https://doi.org/10.48047/AFJBS.6.15.2024.10737-10750

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Photodynamic Therapy as an Adjunctive Therapy in Patients with Aggressive Periodontitis : A Systematic Review

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Volume 6, Issue 15, Sep 2024

Received: 15 July 2024

Accepted: 25 Aug 2024

Published: 25 Sep 2024

doi: 10.48047/AFJBS.6.15.2024.10737-10750

Abstract

Objective: Aggressive periodontitis comprises a group of rare, severe, rapidly progressive form of periodontitis. Conventional treatment includes mechanical debridement augmented with adjunctive antimicrobial therapy. Development of antibiotic resistance has led to use of lasers. Photodynamic therapy (PDT) is a novel non-invasive therapeutic approach with increased site and pathogen specificity. The aim of this study was to determine the efficacy of photodynamic therapy as adjunctive therapy in aggressive periodontitis after scaling root planning (SRP).

Method: Electronic literature searches were conducted 2011 to 2021 using the following database PubMed, Cochrane and Wiley using terms limited to randomized control clinical trialsin English and using the PICOS format. The main clinical parameters used were Periodontal Pocket Depth (PPD), and additional clinical parameters using Bleeding on Probe (BOP), Clinical Attachment Level (CAL) were recorded at baseline & third month.

Result: The research is conducted to identify all full articles and were done manually from 151 articles, and four studies met the eligibility criteria. The analysis of all studies showed an increase in changes in BOP as the main parameter within three months after baseline.

Conclucion: With the available data, it is concluded that photodynamic therapy the statisticallysignificant that PDT may have additional effect on the reduction in pocket depth.

Keywords: periodontal disease or aggressive periodontitis, photodynamic, scalling root planning.

Introduction

Aggressive periodontitis (AgP) is a rapidly progressive periodontal disease, which is not coincident with the amount of oral biofilm and typically shows no association with any systemic disease The treatment strategies for AgP is challenging as there are no outright procedures and standards for its effective management Aggressive periodontitis comprises a group of rapidly progressing forms of periodontal disease that occur in otherwise clinically healthy individuals. It is accepted that, compared with patients with chronic periodontitis, patients with aggressive periodontitis show a more rapid attachment loss and bone destruction that occurs earlier in life. The patient's age when attachment loss is detected is often the criterion used by clinicians to diagnose aggressive periodontitis and to distinguish aggressive periodontitis from chronic adult periodontitis.(1)

Typically, aggressive periodontitis runs in families (familial aggregation), pointing towards a genetic predisposition. These three features (i.e. rapid attachment loss, bone destruction that occurs early in life and familial aggregation) are considered to be the primary features of this disease. It can also be argued that because aggressive periodontitis, although not rare, is a fairly uncommon condition, little is known about its optimal manage- ment. Protocols for treating chronic periodontitis are fairly well established.(2)

Aggressive periodontitis comprises a group of rare, severe, rapidly progressive form of periodontitis. Conventional treatment includes mechanical debridement augmented with adjunctive antimicrobial therapy. Development of antibiotic resistance has led to use of lasers. Photodynamic therapy (PDT) is a novel non-invasive therapeutic approach with increased site and pathogen specificity. Aggressive periodontitis, is a unique type of periodontitis comprising of rapid destruction of periodontal ligament and alveolar bone in systemically healthy

individuals generally of a younger age group but patients may be older. Its prevalence is less than chronic periodontitis, and result in early tooth loss in the affected individuals.[3]

The most important goal of therapy is to reduce or eliminate these subgingival microorganisms, regenerate the lost tissues and maintain periodontal health. Scaling and root planing is considered as a gold standard to attain and maintain periodontal health by elimination of bacterial plaque. Although mechanical treatment significantly decreases the prevalence and levels of subgingival microorganisms, it does not necessarily eliminate all pathogens. As the probing depth increases, the effectiveness of scaling and root planing decreases, leaving subgingival plaque, calculus on root surfaces and presence of persistent periodontopathogens. A more efficient and atraumatic technique is the use of lasers for periodontal treatment. Conventional non-surgical periodontal treatment, primarily consisting of scaling and root planing (SRP), aims to arrest this tenacious disease by mechanically eliminating the calculus and bacterial deposits from supra- and subgingival regions of the root surface. SRP, as the gold standard of periodontal therapy, has been proved to be both safe and effective in treating chronic periodontitis in the vast majority of cases . However, SRP alone may fail to completely eradicate periodontal pathogens located in areas where there is limited access to mechanical instrumentation, such as deep pockets, furcation sites, root curvature and concavities. [3][4]

Scaling and root planing (SRP) remains a gold standard for non-surgical periodontal treatment where root surface is debrided with either hand or ultrasonic instruments that facilitates periodontal reattachment. This therapeutic approach is demanding, nevertheless, it is associated with several physical limitations, mainly related with the inability to completely debride root surface in deep periodontal pockets and inaccessible furcation defects, incomplete elimination of periopathogenic bacteria and hence recurrence of the disease.[5]

To overcome the limitations of scaling and root planing and to reduce the bacterial load, antimicrobial photodynamic therapy (aPDT) has been proposed as a treatment strategy for AgP. The mechanism of action of aPDT involves the excitation of photosensitizer dye molecules by laser light or visible light of specific wavelength. This undergoes transition of dye molecule from ground singlet state to excited state triplet. The triplet state photosensitizer reacts with endogenous oxygen resulting in the formation of highly reactive singlet oxygen. These reactive oxygen species are highly cytotoxic causing bacterial cell death. The benefits of aPDT includes instant eradication of causative bacteria, least antibiotic resistance, absence of systemic disturbance and undesirable effects on the healthy periodontal tissue [(6)]

Photodynamic therapy (PDT) is a noninvasive therapeutic approach that involves the use of photoactivatable compound or photosensitizer which binds to the target cell followed by use of low-level laser light of a suitable wavelength to excite the photosensitizer in the presence of oxygen. During this process, free radicals are formed (among them singlet oxygen) which can lead to cytotoxicity and eventually cell death . The target cell could be tumor tissue as in the treatment of cancers or microorganisms The use of PDT in treating infections by eradicating microorganisms is often referred to as antimicrobial PDT (a-PDT). In dentistry, a-PDT has gained popularity as an important novel procedure that has been used in the treatment of periodontal diseases peri-implantitis and endodontic infections. [(7)]

Photodynamic therapy combines low level laser light with a photosensitizer (a non-toxic dye), which binds to the target cells. Photosensitizers, like for example toluidine blue O, methylene blue and malachite green, absorb light of a specific wavelength. In the excited state theses molecules can react with molecules from the environment, for example with oxygen. Reactive oxygen species can be generated, which can cause oxidative damage to the target cells. Several photosensitizers are available which work in combination with a low level laser

(wave length of λ = 630-670 nm) to destroy microorganisms. Therefore, photodynamic therapy can be an alternative for reducing the bacterial load in periodontal pockets. The effects of aPDT on periodontal biofilm have been tested in vitro and its cytotoxic action against many periodontal pathogens, including *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, and Fusobacterium nucleatum,* has been demonstrated. [(8)(9)]

Antimicrobial photodynamic therapy (aPDT) recently has been proposed as an adjunctive treatment strategy to SRP. The application of aPDT is based on the following principle. A photoactivatable agent (photosensitizer) that absorbs light is able to be taken up preferentially by bacteria. When the photosensitizer is exposed to light of an appropriate wavelength (such as that emitted by a low-power laser) in the presence of oxygen, it generates singlet oxygen and free radicals that are cytotoxic to microorganisms and their products. Many oral bacteria are susceptible to infrared laser in the presence of photosensitizers, such as toluidine blue O, methylene blue and malachite green. These findings suggest that aPDT could be potentially advantageous in periodontal therapy, as well as in the treatment of perimplantitis and endodontic infections.[(10)]

*Photodynamic Therapy (PDT) is an adjunct method after scaling and rootplaning in the treatment of periodontitis. This method was first used in 1990 for cancer treatment. It was determined that its use stimulates autophagy (a method of cell catabolism, which leads to the destruction of abnormal cells) in resistant cancer cells or precancerous cells. In this method, the wavelengths between 650-900 nm are in the visible red light and near infrared, and have a great influence on the biological tissue used. So far, more than 400 substances have been identified as photosensitizers, including Indocyanine Green. Upon excitation with light, this substance acquires properties such as wound healing, antibacterial effect in the treatment of chronic skin and mucosal infections*This systematic review aims to evaluate the efficacy of

photodynamic therapy as an adjuntive therapy with Aggressive Periodontitis after receiving scalling root planning (SRP). [11]

Methods

Search Strategy

This study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systemic Review and Meta-Analysis) guidelines for systematic reviews. Using the Focused Question PICO concept which stands for Population Intervention Comparison and Outcome. The population in this study were patients who had aggressive periodontitis and had received scaling root planning treatment previously. Comparison: assessment of the effectiveness of photodynamic therapy in patients who had undergone SRP on the parameters Periodontal Pocket Depth (PPD), and additional clinical parameters using Bleeding on Probe (BOP), Clinical Attachment Level (CAL) were recorded at baseline & third month. Outcome changes in PPD as the main parameter within three months after baseline.

Several search engines were used to search the literature to answer focus questions, including Pubmed, Google Scholar, Wiley, and Cochrane. The MeSH keywords used periodontal disease or aggressive periodontitis, photodynamic, scalling root planning. The search was limited to English-language studies, in the last 10 years period. This systematic review looked at only randomized controlled trials that were monitored at baseline and 3 months after treatment SRP. After determining the literature, the data is then extracted and some differences are then included in the discussion.

Study Inclusion and Exclusion Criteria

This review included a randomized controlled trial (RCT) with follow-up periods were performed prior to treatment (baseline) and at 3 months after scalling root planning procedure. Exclusion criteria include literature review, systematic review and meta-analysis of articles, no available full text, non-English studies, and duplicate studies.

Outcome Variables

The outcome variable was the clinical outcome taken to treatment (baseline) and at 3 months after scalling root planning procedure as measured by the VAS (Visual Analogue Scale) method.

Data Extraction

The author uses specific keywords and the article is screened based on the title and abstract. The full text of the article is then screened based on the topic of the systematic review that has been determined and then analyzed based on the inclusion criteria that have been determined to get a list of references for the final article that will be used. All selected articles were also screened from the exclusion criteria. The final article is then discussed. Data taken from the article include the author, number of participants, clinical intervention, measurement of effectiveness of photodynamic therapy in patients who had undergone SRP as measured by VAS (Visual Analogue Scale) at baseline and follow-up at 3 and 6 months after scalling root planning procedure.

Quality Evaluation

First, all authors screen eligible studies by tittle and abstract based on inclusion criteria. Then, all authors screened the full article from all the collected studies. The authors held a

meeting and agreed on very relevant publications to be includedin this study. All autors conducted an independent assessment of the quality of the study of the study and disagreement were resolved through discussion. All inherent aspects of the study, including study quality, variables for which were sought, were assessed byall authors independently. The writers then get together again to discuss any conflicting points.

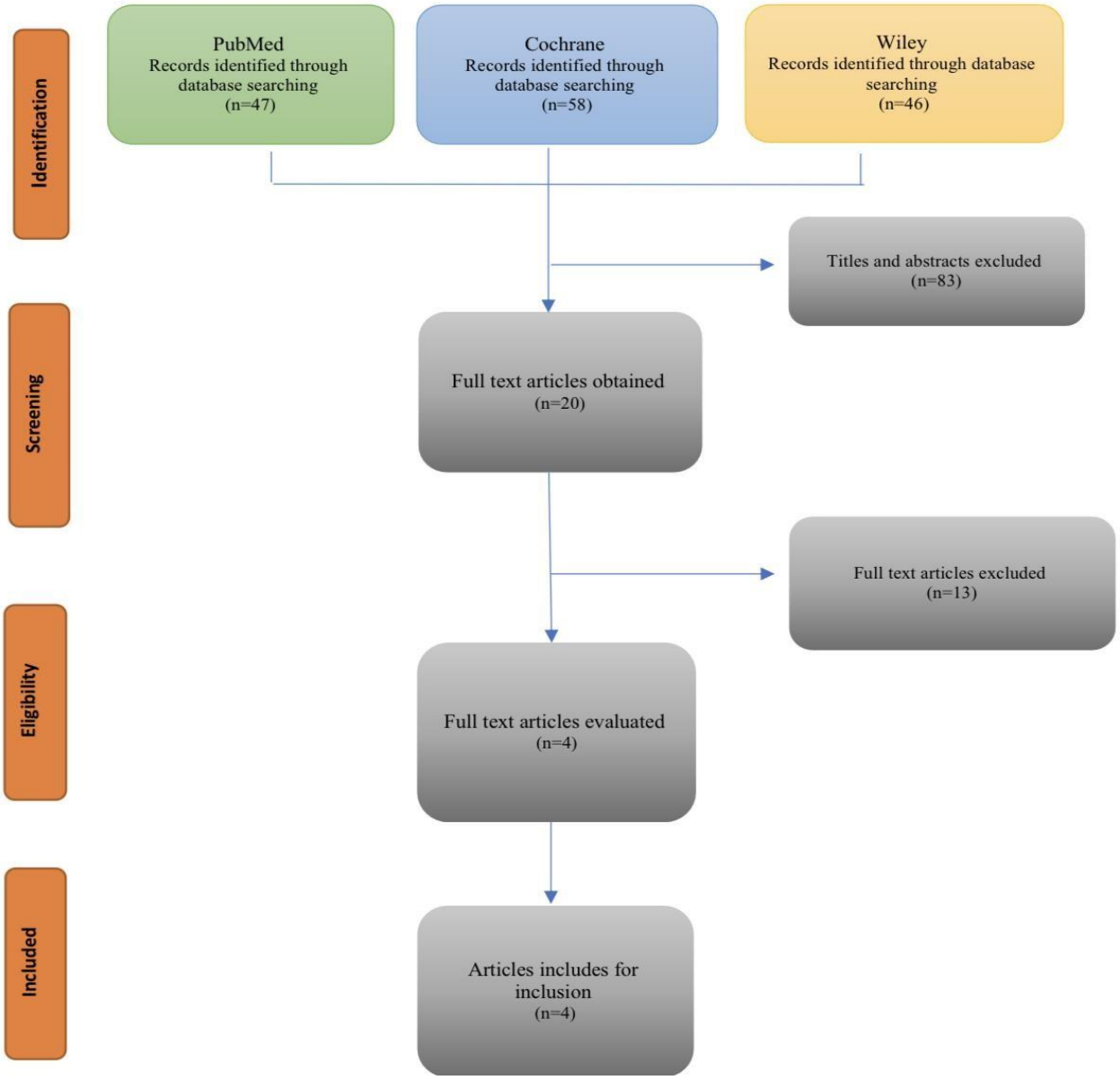

Figure 1. Flowchart PRISMA

Result

A search of data from three databases yielded 151 articles, which were then selected based on duplication, and which were marked as ineligible by automated tools, as well as by other reasons and yielded 83 articles. Then it was filtered again based on the excluded articles in addition to the last 10 year articles and randomized clinical trials and resulted in 20 articles. Then filtered some articles that could not be opened and produced 13 articles., and four articles were screened from 13 articles because the treatment discussed efficacy of photodynamic therapy as an adjuntive therapy with Aggressive Periodontitis after receiving scalling root planning (SRP) and with follow-up periods were performed prior to treatment (baseline) and at 3 months after scalling root planning procedure. The flow article selection can be seen in figure 1.

The three of studies were randomized clinical trials (RCTs), review aims to evaluate the efficacy of photodynamic therapy as an adjuntive therapy with Aggressive Periodontitis after receiving scalling root planning (SRP). This study was conducted between 2011 to 2021. The three studies evaluated and to see if there is any effect of Photodynaamic therapy as an additional treatment in patients with aggressive Periodontitis. The study was then evaluated through clinical outcomes from baseline to 3 months after the procedure.

The studies used were published in 2013, 2016 and 2018. Participants in this study were an average of 15 to 18 patients. Each study has a different treatment, namely there is only SRP, there is also SRP with diode laser, SRP with photodynamic therapy, SRP with AB (clarithromycin), there is also only PDT intervention. Each study provides a comparison of therapeutic effect index scores in Aggressive Periodontitist patients at different treatment groups on the first day (baseline) of the procedure and on the third month after the procedure. The clinical parameters are shown in table 1.

Sreeder et al reported that the intervention that showed an improvement or decrease effect was on SRP + PDT with a baseline value of 3.27±0.34 and after 3 months of intervention there was a decrease in score of 1.53±0.23 on the Bleeding Of Point parameter. Where this significant change means that the SRP + PDT intervention has a Bleeding Of Point improvement effect in aggressive periodontitis patients after 3 months of intervention.

Bechara et al, using 18 patients reported that the intervention that showed an improvement or decrease effect was on SRP + AB (CLARITROMYCIN 500MG) + PDT with a baseline value of 6.7 ± 1.3 and after 3 months of intervention there was a significant decrease in score of 3 ,2±0.3 on the Periodontal Pocket Depth parameter. Where this significant change means that the SRP + AB (CLARITROMYCIN 500MG) + PDT intervention has the effect of increasing PPD repair in aggressive periodontitis patients after 3 months of intervention.

Nicole et al , only used two types of intervention, namely in 17 patients only Photodynamic therapy intervention and in 18 patients only given antibiotics after Scaling Root Planning was carried out. In this study, it was reported that the intervention that showed the effect of improving or decreasing scores was in patients who were only given photodynamic therapy with a baseline value of 70.4 ± 22.4 and after 3 months of intervention there was a decrease in score of 37.7 ± 21.3 on the Bleeding Of Point parameter. Where this significant change means that photodynamic therapy intervention has the effect of increasing Bleeding Of Point healing in aggressive periodontitis patients after 3 months of intervention.

Table 1. Overview of data from three studies

Study	Study type	N (subject)	Intervention	Baseline			3rd Months		
				BOP	PPD	CAL	BOP	PPD	CAL
Sreedar Annaji et al 2016	RCT	15 Patients	SRP ONLY	3.16±0.35	6.08±0.21	9.41±0.51	1.72±0.20	5.79±0.20	9.13±0.46
			SRP + LASER DIODE	3.28±0.35	6.13±0.35	9.63±0.77	1.58±0.23	5.63±0.47	9.17±0.84
			SRP + PDT	3.27±0.34	6.20±0.25	9.52±0.58	1.53±0.23	5.59±0.53	8.87±0.71
Bechara et al 2018	RCT	18 patients	SRP ONLY	100%	7.1±1.0	7.1±1.0	33,30%	5.0±1.0	5.1±1.0
			SRP + PDT	100%	7.2±1.2	7.3±1.2	33,30%	4.4±0.9	4.8±1.7
			SRP + AB (CLARITROMYCIN 500MG)	100%	6,8 ± 2,64	7.5±2,8	11,10%	3,7±0.8	4.4±1.6
			SRP + AB + PDT	100%	6,7 ± 1,3	6,7 ± 1,3	22.2%	3,2±0,3	3,6±1,3
nicole at al 2013	RCT	17 patients	PDT ONLY	70.4 ± 22.4	5.1 ± 0.5	5.7 ± 0.8	37.7 ± 21.3	4.0 ± 0.8	4.7 ± 1. 1
		18 patients	SYSTEMIC AB	85,7± 15,9	5,0 ± 0,8	5,5 ± 1,1	34,6 ± 22,8	3,2 ± 0,4	3,9 ± 1,0

Discussion

The use of Photodynamic Therapy in addition to scaling and root planing can affect Pocket Depth and Clinical Attachment Loss. Several studies have also shown changes in the position of the gingival margin after treatment. On the other hand, multiple trials and combined estimates pooled additional gains in clinical outcomes when compared to those expected after the conventional approach (SRP) for mechanical debridement of the root surface. (12)

In this study, three randomized control trials (RCTs) were selected. This review included a randomized controlled trial (RCT) with follow-up periods were performed prior to treatment (baseline) and at 3 months after scalling root planning procedure. To overcome the limitations of scaling and root planing and to reduce bacterial numbers, antimicrobial photodynamic therapy (aPDT) has been proposed as a treatment strategy for AGP. The mechanism of action of aPDT involves the excitation of photosensitizer dye molecules by laser light or visible light of certain wavelengths. The benefits of aPDT include instant eradication of causative bacteria, minimal antibiotic resistance, absence of systemic disturbances and undesirable effects on healthy periodontal tissues. (6)

Based on this, The aim of this study was to determine the efficacy of photodynamic therapy as adjunctive therapy in aggressive periodontitis after scaling root planning (SRP).

Sreeder et al (13), Photodynamic therapy obviates these disadvantages by combining soft laser irradiation with photosensitizer dye. It has adjunctive benefit at sites with deep periodontal pockets, furcations and root concavities. In order to explore the effectiveness of photodynamic therapy in destroying periodontal bacteria in vivo the present prospective controlled split mouth study was carried out using 810nm diode laser as an adjunct to scaling and root planing. Toluidine blue was chosen as the photosensitizer in this study, because it has been shown to be potentially one of the safest photosensitizers for treating periodontal disease.

When compared in each group all clinical parameters showed a significant decrease in their values between baseline to 3 months indicating the effectiveness of individual therapy. Scaling and root planing (SRP) is one of the most commonly used clinically effective procedures for the treatment of periodontal disease and is considered a gold standard treatment which has been supported by various studies.

Bechara et al [(14)] , the aim of this randomized clinical trial was to assess whether single application of clarithromycin-associated aPDT would bring about clinical benefit in the non-surgical periodontal treatment of GAgP. In addition, this study was intended to determine whether the results of aPDT and clarithromycin are comparable. To the best of the authors' knowledge, this is the first study to evaluate the effects of aPDT associated with systemic antibiotics. Following the same trend, a systematic review also showed that probing depth had a greater reduction at 3-month follow-up than at 6-month follow-up. This suggests that aPDT adds short-term clinical benefit to SRP but long-term effectiveness as an adjunct to SRP is dubious. Thus it is also necessary to test antimicrobial treatments such as systemicantibiotics.

Nicole et al [(15)] ,it has been scientifically proven that periodontitis is an infec- tious disease, the successful treatment of which is based on eliminating the infection. The aim of the present study was to determine the efficacy of photodynamic therapy (PDT) compared to systemic antibiotics (AB) in addition to scaling and root planing (SRP) in patients with aggressive periodontitis. In numerous studies it has been shown that treatment with the antibiotics metronidazole and amoxicillin in combination with SRP significantly improves the clinical results compared to treatment with SRP alone. The results of the present study show that both treatment approaches (SRP plus systemic antibiotics [AB] and SRP plus PDT) significantly improve the parameters examined: PPD, CAL, and BOP. This positive effect of PDT on BOP has also been reported in previous studies .

Conclusion

With the available data, it is concluded that the statistically significant photodynamic therapy that Photodynamic therapy may have an additional effect on reduction of Bleeding Of Pocket in the Agrresive periodontitist patients.

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