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Research Article

Photo Dynamic Therapy as An Adjunct to Mechanical Debridement on Non-Surgical Management of Peri-Implantitis - A Systematic Review

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INTRODUCTION

Dental implants have become much more widely used in medical practice over the past few decades. Due to its excellent success rates, it is regarded as a secure and practical treatment option for people who are partially or completely edentulous [1,2,3]. The prevalence of related implant problems and diseases has increased as a result of the large rise in implant placements [4]. Peri implantitis (PI), which affects 19% of patients, and peri-implant mucositis (p-iM) are the two most significant illnesses [5]. At the World Workshop on the Classification of Periodontal and Peri-implant Conditions and Diseases, Berglundh et al. [6] defined peri-implantitis (PI) as a plaque-associated pathological condition occurring in tissues around dental implants, characterized by swelling in the peri-implant mucosa and ensuing gradual bone loss as a result. The locations that display PI are linked to indications of clinical inflammation, elevated probing depth (PD) values with or without recession, bleeding on probing (BOP) values with or without pus, and radiographic bone loss evidence(1)

Decontaminating implant surfaces is a difficult objective. The literature has suggested a number of various treatments [7,8,9]. In conjunction with topical or systemic antibiotics, surfaces can be cleaned mechanically (with dental curettes, ultrasonic scalers, and airpowder abrasive) and chemically (with citric acid, H2O2, chlorhexidine digluconate, and EDTA) [10, 11]. Lasers can be used to clean the surfaces of implants. Due to their hemostatic qualities, ability to target specific calculi, and bactericidal effects, diode, erbium, and CO2 lasers are the most often employed (12). The combination of conventional care and photodynamic therapy (PDT) is an alternate method for decontaminating dental implants. Photodynamic therapy includes the use of a low-power diode laser in combination with photosensitizing compounds. These components are linked to the bacterial membrane and, when excited, react with the substrate. The photosensitizer binds to the target cells and when it is irradiated with light of specific wavelength, in the presence of oxygen, it undergoes a transition from a low-energy ground state to an excited singlet state; then singlet oxygen and other very reactive agents are produced, which are toxic to these target cells [13]. In recent years, photodynamic treatment (PDT) has drawn increased attention in dentistry. Killing of periodontal bacteria is promoted by the application of photosensitive dyes into pockets and their activation with light. Clinical trials in people with chronic periodontitis have shown that PDT has positive benefits on reducing gingival inflammation (14). Dogs were used to study the effects of PDT on the management of ligature-induced peri-implantitis. Prevotella intermedia/nigrescens, Fusobacterium spp., and beta-

haemolytic Streptococcus bacterial populations all decreased, according to the findings [15]. In antimicrobial PDT, photosensitizers such as toluidine blue and methylene blue are employed. Similar physicochemical and chemical characteristics can be seen in these photosensitizers.[16] Prevotella intermedia and Aggregatibacter actinomycetemcomitans counts significantly decreased as a result of TBO, however Porphyromonas gingivalis was unaffected.[17,18]. Authors have shown that PDT does not harm titanium surface [19]. Indocyanine green (ICG), a different photosensitizer with an activation wavelength of 805 nm and low power diode laser radiation, also eliminated periodontal infections like P. gingivalis during PDT. [20] Hopp and Biffar combined PDT and ICG, which had the long-term effect of stabilizing periodontitis/peri implantitis.[21] Near infrared light (800–1100 nm) can reach a depth of 6 mm while visible red light (650 nm) can only penetrate biological tissues up to 3-3.5 mm. As a result, when compared to other chemicals, the ICG, which has a wavelength of 805 nm, can permeate biological tissues more deeply.[22] Additionally, the ICG is non-toxic and has received approval from the US Food and Drug Administration for use in medical procedures.[23]

REVIEW METHODS:

Protocol and Registration

This systematic review and meta-analysis were performed in accordance with Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA 2020)(Ref 1) statement guidelines, the Cochrane Handbook for systematic reviews of interventions,(Ref 2) version 5.1.0 and is registered at PROSPERO under the registration code, CRD----------. In the Patient, Intervention, Comparison and Outcome (PICO) format the following focused question was proposed "Is there a difference in the effect of Photo dynamic therapy as an adjunct to mechanical debridement as compared to mechanical debridement alone in non-surgical management of patients with peri-implantitis?"

Literature Search

A systematic search was carried out in databases; PubMed, MEDLINE, DOAJ, Cochrane library, and Scopus until July 2023 to retrieve articles in the English language. Relevant MeSH terms and free text terms were used based on Population, Intervention, Comparison, Outcomes and Study (PICOS) (Table 1). The search strategy was framed using Boolean operators (OR, AND) with #1AND #2AND #3AND #4AND #5. Apart from these databases, the articles were also screened by cross reference, citation chasing, and Grey literature were conducted using Google Scholar, Greylist and OpenGrey along with hand searching from specialty journals. A specific electronic search of journals presented in Table 1 was conducted.

Eligibility Criteria

Inclusion criteria outline according to the PICOS strategy

Population (P): Studies with Patients clinically diagnosed with peri- implantitis diagnosed clinically by peri-implant bone loss, pocket depth and level of attachment or radiographic evidence of bone loss with a range of 0.5–2 mm from the time when the prosthetic reconstruction was delivered to prescreening appointment II irrespective of age, gender, ethnicity, and nationality.

Interventions (I): Studies using photodynamic therapy as an adjunctive treatment to mechanical debridement for the management of peri-implantitis.

Comparison (C): Studies using mechanical debridement alone for non-surgical management of patients with peri-implantitis.

Outcome (O): Primary outcome: Studies assessing either or all of the following outcomes at minimum of one week follow-up interval:

i. Bleeding on Probing: Bleeding after placing the probe apical to the gingival margin at six sites per implant, for the presence or absence of bleeding subsequent to probing
ii. Periodontal Probing Depth: The depth of the gingival sulcus measured from the gingival margin
iii. Clinical Attachment Loss: Measured from a reference point (acrylic stent) to the bottom of the probable pocket
iv. Gingival Recession: Measured as the distance from a reference point (acrylic stent) to the gingival margin

Secondary outcome: Studies assessing gingival index, plaque index, pain along with either or all of the primary outcomes at minimum of one week follow-up interval.

Study design (S): Only randomized controlled trials assessing the effect of Photo dynamic therapy as an adjunct to mechanical debridement as compared to mechanical debridement alone in non-surgical management of patients with peri-implantitis

Exclusion criteria

- Studies involving participants who had a history of significant medical conditions, or took any medication that may affect the effect of the agents.
- Studies involving combination of treatment other than photodynamic therapy with mechanical debridement
- Single intervention trials without the control group will be excluded
- Observational study designs, case reports, case series, cross-sectional studies, non-randomised control trials and reviews.
- Article reporting only abstracts and full-texts were not available in the database.

Screening and Selection of Studies

Two reviewers independently (----- and ---) undertook a three-step selection of studies in the databases based on eligibility criteria. In 1st step, the titles of the articles were screened and irrelevant articles were excluded. The second step included the screening of remaining articles

based on the abstract, and the third step screened articles after reading the full text to verify the degree of compliance that the studies had with eligibility criteria and make a final decision of their inclusion in this review. Duplicate records were removed using the software. The level of concordance, calculated through Cohen's kappa, between the two reviewers was 0.92 for titles and abstracts and 0.94 for full texts. Discrepancies among authors/reviewers were resolved by the third author (XYZ) through careful discussion. If needed, authors of the included studies were contacted by e-mail for clarification of any doubts and missing data.

Data Extraction

A standardized data extraction form was prepared in a Microsoft Excel version (2013) spreadsheet assisted by an expert, before proceeding with data extraction. A pilot form with data extraction of two articles under headings; author's name, year of publication, study design, sample size, age group, intervention and comparison description, outcome measures and author's conclusion were completed. After the consensus of both authors with the data extracted, further extraction was commenced.

Assessments of the risk of bias and quality

Cochrane ROB assessment tool (Ref 3) was used for categorizing the studies into high, medium, and low risk for further inclusion in quantitative analysis. The ROB tool consisted of critically appraising the studies based on domains; random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, risk of other potential sources of bias, and overall, ROB.

Statistical Analysis for Quantitative Synthesis

Review Manager (RevMan) 5.3 was used for statistical analysis. The combined results were expressed as mean and standard deviation for the continuous data at 95% confidence intervals (CIs) and $P<0.05$ was considered significant. Chi-square and Tau-square were used to assess whether the observed difference was homogeneous or heterogeneous among the studies. Statistical heterogeneity was assessed by the I^2 test at $\alpha=0.10$. Subgroup analysis was conducted to reduce the heterogeneity among the studies. For $I^2>50\%$, the random-effects model was applied. Also, the statistical significance was set at p-value (two-tailed) <0.05. Detection of publication bias using funnel plots were done for studies exceeding 10 in number for each outcome assessed (Ref 4).

Table 1: The search strategy and PICOS tool

Search strategy	
Focused Question	Is there a difference in the effect of Photo dynamic therapy as an adjunct to mechanical debridement as compared to mechanical debridement alone in non-surgical management of patients with peri-implantitis?
Search strategy	
Population	("peri-implant mucositis" [Text Word]) OR ("Peri-Implant Diseases"[Text Word])) OR (peri-implantitis [MeSH Terms])) OR (Peri Implantitis [Text Word])) OR (Peri-Implantitides [Text Word])) OR (Periimplantitides [Text Word]))
Intervention (#1)	((Photochemotherapy [MeSH Terms])) OR (Photodynamic Therapy [Text Word])) OR (Photochemotherapies [Text Word])) OR (Therapy, Photodynamic [Text Word]))) OR (Photodynamic Therapies [Text Word])) OR (Therapies, Photodynamic [Text Word])) OR (diode laser therapy [Text Word])) OR (Diode Laser [Text Word] OR (Laser therapy [Text Word] OR "Adjunctive Antimicrobial Photodynamic Therapy" [Text Word]))
Comparisons (#2)	(("mechanical Debridement" [Text Word] OR "scaling and root planing"[Text Word]) OR ("Non-Surgical Treatment" [Text Word]))
Outcomes (#3)	(Bleeding on Probing [Text Word] OR Clinical Attachment Loss [Text Word] OR Gingival Recession [Text Word] OR Gingival Recession [MeSH] OR Probing Depth [Text Word] OR Plaque Index [Text Word] OR Gingival Bleeding Index [Text Word] OR Full Mouth Bleeding Index [Text Word])
Study design (#4)	((Randomized controlled studies [Text Word] OR randomized control trials [MeSH] OR randomized control clinical trial [MeSH]))
Search Combination	#1 AND #2 AND #3 AND #4
Database search	
Language	Articles in English language
Electronic Databases	PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, Scopus, DOAJ
Period of Publication	Studies published between 1-1-2010 to 31-07-2023

Figure 1: PRISMA flow diagram

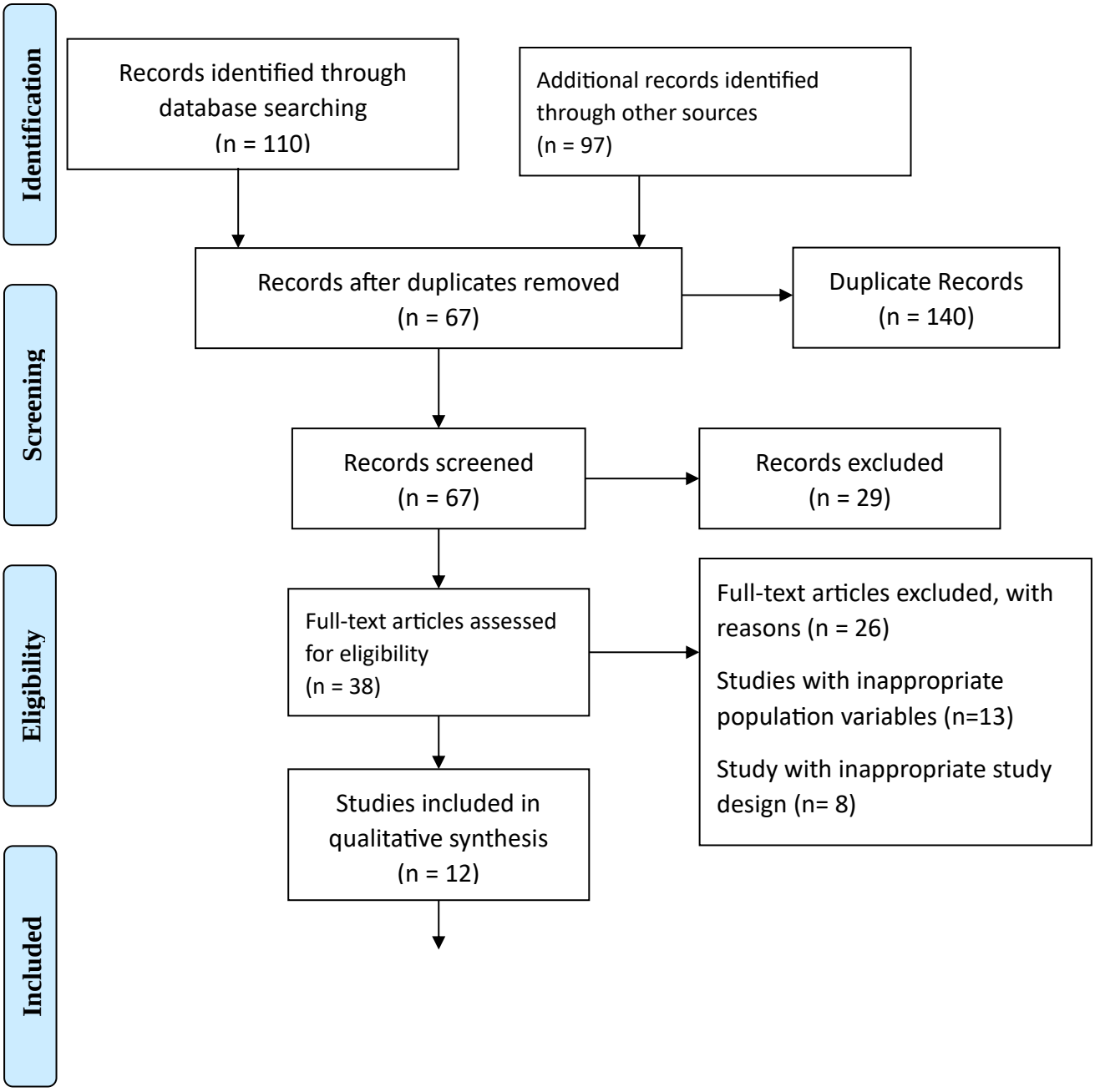


Table 2- Study Characteristics

Study Id	Place of study	Sample Size I/C	Age I/C	Confirmatory test	Instrument used for assessment	Intervention group	Control group	Type of Laser	Type of dye	Wavelength/Power/Density/Mode	Time of application	Technique Control group	Time interval	Outcome assessed	Authors Conclusions
Altindal D et al 2023	Turkey	20/20	36-68	Clinical parameters	Calibrated Williams periodontal plastic probe	MD + aPDT	MD+ sham	Diode laser		940-nm/ 1.5 W/ 15 J/cm2/ uninitiated mode	First week and second week for 3 times	Air flow and titanium curettes and irrigation of peri-implant grooves with 0.12% chlorhexidine gluconate	B 3-M	PI, GI, BOP, PPD, CAL	940-nm diode laser in addition to the nonsurgical therapy of PI provided clinical, but not biochemical benefits
Tan J 2023	USA	18/12	60-70	2017 World Workshop for Periodontal Classification	Colored periodontal probe	MD + aPDT	MD + sham	Diode laser	methylene blue at a concentration of 0.01%	660 nm/100mW /10 J/site/-	Baseline as a one-time therapy	Titanium curettes and piezo ultrasonic titanium tips + Sham lasers	6-W, 12-W	BOP, PD, PI, CAL, buccal keratinized gingiva	Mechanical debridement with the adjunctive use of aPDT was equivalent to mechanical debridement alone in all clinical outcomes
Pourabbas R et al 2023	Iran	25/25	26–58	Clinical and radiographic	Periodontal probe	MD + aPDT	MD alone	Laser	indocyanine green photosensitizer	805-nm/ 0.5 W/-/-	Baseline as a one-time therapy	Sonic scaler which was followed by the use of titanium curettes and a glycine-based polishing powder	B, 2 W, 3 M	BOP, PD, CAL, GR, pain on probing, suppuration	Addition of PDT to mechanical therapy did not provide any additional improvements in the clinical or biologic parameters of peri-implant mucosal inflammation
Soundarajan S et al 2022 Unclear data with time interval	India	36/36	42.7 ± 2.8	Clinical parameters	William's periodontal probe	MD + aPDT	MD alone	InGaAs Semi-conductor diode laser	1% methylene blue	660 nm/ 70 mW/ 16.72 J/cm2/ continuous wave mode	B, 1W, 2W, 3W	Gracey curettes and a piezoelectric ultrasonic scaler unit	B, 3M, 6M	PI, GI, PPD, CAL	Nonsurgical periodontal therapy of chronic periodontitis using a-PDT as an adjunct to SRP was significantly more effective than SRP alone in

															reducing PD, CAL, GI, and PI at 3 months follow up.
Yayli N et al 2022	Turkey	16/17	40-60	Clinical and radiographic	Plastic probe	MD + a-PDT	MD + Sham	Diode laser	-	940 nm/ 0.8 W/ 3 J/cm^2/ continuous mode	Baseline	Titanium Gracey curettes	B, 6M	PI, GI BOP, PD	Similar treatment outcomes were obtained in the mechanical therapy–alone group and the diode laser–assisted mechanical therapy
Al-Askar M et al 2021	Riyadh, Saudi Arabia	16/16	60-70	peri-implantitis was based upon the criteria described in the study by Renvert et al	Plastic graded probe (UNC15 periodontal-probe, Hu-Friedy)	MD + aPDT	MD alone	Diode laser	0.05% methylene blue	660 nm/ 180 mW/cm2/ 60 J/cm2/-	Baseline	Sterile plastic and stainless-steel curettes respectively	B, 3M	PI, GI, PD, Crestal bone loss	PDT seem to be useful adjunct to MD for the treatment of peri-implant soft-tissue inflammation among patients with peri-implantitis.
Garcia M et al 2021	USA	18/16	30-87	2017 World Workshop for Periodontal Classification w	Color-coded periodontal probe	MD + aPDT	MD+ sham	Diode laser	Methylene blue dye (0.01 mg/ml)	660nm/ 100mW/ 10J/site	Baseline	Titanium curettes with piezo ultrasonic titanium tips	B, 6W, 12W	BOP, PPD, PI	There was no statistically significant difference in clinical parameter reduction between test (aPDT) and control (“sham aPDT”) groups

Sheokand N et al 2021	India	not clearly mentioned	25 - 60	Clinical and radiographic	-	aPDT	MD alone	HELBO diode laser	-	670 nm/ -	Baseline	non-metal tip and implant debridement was done with carbon-fiber-reinforced plastic curettes	B, 6 W	PPD BOP	Use of photodynamic therapy added therapeutic benefit to conventional management
Wang H et al 2019	China	66/65	30-60	Clinical and radiographic	Periodontal probe	MD + aPDT	MD alone with saline wash	Light-emitting diode	Toluidine blue	635 nm/ 750 mW/ 60 mW/cm2	Baseline	Subgingival sand-blast using glycine powder	B, 1M, 3M, 6M	PD PLI, SBI, CAL	PDT combined with MD significantly improves PD, CAL, PLI and SBI
Karimi M et al 2016	Iran	15/15	40-60	Clinically and radiographically	Plastic probe	MD + aPDT	MD alone	Light-emitting diode	Toluidine blue 0.01%	630 nm/ 2000 mW/cm2/ -/-	Baseline	Plastic curettes followed by pocket irrigation with sterile saline.	B, 1.5 M, 3 M	GI BOP PPD CAL	Antimicrobial PDT following closed surface scaling resulted in an improvement of clinical parameters, in the treatment of peri-implant diseases.
Romeo U et al 2016	Italy	63/59	34-68	Clinical and radiographic	Plastic probe	MD + aPDT	MD alone	HELBO TheraLite diode laser	Methylene blue	670nm/ 5mW/cm2,/ 25.54J/cm2/-	Baseline	Mechanical and manual decontamination of the oral cavity was performed using air polishing with micronized glycine powder	B, 6W, 12W, 24W	BOP, PD	Antimicrobial photodynamic therapy with diode laser and phenothiazine chloride represents a reliable adjunctive treatment to conventional therapy

Bombeccari GP et al 2013	Italy	20/20	33–64	Clinically and radiographically diagnosed	Plastic constant pressure probe with a 20 g controlled probing force	MD + aPDT	MD alone	Diode laser	Toluidine blue O	810 nm/ 1 W/-/ continuous wave mode	Baseline	curetted with plastic scalers and irrigated with a 0.2% chlorhexidine digluconate solution for 1 minute before treatment	B, 3M, 6 M	PPD, PAL, BOP	Treatment with PDT in patients with periimplantitis was not associated with major reduction of total anaerobic bacteria on the rough surfaces of dental implants as compared with surgical therapy.

aPDT- Adjunctive Photodynamic Therapy, B- Baseline, BOP- Bleeding on Probing, CAL- Clinical Attachment Loss, C- Control, I- Intervention, F- Female, GI- Gingival Index, GR- Gingival Recession, M- Month, MD- Mechanical Debridement, PI- Plaque Index, PII- Periodontal Index, PPD- Periodontal Probing Depth, SRP- Scaling and Root Planning, SBI- Sulcus Bleeding Index, W- Week

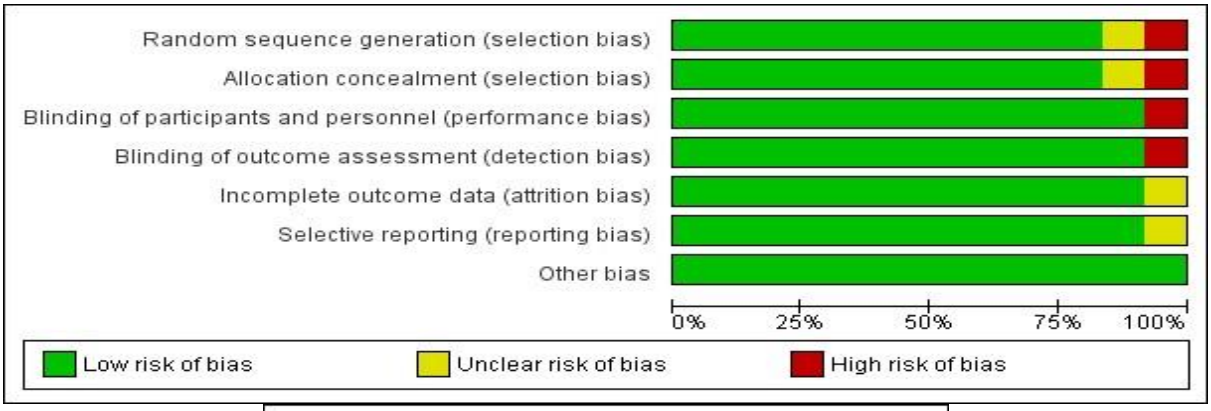
Table 3: Outcome measures assessed in Individual Studies

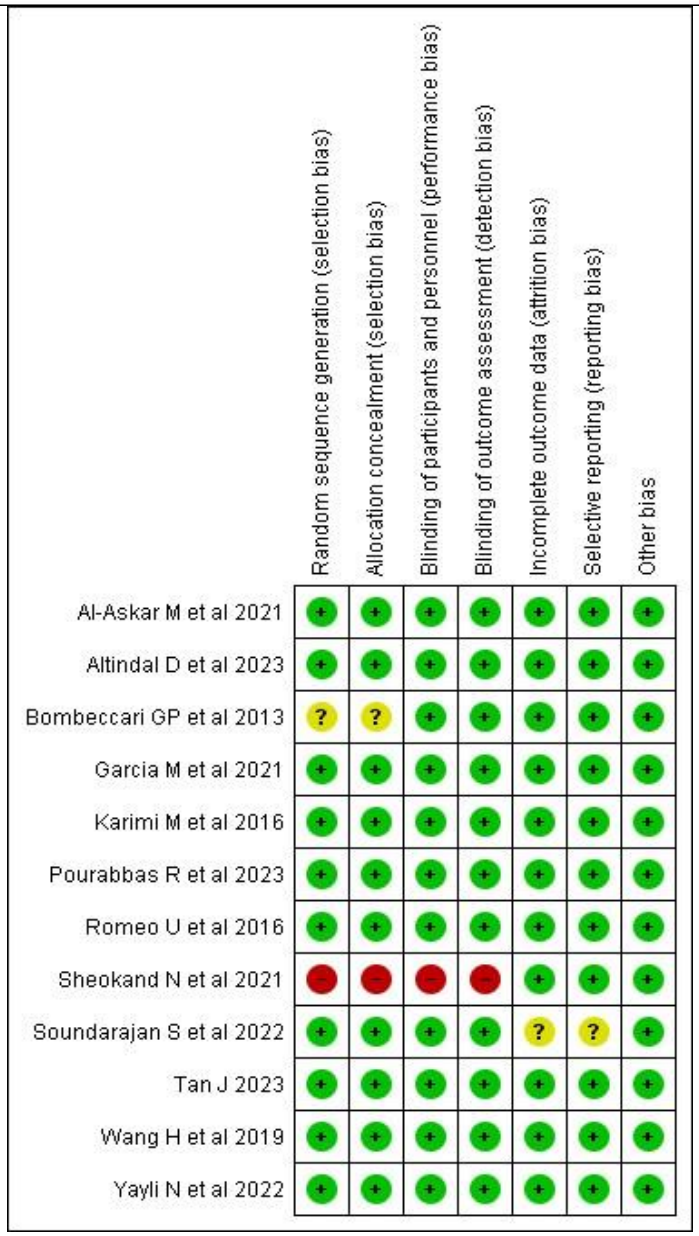
Study Id	Sample Size Intervention/Control	Intervention	Control
Modified Plaque Index			
Altindal D et al 2023	20/20	BL 2.15±0.56 3 M 0.85±0.67	BL 2.06±0.47 3 M 0.88±0.68
Yayli N et al 2022	16/17	BL 1.90 ± 0.62 6M 1.07 ± 0.63	BL 1.64 ± 0.74 6M 1.00 ± 0.68
Al-Askar M et al 2021	16/16	BL 2.77 ± 0.2 3 M 0.5± 0.1	BL 2.56± 0.3 3 M 1.6± 0.3
Garcia M et al 2021	18/16	BL 3.83 ± 0.83 6 M 3.75 ± 1.03 12 M 3.17 ± 0.48	BL 5.09 ± 0.39 6 M 4.30 ± 0.65 12 M 4.33 ± 0.55
Modified Gingival Index			
Altindal D et al 2023	20/20	BL 2.45±0.51 3 M 1.07±0.54	BL 2.44±0.56 3 M 1.28±0.60
Yayli N et al 2022	16/17	BL 1.96 ± 0.31 6M 1.58 ± 0.45	BL 1.92 ± 0.16 6M 1.67 ± 0.32
Al-Askar M et al 2021	16/16	BL 3.3 ± 0.1 3 M 0.2 ± 0.05	BL 3.08 ± 0.2 3 M 2.2 ± 0.08
Probing Depth			
Altindal D et al 2023	20/20	BL 5.11±1.04 3 M 3.73±0.95	BL 4.50±1.15 3 M 3.94±1.14
Pourabbas R et al 2023	25/25	BL 5.44±0.65 2W 3.2±0.76 3M 3.56±0.58	BL 5.37±0.71 2W 3.91±0.88 3M 3.87±1.19
Soundarajan S et al 2022	36/36	3M 4.7 ± 0.6	3M 5.61 ± 0.6
Yayli N et al 2022	16/17	BL 4.14 ± 0.80	BL 4.14 ± 0.64

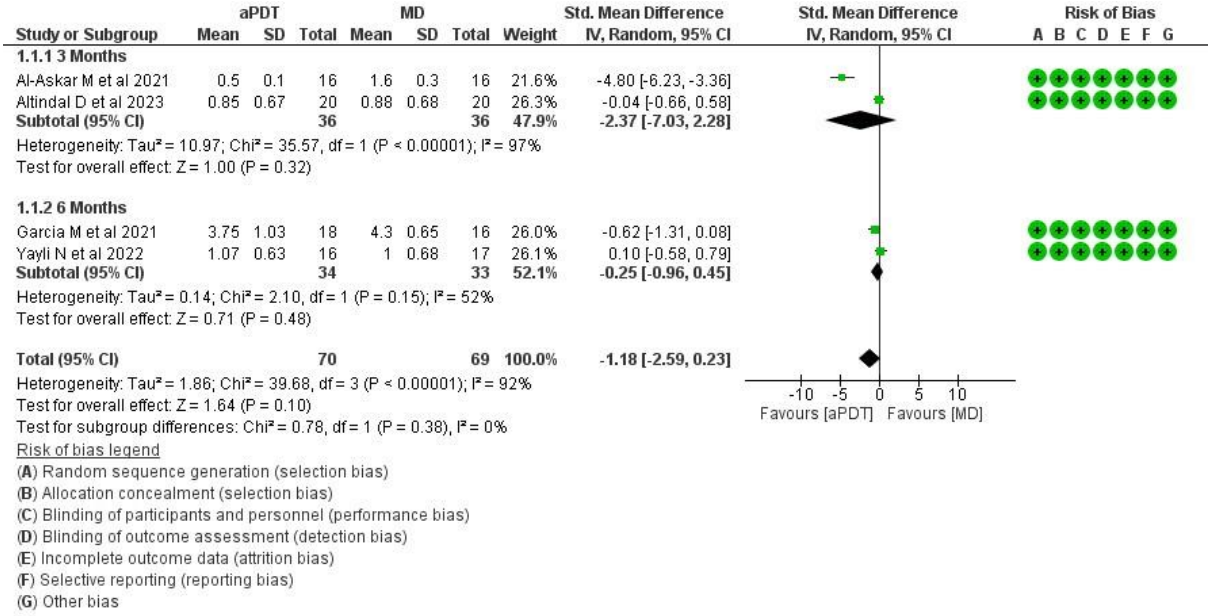
		6M 3.28 ± 1.00	6M 3.62 ± 0.71
Al-Askar M et al 2021	16/16	BL 4.2 ± 0.1 3 M 1.4 ± 0.07	BL 4.4 ± 0.2 3 M 2.7 ± 0.03
Garcia M et al 2021	18/16	BL 5.15 ± 0.34 6 W 4.00 ± 0.42 12M 4.44 ± 0.53	BL 4.97 ± 0.60 6W 3.54 ± 0.54 12 M 3.94 ± 0.48
Wang H et al 2019	66/65	BL 4.93 ± 1.07 1 M 4.23 ±0.94 3 M 3.37± 0.37 6 M 3.06 ±0.29	BL 5.07± 0.72 1 M 3.55 ± 0.47 3 M 3.89 ± 0.22 6 M 4.62 ±0.45
Karimi M et al 2016	15/15	BL 5.36 ± 1.13 1.5 M 3.75 ± 0.9 3 M 3.13 ± 0.54	BL 5.08 ± 1.47 1.5 M 5.09 ± 1.5 3 M 5.08 ± 1.5
Bombeccari GP et al 2013	20/20	BL 5.9 ±0.76 3M 5.2 ± 1.03 6M 4.9 ± 0.47	BL 5.8 ± 0.78 3M 5.7 ± 0.48 6M 5.5 ± 0.52
Clinical Attachment Loss			
Altindal D et al 2023	20/20	BL 5.15±1.05 3 M 3.75±0.91	BL 4.50±1.15 3 M 3.94±1.14
Pourabbas R et al 2023	25/25	6.92±0.81 2W 4.16±0.62 3M 4.8±0.5	6.08±0.71 2W 5.54±0.97 3M 6.12±0.53
Soundarajan S et al 2022	36/36	3 M 6.02 ± 0.6	3 M 7.19 ± 0.6
Wang H et al 2019	66/65	BL 1.85/0.86 1 M	BL 1.49/0.67

		1.85/0.85 3 M 1.48/0.57 6 M 1.32/0.43	1 M 1.49/0.67 3 M 1.48/0.67 6 M 1.49/0.67
Karimi M et al 2016	15/15	BL 7.36 ± 1.57 1.5M 5.57 ± 1.09 3M 4.79 ± 1.36	BL 7.16 ± 1.4 1.5M 7.17 ± 1.4 3M 7.18 ± 1.4
Bombeccari GP et al 2013	20/20	BL 7.11±0.02 3 M 6.58 ±0.02 6 M 6.57±0.02	BL 7.05±0.02 3 M 7.02 ±0.02 6 M 6.95±0.03
Bleeding on Probing			
Altindal D et al 2023	20/20	BL 94.16±15.55 3 M 28.33±28.14	BL 88.33±21.01 3 M 43.33±40.6
Pourabbas R et al 2023	25/25	79.40±13.21 2W 28.56±9.63 3M 51.88±17.69	76.62±15.25 2W 24.41±10.25 3M 30.95±10.82
Yayli N et al 2022	16/17	BL 88.09 ± 17.82 6M 61.90 ± 29.37	BL 72.02 ± 23.93 6M 60.71 ± 29.13
Garcia M et al 2021	11/6	BL 5.27 ± 0.38 6 M 3.4 ± 0.64 12 M 3.44 ± 0.63	BL 3.33 ± 0.33 6 M 2.75 ± 1.11 12 M 2.33 ± 0.61
Bombeccari GP et al 2013	20/20	BL 0.70± 0.48 3 M 0.00±0.00 6 M 0.10±0.31	BL 0.80±0.44 3 M 0.30±0.42 6 M 0.50±0.52
Gingival Recession			

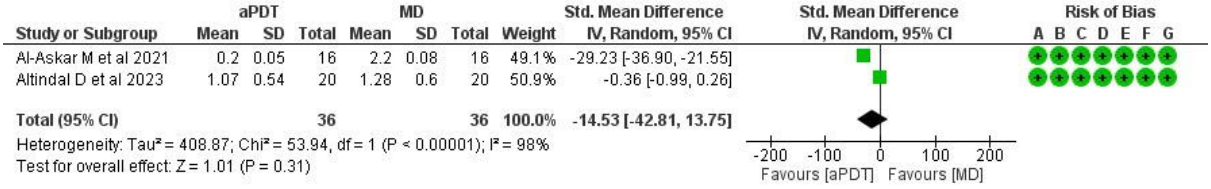
Pourabbas R et al 2023	25/25	BL 1.12±0.78 2W 1.08±0.81 3M 1.4±0.57	BL 1.33±0.86 2W 1.25±0.73 3M 1.5±0.83







Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias



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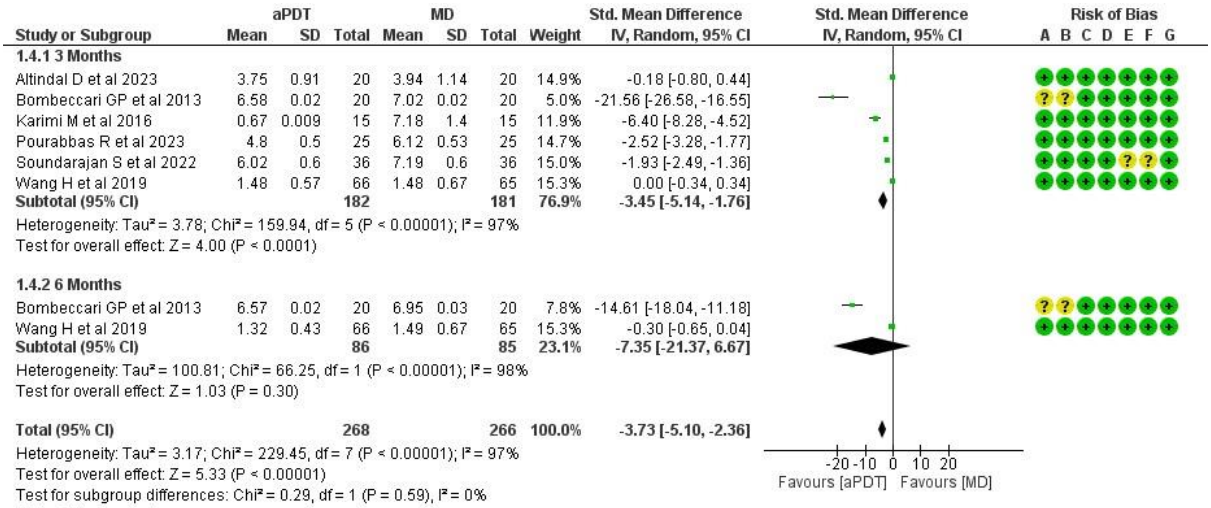

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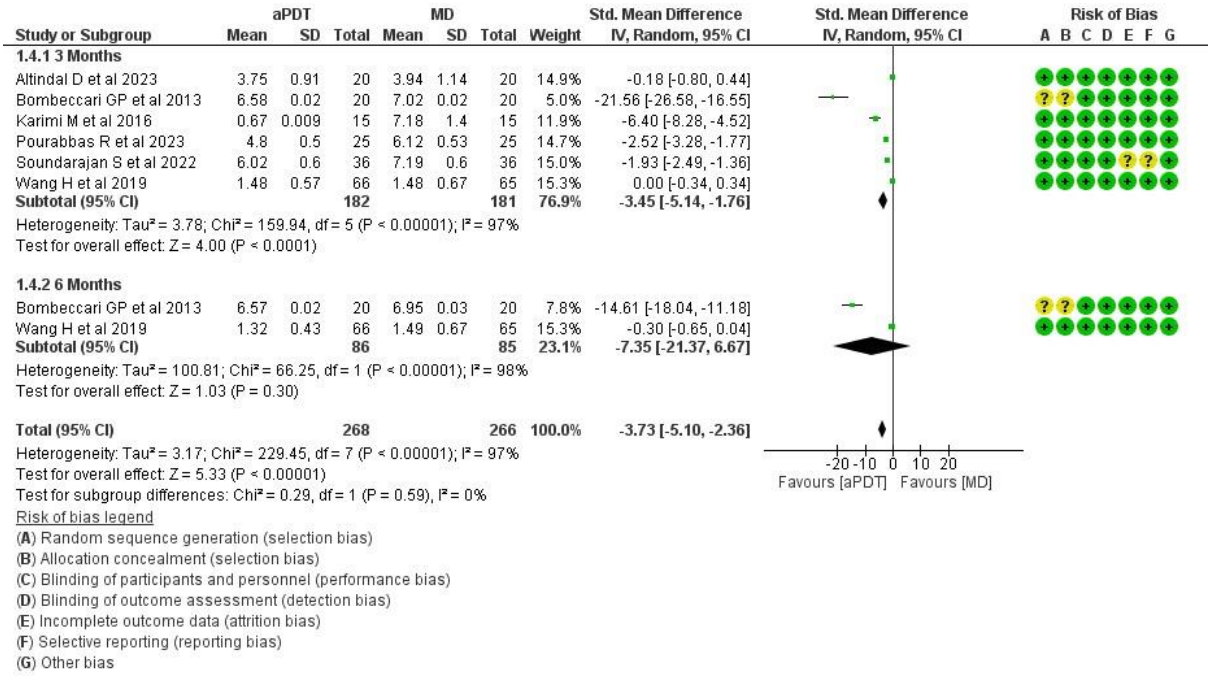

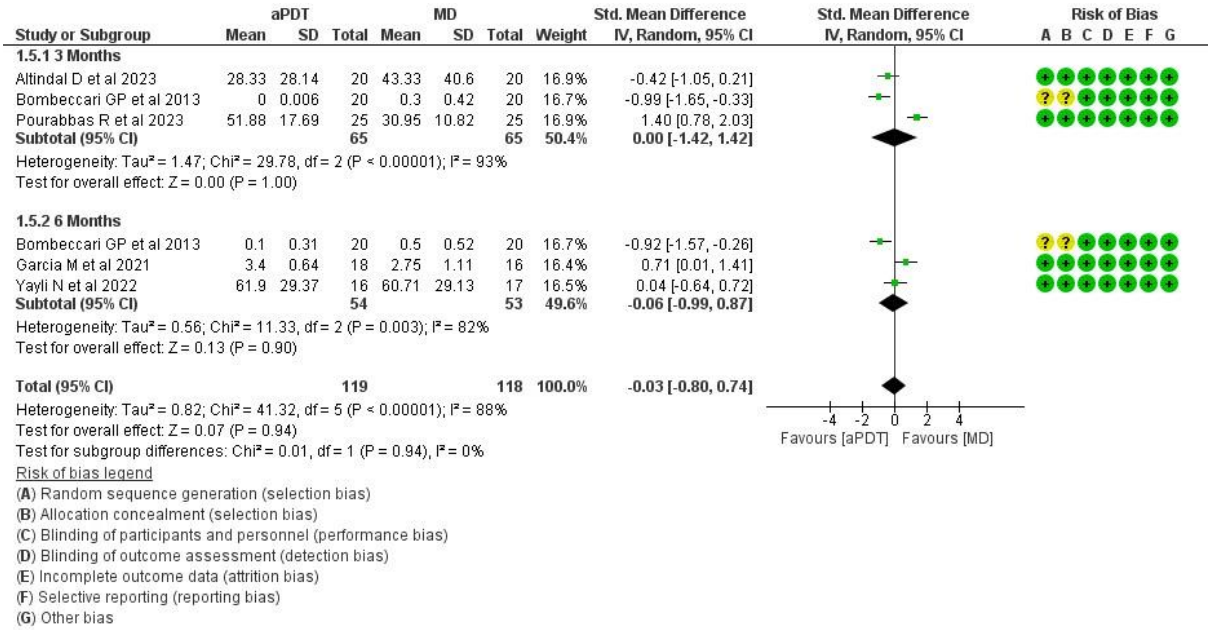

DISCUSSION

Our study's aim was to assess if there is an additional benefit of adjunct to mechanical debridement on non-surgical management of peri-implantitis . Assessing the Plaque Index, Gingival Index, Probing Depth ,Clinical Attachment Loss and bleeding on probing. At 3 months, standardized mean difference for plaque index between both the groups favored the aPDT group but did not show statistically significant difference as (SMD, -2.37, 95% CI = -7.03 - -2.28, p - 0.32, I^2- 97%). At 6 months, standardized mean difference for plaque index between both the groups did not show a statistically significant difference (SMD, -0.25, 95% CI = -0.96 - 0.45, p - 0.48, I^2- 52%).

At 3 months, standardized mean difference for gingival index between both the groups favored the aPDT group but did not show statistically significant difference as (SMD, -14.53, 95% CI = -42.81 – 13.75, p - 0.31, I^2- 98%).

The standardized mean difference for probing depth between adjunctive Photodynamic therapy group and Mechanical Debridement group was carried out as subgroups analysis using random effect model according to the time interval of 3 months and 6 months. At 3 months, standardized mean difference for probing depth between both the groups favored the aPDT group showing a statistically significant difference (SMD, -1.45, 95% CI = -2.37 - -0.53, p - 0.002, I^2- 93%). At 6 months, standardized mean difference for probing depth between both the groups did not show a statistically significant difference (SMD, -1.19, 95% CI = -3.36 - 0.98, p - 0.28, I^2- 0%).

The standardized mean difference for clinical attachment loss between adjunctive Photodynamic therapy group and Mechanical Debridement group was carried out as subgroups analysis using random effect model according to the time interval of 3 months and 6 months. At 3 months, standardized mean difference for clinical attachment loss between both the groups favored the aPDT group showing a statistically significant difference (SMD, -2.42, 95% CI = -3.84 - -0.99, p = 0.0009, I^2- 96%). At 6 months, standardized mean difference for clinical attachment loss between both the groups did not show a statistically significant difference (SMD, -7.35, 95% CI = -21.37 - 6.67, p - 0.30, I^2- 98%). Graumann et al. [15] revealed the antimicrobial effect of a-PDT in bacteria, in the biofilm in the periodontal pocket. a-PDT was also reported to inhibit the adherence of LPS on the implant and prevent bacterial growth in the biofilm [27,28]. In addition, a-PDT was demonstrated to have a continuous antimicrobial effect [25]. Although the mechanism underlying this effect has not yet been clarified, Tanaka et al. [25] hypothesized that a-PDT stimulated the accumulation of neutrophils in the irradiated area and activated their phagocytic effect, in addition to the direct antimicrobial effect of a-PDT, resulting in its continuous antimicrobial effect. Zulaziz et al. [29] reported that a-PDT also enhances the immune response by activating macrophages, which should contribute to the remission of the symptom. Thus, exposure of the gingiva to a-PDT is expected to induce antimicrobial effect and immune response. Therefore, it is possible that a-PDT is effective not only for the treatment but also for the prevention of peri-implant disease (Seigo Ohba, Mika Sato, Sawako Noda, Hideyuki Yamamoto, Kazuhiro Egahira, Izumi Asahina,Assessment of safety and efficacy of antimicrobial photodynamic therapy for peri-implant disease, Photodiagnosis and Photodynamic Therapy,Volume 31,2020,101936,ISSN 1572-1000.

The presence of keratinized mucosa did not have any relation to the effect of a-PDT on peri-implantitis in this study, suggesting that keratinized mucosa do not play a crucial role in treating peri-implantitis by a-PDT in the short term (Table 5). On the other hand, keratinized mucosa is known to be an important factor in keeping implants sound [30]. Keratinized mucosa might be crucial to preven t the initiation of peri-implantitis. However, a long-term assessment is necessary to understand the role of keratinized mucosa in the a-PDT treatment for peri-implantitis. (Thamer Almohareba, Nawaf Alhamoudib,*, Modhi Al Deebc, Mohammed S. Bin-Shuwaisha ,Sameer A Mokeemb, Syed Saad Shafqatd, Fahim Vohrac, Tariq Abduljabbare,f)

PDT can induce dentinal modification which is responsible to introduce exposure of the collagen fibers. The collagen fibers when exposed may help in the attachment and stabilization of newly formed blood clots. This event may result in quicker healing and improved collagen attachment. Due to the increasing conflicts, more clinical trials should be done in this particular area to create an understanding which will be beneficial in achieving optimal clinical outcomes [24,25].

The following limitations should be kept in mind when interpreting our results. First, the treatment results were evaluated at 3 to 6 months and not followed up in the long term, and the sample size was relatively small. Our study had no microbiological analyses and focused on a single biochemical marker. In addition, the wavelength, power, waveform, pulse duration, energy intensity, exposure time, target tissue, and tissue properties may all have strongly influenced the treatment results.

CONCLUSION

We may conclude now, there is minimal level of evidence, and aPDT can only be an adjunct to mechanical debridement, with possible additional clinical benefits of Probing depth reduction and gain Clinical level of attachment .

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I- Intervention
C- Control
M- Male
F- Female
PI- Plaque Index
GI- Gingival Index
BOP- Bleeding on Probing
PPD- Periodontal Probing Depth
CAL- Clinical Attachment Loss
M- Month
W- Week
B- Baseline
MD- Mechanical Debridement

aPDT- Adjunctive Photodynamic Therapy
GR- Gingival Recession
SRP- Scaling and Root Planning
SBI- Sulcus Bleeding Index
PII- Periodontal Index