factors, including the extent of tissue defect, overall health, and age ⁽⁵⁾.

Periodontal therapy relies heavily on scaling and root planning (SRP). Its main objective is to remove both soft and hard microbial residues from the diseased root surfaces. It reduces clinical inflammation and pocket probing depth remarkably well ⁽⁶⁾. However, the efficacy of SRP can be restricted because it is incapable of completely eradicating all bacteria in cases with deep pocket, root concavities, grooves, furcation involvement, and invasion of root surface abnormalities ⁽⁷⁾.

In order to overcome this limitation other treatment modalities began to gain traction as supplementary to mechanical procedures ⁽⁸⁾. Pharmacological disinfectants and antibiotics as adjuncts to SRP may facilitate resolution of the inflammation ⁽⁹⁾. However, Because of the risk of bacterial resistance and the effect on the entire microbiota composition of the human organism that is deeply connected to systemic antibiotic administration, antibiotic use must be critically questioned, especially in terms of its potential added benefit and adverse side effects for the patient ⁽¹⁰⁾.

Due to the ability of laser application to remove inactivated pathogens and subgingival calculus, laser application as an adjuvant to SRP currently exhibits satisfactory bacteriostatic and decontamination capacity, especially in areas where standard periodontal tools cannot reach. Furthermore, lasers offer specific benefits in hemostasis, greater visibility, improved healing, and the potential avoidance of surgical intervention ⁽¹¹⁾.

Photodynamic therapy is one of the recent treatment modalities for periodontitis. It is an oxygen-dependent photochemical process that takes place when a photosensitizing molecule is activated by light, resulting in the generation of cytotoxic reactive oxygen species, primarily singlet oxygen ⁽¹²⁾. PDT efficiency is determined by the correct collaboration of light, oxygen, and photosensitizers (PSs), which are responsible for the production of reactive oxygen species (ROS) and the ablation of the targeted cells ⁽¹³⁾. PSs are dyes consisting of molecules that can absorb light energy and using that to induce chemical reactions in cells and surrounding tissues. PS must be activated by a specific wavelength of light in order to triggering the mechanism required to detect and eliminate harmful tissue ⁽¹⁴⁾.

So this study aimed to evaluate and compare the efficacy of photodynamic periodontal therapy and diode laser as an adjunctive approach to conventional periodontal therapy in management of chronic periodontitis.

SUBJECTS AND METHODS

Thirty patients of both genders suffering periodontitis were considered into this study. They were selected from those attending at the Out-patient clinics of department of Oral Medicine, Periodontology, oral Diagnosis and Radiology, Faculty of Dental Medicine, Al-Azhar University for girls.

The patients were chosen based on clinical and radiographic examination according to the following

inclusion criteria: Patient aged range from 30-40 years old, free from any systemic illness that have an effect on the periodontium and suffering from chronic periodontitis (Fig.1). Pregnant or lactating women, Smokers or chewing any form of tobacco and patients that may have allergy to toluidine blue photosensitizer agent used in this current study were excluded.

All subjects were instructed about the nature and benefits of their involvement in the study prior to the procedure. Satisfactory written consent will be obtained from all patient denoting their convenience about scheduled research program and experimental design. The research protocol was approved by the Research Ethics Committee. Code (REC-ME-22-09).



Figure (1) Showing chronic periodontitis with probing depth 6mm

Sample size:

Power calculation test was performed, setting an effect size = 0.80, $\alpha = 0.05$, and a power at 80%. The sample size calculation showed a requirement for 8 subjects per group. Accordingly, at the present study, 10 subjects were recruited per group.

The 30 enrolled patients were randomly assigned to three groups (I, II, and III) on the basis of the periodontal treatment protocol as follow: Group I (control group): 10 patients received SRP only. Group II (Diode laser group): 10 patients were treated

with SRP with application of a 940-nm diode laser as an adjunctive to the periodontal therapy. Group III (Photodynamic group): 10 patients were treated with SRP with photodynamic treatment protocol, which consisted of low level 635 nm diode laser application in addition to application of (toluidine blue) as photosensitizer. Each tooth was irradiated for 2 min (60 s buccally, 60 s palatally). The tip diameter was 1cm was inserted in the pocket and was operated with a sweeping movement, apically to coronally direction for 30 s.

All patients of the three groups were treated with conventional therapy which includes Supragingival, subgingival scaling and root planning using ultrasound scaler and curettes, chlorhexidine mouth wash for 1 week post periodontal therapy, Oral hygiene instructions. The instruction include brushing teeth with gentle oral brush 3 times daily and flossing once a day.

Groups II and III received laser irradiation in three sessions: the first 48 hours after conventional periodontal therapy, the second on the 7th day of the first session, and the third on the 14th day of the first session.

Outcome measurements:

1- Clinical evaluation:

The clinical results of the study will be evaluated pocket depth measurements ⁽¹⁵⁾, and clinical attachment level ⁽¹⁵⁾. The clinical measurements will be obtained at the baseline, 1month interval, 3 months interval and 6 months interval.

2- Biochemical evaluation:

Samples of gingival crevicular fluid collected from periodontal pockets at the site of periodontal treatment at the baseline (before the starting), 3days, 1week and 1month intervals. Samples were pooled from the selected periodontal sites (in the deepest site). Cotton rolls were used to isolate the sampling

area, which was then cleaned supragingivally with sterile cotton pellets. Until resistance was sensed, a sterile absorbent paper point was pushed into the gingival sulcus or pocket. the paper point was maintained in place for 30s. The samples were immediately placed in Eppendorf tubes, transported to the laboratory, and stored at -80°C . The enzyme linked immunosorbent assay (ELIZA) was used to examine the collected samples for evaluation of nitrate (NO_3), nitrite (NO_2) and total nitric oxide (NO) contents and the following cytokines; interleukin 1β , and interleukin 6.

Statistical analysis:

Statistical analysis was performed by applying One-way ANOVA to compare between normal distributed data followed by Post Hoc test for multiple comparisons between different groups. Statistical analysis for ordinal data was performed by Kruskal-Wallis followed by Mann-Whitney Test for pairwise comparisons between groups. P-value ≤ 0.05 was considered statistically significant (95% significance level), and P-value ≤ 0.001 was considered highly statistically significant (99% significance level). Shapiro Wilk test was used for testing the normality of data. Data were analyzed using the statistical software SPSS (version 23, IBM Co. USA).

RESULTS

Clinical evaluation:

In the term of probing depth (PD):

Before therapy the mean was (6.36 ± 0.56) in the control group, (6.21 ± 0.49) in the laser group, and (6.64 ± 0.75) in the photodynamic group with nonsignificant P-value = 0.423.

After one month of therapy the mean was (5.71 ± 0.64) in the control group, (4.21 ± 0.76) in the laser group, and (4.57 ± 0.84) in the photodynamic

group with significant P-value = 0.006.

After three months of therapy the mean was (5.00 ± 1.00) in the control group, (3.36 ± 0.85) in the laser group, and (3.57 ± 0.53) in the photodynamic group with significant P-value = 0.004.

After six months of therapy the mean of Max PD was (4.57 ± 0.67) in the control group, (3.14 ± 0.75) in the laser group, and (2.43 ± 0.53) in the photodynamic group with highly significant P-value = 0.000.

In the term of clinical attachment loss:

Before therapy the mean was (4.5 ± 0.71) in the control group, (4.71 ± 0.99) in the laser group, and (5.14 ± 0.85) in the photodynamic group with nonsignificant P-value = 0.382.

After one month of therapy the mean of CAL was (3.64 ± 0.85) in the control group, (3.14 ± 0.8) in the laser group, and (3.21 ± 0.7) in the photodynamic group with nonsignificant P-value = 0.453.

After three months of therapy the mean of CAL was (3.29 ± 0.91) in the control group, (2.29 ± 0.91) in the laser group, and (2.29 ± 0.76) in the photodynamic group with nonsignificant P-value = 0.067.

After six months of therapy the mean of CAL was (2.93 ± 0.73) in the control group, (1.86 ± 0.63) in the laser group, and (1.14 ± 0.69) in the photodynamic group with highly significant P-value = 0.000.

So intra group comparison for all group showed, there were significant difference between baseline and three months and also between baseline and 6 months with the highest mean of PD and CAL were achieved before the start of therapy (baseline), while the lowest was achieved after 6 months of therapy. While inter group comparison showed the laser group achieved the lowest mean of PD and CAL after one month of therapy but Photodynamic group showed the lowest mean after 6 months of therapy. (table 1).

Table (1): Mean \pm SD of Max PD and CAL (mm) for all groups at different time intervals.

		Baseline	1 Month	3 Months	6 Months	P-value*
Max PD	Control	6.36 \pm 0.56 ^{Aa}	5.71 \pm 0.64 ^{Aab}	5.00 \pm 1.00 ^{Abc}	4.57 \pm 0.67 ^{Ac}	0.001 ^{HS}
	Laser	6.21 \pm 0.49 ^{Aa}	4.21 \pm 0.76 ^{Bb}	3.36 \pm 0.85 ^{Bbc}	3.14 \pm 0.75 ^{Bc}	0.000 ^{HS}
	Photodynamic	6.64 \pm 0.75 ^{Aa}	4.57 \pm 0.84 ^{Bb}	3.57 \pm 0.53 ^{Bc}	2.43 \pm 0.53 ^{Bd}	0.000 ^{HS}
	P-value**	0.423 ^{NS}	0.006 ^S	0.004 ^S	0.000 ^{HS}	
CAL	Control	4.5 \pm 0.71 ^{Aa}	3.64 \pm 0.85 ^{Aab}	3.29 \pm 0.91 ^{Ab}	2.93 \pm 0.73 ^{Ab}	0.008 ^S
	Laser	4.71 \pm 0.99 ^{Aa}	3.14 \pm 0.8 ^{Ab}	2.29 \pm 0.91 ^{Abc}	1.86 \pm 0.63 ^{Bc}	0.000 ^{HS}
	Photodynamic	5.14 \pm 0.85 ^{Aa}	3.21 \pm 0.7 ^{Ab}	2.29 \pm 0.76 ^{Abc}	1.14 \pm 0.69 ^{Bc}	0.000 ^{HS}
	P-value**	0.382 ^{NS}	0.453 ^{NS}	0.067 ^{NS}	0.000 ^{HS}	

-HS =highly significant ($P \leq 0.001$) -S = significant ($P \leq 0.05$) -NS =Non significant ($P > 0.05$)

Biochemical evaluation: intra group comparison for all groups showed the highest of IL1, IL6, NO, NO2 and NO3 were achieved before the start of therapy (baseline), while the lowest mean of all was achieved after one month of therapy. In regard to IL1, IL6, NO and NO2 there were a significant difference between all time intervals, and the overall p value was statistically significant. But in regard to NO3 there was no significant difference between all time intervals, and the overall p value was not statistically significant (table 2).

While intergroup comparison showed the laser group achieved the lowest IL1, IL6 and NO2

after one day and one week but the photodynamic group achieved the lowest value after one month of therapy. There was no significant difference between the three groups at base line, 3 days and one week while there was a statistically significant difference between groups after one month.

In regard to NO, NO3 intergroup comparison showed the photodynamic group achieved the lowest value at all time intervals. While there was a statistically significant difference of NO after one week and one month of therapy but there was no significant differences of NO3 between the three groups at all time interval (See table2).

Table (2) Mean \pm SD of Biochemistry variables for all groups at different time intervals.

		Baseline	3 Days	1 Week	1 Month	P*
Interleukin 1 (ng/ml)	C	246.39 \pm 56.38 ^{Aa}	198.30 \pm 58.40 ^{Aab}	171.89 \pm 47.41 ^{Aab}	158.58 \pm 43.32 ^{Ab}	0.021 ^S
	L	234.8 \pm 55.96 ^{Aa}	162.4 \pm 56.76 ^{Aab}	126.8 \pm 40.02 ^{Ab}	117.46 \pm 86.56 ^{ABb}	0.007 ^S
	Ph	230.51 \pm 33.2 ^{Aa}	169.33 \pm 37.57 ^{Ab}	134.04 \pm 28.68 ^{Abc}	90.24 \pm 34.59 ^{Bc}	0.000 ^{HS}
	P**	0.828 ^{NS}	0.406 ^{NS}	0.099 ^{NS}	0.034 ^S	
Interleukin 6 (ng/ml)	C	4.14 \pm 0.96 ^{Aa}	3.24 \pm 0.89 ^{Aab}	2.15 \pm 1.03 ^{Ab}	2.11 \pm 0.95 ^{Ab}	0.001 ^{HS}
	L	3.8 \pm 1.19 ^{Aa}	2.43 \pm 0.75 ^{Ab}	1.33 \pm 0.49 ^{Abc}	1.27 \pm 0.36 ^{Bc}	0.000 ^{HS}
	Ph	3.79 \pm 0.8 ^{Aa}	2.62 \pm 0.77 ^{Aab}	1.57 \pm 0.83 ^{Abc}	0.84 \pm 0.98 ^{Bc}	0.000 ^{HS}
	P**	0.761 ^{NS}	0.176 ^{NS}	0.179 ^{NS}	0.028 ^S	

		Baseline	3 Days	1 Week	1 Month	P*
NO	C	76.42±14.86 ^{Aa}	69.38±16.35 ^{Aa}	63±17.27 ^{Aa}	67.21±19.07 ^{Aa}	0.307 ^{NS}
	L	76.92±12.72 ^{Aa}	55.57±7.74 ^{Ab}	46.4±9.65 ^{Abb}	50.51±9.65 ^{Ab}	0.000 ^{HS}
	Ph	78.94±12.3 ^{Aa}	55.22±13.62 ^{Ab}	37.28±8.41 ^{Bc}	41.2±13.53 ^{Abc}	0.000 ^{HS}
	p**	0.933 ^{NS}	0.096 ^{NS}	0.004 ^S	0.021 ^S	
NO2	C	3.08±0.52 ^{Aa}	2.32±0.67 ^{Aab}	1.81±0.66 ^{Aa}	1.79±0.77 ^{Ab}	0.004 ^S
	L	3.03±0.5 ^{Aa}	1.75±0.28 ^{Ab}	1.31±0.39 ^{Aac}	0.86±0.5 ^{Bc}	0.000 ^{HS}
	Ph	3.04±0.3 ^{Aa}	2.11±0.48 ^{Ab}	1.29±0.55 ^{Ac}	0.76±0.66 ^{Bc}	0.000 ^{HS}
	p**	0.971 ^{NS}	0.134 ^{NS}	0.164 ^{NS}	0.015 ^S	
NO3	C	7.36±1.69 ^{Aa}	6.75±1.38 ^{Aa}	6.28±1.38 ^{Aa}	6.11±1.16 ^{Aa}	0.371 ^{NS}
	L	8.46±2.27 ^{Aa}	7.47±2.04 ^{Aa}	6.68±2.14 ^{Aa}	6.23±2.31 ^{Aa}	0.266 ^{NS}
	Ph	8.32±2.51 ^{Aa}	6.74±2.79 ^{Aa}	5.79±3.12 ^{Aa}	5.44±3.37 ^{Aa}	0.291 ^{NS}
	p**	0.596 ^{NS}	0.768 ^{NS}	0.776 ^{NS}	0.814 ^{NS}	

-HS =highly significant ($P \leq 0.001$) -S = significant ($P \leq 0.05$) -NS =Non significant ($P > 0.05$)

DISCUSSION

Following SRP, excellent dental hygiene can significantly minimize microbial diversity in pockets less than 5mm depth. As a result, periodontal pockets more than 5mm in depth were chosen to test the efficacy of various treatment options⁽¹⁶⁾.

According to the findings of this research, there was no substantial difference in terms of clinical parameters. (PI, GI, PD, CAL) at the base line examination. a finding that ensured comparable treatment outcomes at the follow up.

Regarding to PD, there were a significant improvement in PD with laser and photodynamic groups than control group after one, three and six months of therapy. But there was no substantial difference between laser and photodynamic group with only a propensity for higher reduction of PD in photodynamic group after 6month of therapy.

Regarding to CAL, there were no significant difference between the three groups after one, three months of therapy. While there was marked improvement in laser and photodynamic groups

than control group after 6month of therapy with no substantial difference between laser group and photodynamic group.

This finding is supported by a study evaluating the effect of PDT with 660 nm diode laser and methylene blue as an alternative to scaling and root planning (SRP) on clinical periodontal indices and observed that PDT improved PD considerably when compared to SRP alone⁽¹⁷⁾.

A study made for a group of patients with chronic periodontal disease, evaluated the efficiency of adjunctive photodynamic low-level laser therapy (670 nm) with methylene blue as a photosensitizer and a diode laser (940 nm) with traditional non-surgical mechanical treatment. In terms of probing depth, CAL, and bleeding on probing 6 months after treatment, the results of this study demonstrated no additional clinical benefit when employing diode or photodynamic laser therapy in conjunction with standard SRP compared to mechanical therapy alone which contradict with the finding of this study⁽¹⁸⁾.

In the term of biochemical evaluation, the results of current study showed that no substantial

difference between groups in (IL-1 β , IL6, NO, NO₂ and NO₃) at the base line.

Regarding to IL-1 β and IL6, there were no significant differences between the three groups at 3 days and one week. While there was a significant improvement in laser and photodynamic groups than control group after 1month of therapy with no significant difference between laser group and photodynamic group.

These findings are supported by another study made to assess the efficacy of PDT as an adjuvant to NSPT and its effects on GCF levels of IL-6, IL-8, and IL-10 in chronic periodontitis. At 3 months, the PDT group exhibited lower levels of pro-inflammatory cytokines (IL-6 and IL-8) than the control group⁽¹⁹⁾.

Regarding nitric oxide (NO), there were no significant differences between the three groups at 3days and one month while there was a significant difference between groups after one week. These results probably occurred due to NO is un stable biomarker so it is gradually return to its level by time.

Regarding to nitrite (NO₂), there were no significant differences between the three groups at 3days, and one week while there was a significant improvement in laser and photodynamic groups than control group after 1month of therapy with no significant difference between laser group and photodynamic group.

Regarding nitrate (NO₃), there was no significant differences between all time intervals, and the overall p value was not statistically significant.

The findings of this study are similar to those of other researcher, who focused on nitric oxide, nitrite, and nitrate levels in chronic periodontitis patients treated with IPT and probiotic dietary supplements and found that both groups resulted in a decrease in NO and NO₂. In contrast to the control group, adding probiotic-rich dietary supplements to IPT resulted in a significant reduction in NO and NO₂ levels for up to 6 months of follow-up. NO₃ levels did not alter much⁽²⁰⁾.

CONCLUSION

Diode laser and photodynamic therapies add a beneficial effect in clinical and biochemical parameters when used as adjunctive to scaling and root planning but there was no significant difference between them.

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RECOMMENDATION

Further studies on the effect of diode laser and photodynamic therapies on the concentration of nitric oxide and its end product in periodontitis.

CONFLICT OF INTEREST

There was no conflict of interest.

FUNDING

No funding had been received for this study.

REFERENCES

1. Kazi M, Bharadwaj R. Role of herpesviruses in chronic periodontitis and their association with clinical parameters and in increasing severity of the disease. *Eur J Dent.* 2017,11:299-304.
2. Ishikawa T, Sasaki D, Aizawa R, Yamamoto M, Yaegashi T, Irié T, Sasaki M. The Role of Lactic Acid on Wound Healing, Cell Growth, Cell Cycle Kinetics, and Gene Expression of Cultured Junctional Epithelium Cells in the Pathophysiology of Periodontal Disease. *Pathogens.* 2021,10:1507-18.
3. Xu W, Zhou W, Wang H, Liang S. Roles of Porphyromonas gingivalis and its virulence factors in periodontitis. *Adv Protein Chem Struct Biol.* 2020,120: 45-84.
4. Pan W, Wang Q, Chen Q. The cytokine network involved in the host immune response to periodontitis. *Int J Oral Sci.* 2019,11:30-43

5. Könönen E, Gursoy M, Gursoy UK. Periodontitis: A Multifaceted Disease of Tooth-Supporting Tissues. *J Clin Med*. 2019;8:1135-47.
6. Ramanauskaite E, Machiulskiene V. Antiseptics as adjuncts to scaling and root planing in the treatment of periodontitis: a systematic literature review. *BMC Oral Health*. 2020;20:143-62.
7. Cobb CM, Sottosanti JS. A re-evaluation of scaling and root planing. *J Periodontol*. 2021;92:1370-78.
8. Alroufhan I E, Gamal M, Ganji KK, Khan AM, Alsharari KN, Alruwaili MK, Al Waqdani NH. The Effectiveness of Mouthwashes With Various Ingredients in Plaque Control: A Systematic Review and Meta-Analysis. *Altern Ther Health Med*. 2021;27:52-7.
9. Donos N, Calciolari E, Brusselaers N, Goldoni M, Bostanci N, Belibasakis GN. The adjunctive use of host modulators in non-surgical periodontal therapy. A systematic review of randomized, placebo-controlled clinical studies. *J Clin Periodontol*. 2020;47:199-238.
10. Pretzl B, Sälzer S, Ehmke B, Schlagenhauf U, Dannewitz B, Dommisch H, Eickholz P, Jockel-Schneider Y. Administration of systemic antibiotics during non-surgical periodontal therapy-a consensus report. *Clin Oral Investig*. 2019;23: 3073-85.
11. Cobb CM. Lasers and the treatment of periodontitis: the essence and the noise. *Periodontol 2000*. 2017;75:205-95.
12. Stájer A, Kajári S, Gajdács M, Musah-Eroje A, Baráth Z. Utility of Photodynamic Therapy in Dentistry: Current Concepts. *Dent J (Basel)*. 2020;8:43-55.
13. Simões JCS, Sarpaki S, Papadimitroulas P, Therrien B, Loudos G. Conjugated Photosensitizers for Imaging and PDT in Cancer Research. *J Med Chem*. 2020;63:14119-50.
14. Kwiatkowski S, Knap B, Przystupski D, Saczko J, Kędzierska E, Knap-Czop K, Kotlińska J, Michel O, Kotowski K, Kulbacka J. Photodynamic therapy - mechanisms, photosensitizers and combinations. *Biomed Pharmacother*. 2018;106: 1098-107.
15. Su CW, Yen AF, Lai H, Lee Y, Chen HH, Chen SS. Effects of risk factors on periodontal disease defined by calibrated community periodontal index and loss of attachment scores. *Oral diseases*. 2017; 23:949-55.
16. Gandhi KK, Pavaskar R, Cappetta EG, Drew HJ. Effectiveness of Adjunctive Use of Low-Level Laser Therapy and Photodynamic Therapy After Scaling and Root Planing in Patients with Chronic Periodontitis. *Int J Periodontics Restorative Dent*. 2019;39: 837-43.
17. Derikvand N, Ghasemi SS, Safiaghdam H, Piriaei H, Chiniforush N. Antimicrobial Photodynamic Therapy with Diode laser and Methylene blue as an adjunct to scaling and root planning: A clinical trial. *Photodiagnosis Photodyn Ther*. 2020;31:101818.
18. Katsikanis F, Strakas D, Vouros I. The application of antimicrobial photodynamic therapy (aPDT, 670 nm) and diode laser (940 nm) as adjunctive approach in the conventional cause-related treatment of chronic periodontal disease: a randomized controlled split-mouth clinical trial. *Clin Oral Investig*. 2020;24:1821-27.
19. Kharkar VV, Kolte AP, Kolte RA, Bawankar PV, Lathiya VN, Bodhare GH. Influence of Adjunctive Photodynamic Therapy on Interleukin-6, Interleukin-8, and Interleukin-10 Gingival Crevicular Fluid Levels in Chronic Periodontitis - A Randomized Controlled Trial. *Contemp Clin Dent*. 2021;12: 235-40.
20. Kuka GI, Gursoy H, Emekli-Alturfan E, Ustundag UV, Kuru B.: Evaluation of nitric oxide levels in chronic periodontitis patients treated with initial periodontal therapy and probiotic food supplements: A double blind, randomized controlled clinical trial. 2019;33: 974-9.