

Effect Of Photodynamic Therapy In The Management Of Periodontal Disease - A Systematic Review

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Abstract: Background: Periodontitis is multi factorial disease which is initiated with plaque formation that will initiate an inflammatory response which can cause destruction of tissues & tooth supporting structure. If left untreated it will cause gingival recession and bone destruction which will lead to tooth mobility. Sometimes it is difficult to eliminate periodontal pathogens completely from deepest areas of periodontal pockets, to overcome these issues photodynamic therapy (PDT) was used as it is local non-invasive treatment modality without any side effects. Aim: The aim of present study was to investigate the effectiveness of Photodynamic Therapy (PDT) as an Adjunct To Scaling & Root Planing in the management Of Periodontal Disease. Material And Methods: Literature was searched systemically and studies were identified based on the- PICO (Glossary of Evidence Based Terms 2007). Electronic database search of Pubmed, Google scholar, Medline and scopus was performed using (MESH) terms- Photodynamic therapy, periodontitis, microbiological assessment. Articles published between year 2009- 2019 were reviewed. Patient treated with SRP alone on one side and other side with SRP+ PDT. Recording of Clinical parameters like PPD,CAL,BOP,PS,GR were done from baseline to 3,6 month. Microbiological and biochemical analysis were also evaluated to check level of RANKL/OPG, IL-1 β , TNF- α , Aggregatibacter actenomycetocomitans, Porphyromonas gingivalis, Tanerella forsythia Conclusion:: A large evidence suggest that PDT when used along with SRP resulted in significant improvement in clinical parameters. Significant improvement in biochemical parameters such as IL-1 β , Tnf- α , RANKL/OPG were also seen after periodontal therapy along with PDT when compared with SRP alone. [Saini A Natl J Integr Res Med, 2021; 12(3): 72-78]

Key Words: Periodontitis, Photodynamic Therapy, Scaling & Root Planning

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Introduction: Periodontitis is a chronic inflammatory disease that results in destruction of tissues and surrounding structure of the teeth, If left untreated can cause loss of teeth. It is characterized by destruction of bone and connective tissues following an inflammatory host response secondary to infection by periodontal bacteria. In Periodontal disease, inflammatory mediators like IL-6, IL-8 and TNF- α promote degeneration of inflamed periodontal tissues. In some studies increased level of cytokines in gingival tissues and GCF has also been demonstrated¹.

It has been demonstrated that conventional scaling and root planing (SRP) do not completely remove pathogens, especially in deep pockets , and cannot prevent bacteria from spreading to deeper periodontal soft tissues ; SRP may even favour bacteraemic and endotoxaemic events⁴. To overcome these issues, novel therapeutic approaches complementary to the classical strategies are required – one of which are lasers².

Photodynamic Therapy (PDT) was introduced 100year ago by Oscar Raab , he studied effect of light and dyes on Paramecia . Later in 1970's Dougherty (was working with Porphyrin compounds, he discovered PDT) thus he is also called as Father of PDT³. It involves a photosensitizer, light & oxygen.

Photosensitizer are chemical compounds which when administered to the patient, are taken up selectively by the diseased tissue and readily undergoes photo excitation when exposed to suitable wavelength. Photosensitizers can be classified (Mark Wainwright 1998)⁴ as Acridines, Cationic-azinephotosensitizers- Phenothiazinium , Porphyrin ,Natural product photosensitizers, Methylene blue, acridine orange ,toluidine blue, are potent photosensitizers.

Light: activates the photosensitizer by exposure to low-power visible light at a specific wavelength. Tissue transmits red light efficiently, thus activation of wavelength of the

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photosensitizer results in deeper light penetration. Light systems for the photodynamic therapy are: 1. Diode laser systems 2. Noncoherent light sources 3. Nonlaser light sources include light emitting diodes (LED)⁵. The low-level laser wavelength in photodynamic antimicrobial chemotherapy through a suitably administered photosensitizer, have the following advantages than conventional laser:

- Primary interaction is indirect, through chemical mediator
- Little risk of collateral damage within target sites
- Use of non-collimated light through a diffuser tip can overcome limited access and be further compensated by scatter through the body of the liquid sensitizer

Application Of Photodynamics In Periodontal Disease⁶: It was seen that PDT with chlorin e6 shows advantageous results in suppressing periodontal pathogenic bacteria.

PDT not only kills the bacteria, but can also lead to the detoxification of biological activity.

It was seen that additional treatment by PDT after SRP, will show reduction in Gingival Inflammation & MMP-8 level. IL-1 β , IFN- γ , PGE2.

Material & Methods: The aim of present study was to investigate the effectiveness of

Photodynamic Therapy (PDT) as an Adjunct To Scaling & Root Planning in the management Of Periodontal Disease.

Search Strategy: Literature was searched systemically and studies were identified based on the- PICO (Glossary of Evidence Based Terms 2007). Patients with Chronic Periodontitis as per AAP 1999 Classification.

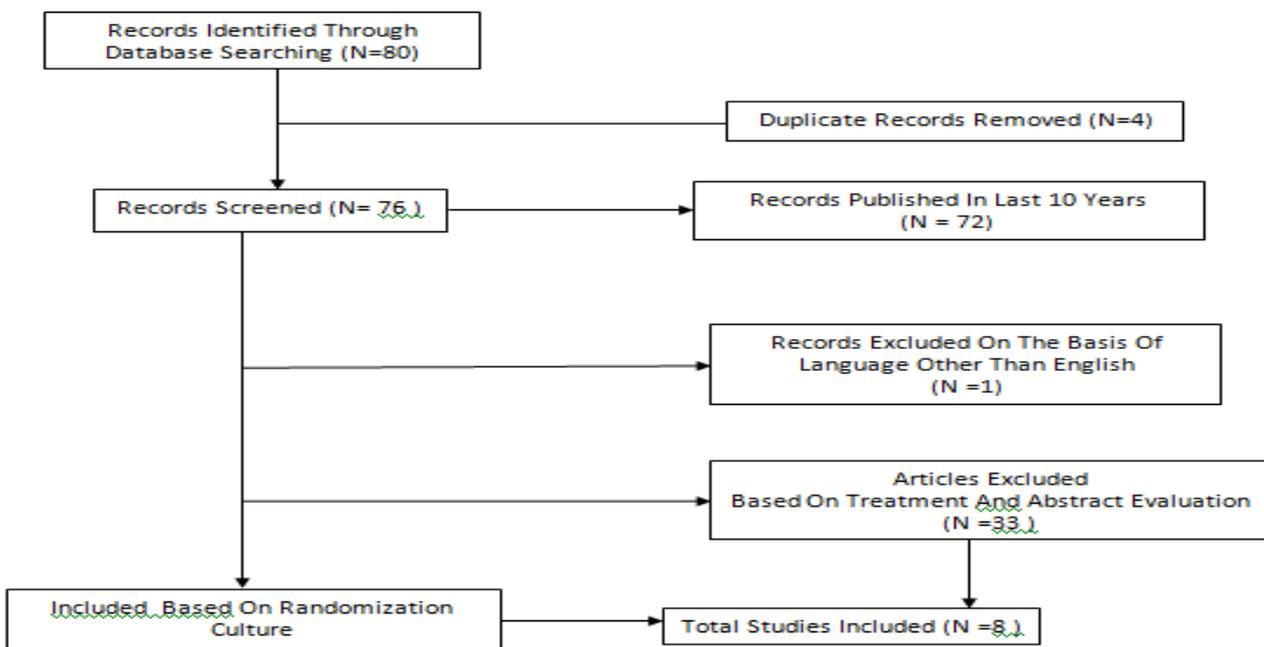
Interventions: Interventions with Photodynamic therapy (PDT) compared to accepted treatment protocol of SRP.

Outcome Measured : Analysis Of Periodontal Probing Depth (PPD), Clinical Attachment Level (CAL), Plaque Index (PI), Gingival Index (GI), Bleeding On Probing (BOP). Electronic database search of Pubmed, Google scholar, Medline and scopus was performed using (MESH) terms- Photodynamic therapy, periodontitis, microbiological assessment. Articles published between years 2009 - 2019 were reviewed. The selected titles were reviewed by two authors- Saini A & Chhina S and were included based on inclusion and exclusion criteria.

Inclusion Criteria: Systematic Review. Meta-Analysis. Cohort Study. Radiologic Trial.

Exclusion Criteria: Animal Studies. In Vitro studies. Systemic Disease. Patient on medication from last 6 months. Studies Other than English.

Figure 1: Schematic Diagram For Procedural Methodology



Results: Database searching yield 80 records. 4 duplicate records were removed from total of 80, leaving 76 records to be screened further. Only Records published in last 10 years were included. 76 Records were further reviewed and 1 record was excluded on the basis of language other than English.

From a total 76 articles, 33 articles excluded based on treatment and abstract evaluation. A total of 43 articles were further evaluated on the basis of exclusion & inclusion criteria and 35 records were removed. Total studies that were systematically reviewed came out to be.⁸

Table 1: Database

Study Design And Author	Sample Size	Mean Age (Years)	Intervention	Parameters Evaluation	Results
Vidal et al (2017)	Subject (37) 11 men 26 women	33 -74 years (55 ± 2)	Test group SRP + aPDT (18 sites) Control group: SRP alone (19 sites)	CAL PPD BOP	No significant difference was found between both treatment end A decrease in A. Actinomy cetemcomitans burden was found when SRP was combined with PDT.
Edvin X et al (2017)	Subjects (27) 11 M 16 F	44-70 (55.5 ± 7.9 years)	Test group SRP + aPDT (36 sites) Control group: SRP alone (36 sites)	PPD CAL BOP	Test sites showed significant improvement in PPD reduction and CAL gain at 3 months, as compared to control sites. A decrease in IL- 1 β level was found in both treatment end at 3 month.
Ravi raj K et al (2016)	Subject (20) 12 F 8 M	30-50	Test group SRP + aPDT (10 patients) Control group: SRP alone (10 patients)	CAL PPD	Statistical significant difference was found between both treatment end at 3 month. A decrease in P.gingivalis, T.denticola, T.forsythia level was found with test group at 3 month.
Pulikkotil et al(2016)	20 patients	45.2 ± 6.7 years	Test group SRP + aPDT (N= 16) Control group: SRP alone (N= 16)	CAL PPD BOP PS	Statistical significant difference was found between both treatment end in relation to CAL, PPD,PS. No reduction of A.actinomycetemcomitans burden was found at baseline and at 3 months
Correa et al (2015)	Subjects (15)	48.1±7.5 years	Test group SRP + aPDT (n=20 sites) Control group: SRP alone (n=20 sites)	RCAL PPD BOP	A significant reduction of BoP in both treatment end at 3 months. At 3 months, a reduction in PPD in both test groups . whereas an increase in RCAL was detected only in test group when compared to baseline. A decrease in A. actinomycetemcomitans burden was found when SRP was combined with PDT

Pourabbas et al(2014)	Subjects 22	18 to 70 years mean age (46± 8 years)	Test group SRP + aPDT (n=20 sites) Control group: SRP alone (n=80 sites)	CAL PPD GR	Statistical significant difference was found between both treatment end in relation to CAL, PPD,BOP,GR after 3 months. A decrease in TNF-α level was found when SRP was combined with PDT.
Queiroz et al (2013)	Subjects (20) 9M 11F	35to 55years; mean age (46.05±6.38 year)	Test group SRP + aPDT (n=121 sites) Control group: SRP alone (n=64 sites)	CAL PD	No statistical significant difference was found between both treatment end in relation to CAL, PPD,GR in smokers. A decrease in IL-1β level when SRP combined with PDT.
Haider et al (2013)	Subject (16) 5 M 11 F	20-50 (40.9 ± 13.34 years)	Test group SRP + aPDT (63 sites) Control group: SRP alone (73 sites)	PPD CAL BOP	Significant difference was found between both treatment end in relation to CAL, PPD,BOP at 3 month.

Discussion: Periodontitis is an inflammatory disease, affecting tissues supporting the teeth in their socket.. Periodontal disease initiation and propagation is through dental plaque, which interact with the immune defences of the host, leading to inflammation and disease⁷.

The main objective of periodontal therapy is to eliminate the bacterial deposits on root surface of teeth by scaling and root planning (SRP), but it is difficult to eliminate periodontal pathogens completely from deepest areas of periodontal pockets. To overcome these issues photodynamic therapy (PDT) was employed⁸.

PDT is a new treatment modality developed for several diseases like periodontitis, which involves the use of photosensitizer that is activated by exposure of light of a specific wavelength in the presence of oxygen. Methylene blue, toluidine blue and acridine orange are potent photosensitizers⁹, which when administered to the patient are taken up selectively by the diseased tissue and readily undergoes photo excitation when exposed to suitable wavelength.

PDT require source of light to activate photosensitizer by exposure to low power visible light at specific wavelength. Mostly photosensitizer are activated by red light between 630nm and 700nm, penetration depth 0.5-1.5 cm. Currently helium-neon lasers,

gallium-aluminum-arsenide & argon lasers are used¹⁰.

PDT fastens wound healing, & has biostimulatory effect on osteoblast like cells during 72hrs after irradiation as well as increase in collagen fiber deposition. PDT also inhibit inflammatory mediators thus favouring cellular chemotaxis and promotes vasodilation & angiogenesis, act on neutrophils and promotes their migration and integration¹⁰.

The aim of this systematic review was to check if additional treatment with PDT will provide additional clinical benefits or not with Nonsurgical periodontal therapy. Clinical parameters like PPD, CAL, BOP, GI, GR, PI were compared at baseline.

Bleeding on probing is easily detected clinically and therefore it is of value for early diagnosis & prevention of periodontal inflammation¹¹. Study by Pulikkotil et al (2016)¹², Correa et al (2015)¹³, Haider et al (2013)¹⁴ found significant decrease in bleeding on probing, when treated with SRP or SRP with PDT (p<0.001), on the other hand Vidal et al (2017)¹⁵ study found no significant difference after the treatment (p>0.05).

The pocket probing depth was recorded to the nearest millimetres the distance from the crest of gingival margin to the base of the pocket by

using UNC-15. Edwin X et al (2017)¹⁶, Ravi raj et al (2016)¹⁷, Hider et al (2013)¹⁴, Pulikkotil et al (2016)¹², Correa et al (2015)¹³, Pourabbas et al (2014)¹⁸ found statistical significant difference. Vidal et al (2017)¹⁵ study found no significant difference after the treatment ($p>0.05$).

Clinical attachment level is the distance measured from the cemento-enamel junction to the tip of a periodontal probe during periodontal diagnostic probing. It is measured with the help of UNC-15 probe. Gingival Recession is the displacement of marginal tissue apical to cemento-enamel junction (CEJ), Study by Pourabbas et al (2014)¹⁸ showed significant difference when treated with SRP and PDT whereas Edwin X et al (2017)¹⁶ study showed no significant difference ($p<0.001$).

Plaque Index is used to measure the thickness of Plaque on the gingival one third. Used as full mouth index or Simplified index. Pulikkotil et al (2016)¹² study showed statistical significant difference in patient treated with SRP alone or in combination with PDT ($p>0.05$).

Microbiological analysis done to check the level of A.A, P.g, T.d before and after the treatment as it was seen that there level increase in patient with periodontitis. Human microbiota should be monitored as it can be considered as resources for genetic diversity, a modifier of disease, essential component of immunity. It helps the clinician to monitor the disease & to check effectiveness of treatment. *Aggregatibacter Actinomycetemcomitans* is a Gram negative facultative anaerobe which is non motile bacterium. It has some virulence factors which enable it to invade tissues¹⁹. Vidal et al (2017) and Correa et al (2015) study showed significant decrease in A.A level when SRP combined with PDT ($p<0.001$), but as study by Pulikkotil et al (2016) showed no significant decrease from baseline to 3 months after treatment with SRP and PDT ($p<0.05$).

Porphyromonas gingivalis (P.g) is non motile, Gram-negative, rod-shaped, anaerobic, pathogenic bacterium, involved in pathogenesis of periodontitis. It has the ability to invade cells & tissues, thus avoiding its killing by immunity²⁰.

Study by Ravi Raj K et al (2016) showed significant decrease in P.g level at 3 month ($p<0.005$). Vidal et al (2017) and Correa et al

(2015) showed no significant decrease in P.g level after the treatment. ($p<0.001$).

Treponema denticola (T.d) is Gram negative, obligate anaerobic, motile and highly spirochete. It has been associated with early onset periodontitis, NUG, Acute pericoronitis. It has several non-classic virulence determinants which enable it to interact with other pathogenic bacteria to promote disease progression²¹. Vidal et al (2017) showed no significant decrease in T.d level after the treatment. ($p<0.001$) whereas study by Study by Ravi Raj K et al (2016) showed significant decrease in P.g level at 3 month ($p<0.005$).

Biochemical Analysis were done for the determination of RANKL/OPG, Tnf- α level, IL-1 β level. RANKL also known as tumor necrosis kappa-B ligand, is member of TNF superfamily. It affects the immune system and control bone regeneration and remodeling. RANKL is also a binding partner for OPG, can control cell proliferation by modifying protein levels²². A Randomized controlled trial was done by Vidal et al (2017) and they showed no significant increase in their level when SRP was combined with PDT. ($P<0.001$).

IL-1 β (Lymphocyte stimulating factor) is a cytokine protein produced by activated macrophages that is crucial for host defence responses to infection & injury²³. Edwin X et al (2017) checked IL-1 β level after treating patient with SRP alone or along with PDT, they showed significant reduction in the level of IL-1 β for both the group. ($p<0.001$).

Tumor necrosis factor – alpha (TNF- α) is a proinflammatory cytokine released by macrophages which is one of the biomarkers in the connective tissue breakdown associated with periodontitis. Significant difference in SRP and PDT group as compared to SRP group was observed by Pourabbas et al (2014)¹⁸. ($p<0.001$) ADVANTAGES OF PHOTODYNAMIC THERAPY (Seguier S et al 2010) is that it is minimally invasive technique, it has broad spectrum of action, No adverse effect such as ulcer or sloughing, & economical to use²⁴.

PDT has some adverse effect like adverse reaction on eye if irradiation was dose accidentally, or thermogenesis can occur as a result of interaction of laser with the tissues²⁵.

Conclusion: This Systematic review revealed that Photodynamic therapy along with SRP results in Significant improvement in CAL, PPD, BOP, GR and microbiological assessment showed significant decrease in no of periopathogens such A.a, P.g, T.d when subject were subjected to SRP with adjunctive PDT. Significant improvement in biochemical parameters such as IL-1 β , Tnf- α , RANKL/OPG were also seen after periodontal therapy along with PDT when compared with SRP alone.

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