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Review Article

Efficacy of Antimicrobial Photodynamic Therapy as an adjunct periodontal intervention in periodontally diseased subjects undergoing orthodontic therapy - A Systematic Review.

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ABSTRACT:
Photodynamic therapy in fixed orthodontic patients with gingival disease might be beneficial, being non-invasive and having accessibility to difficulty to reach areas like, interdental region with the presence of wires and brackets. This systematic review was designed to analyze the available evidence on the efficacy of antimicrobial photodynamic therapy as an adjunct to scaling in reduction of gingival inflammation in periodontally diseased subjects undergoing fixed orthodontic treatment. Comprehensive search was conducted in electronic databases like PubMed, Scopus and Google scholar along with hand search in relevant journals. Five studies satisfied the criteria and were included in qualitative synthesis of the systematic review. The results of the primary outcome showed adjunctive aPDT did not result in any difference in reduction of gingival inflammation (BOP) compared to scaling alone in fixed orthodontic patients. Only one study showed a significant reduction of gingival inflammation with aPDT, whereas it was better in the scaling group (one study) or no significant difference (3 study) in the other studies. However, aPDT resulted in significant reduction of most of the bacterial species count and proinflammatory cytokine levels in GCF compared to scaling alone. Within the limitations of this systematic review, there is no clear evidence that aPDT adjunctive to scaling has a better effect in reducing gingival inflammation in fixed orthodontic patients. Future studies addressing this area should focus on well planned standardized, long term RCTs that will aid clinicians in making a more evidence-based decision.

Keywords: Photodynamic therapy, Gingival disease, fixed orthodontic therapy

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INTRODUCTION

Malalignment of teeth is one of the primary concerns for both the young and adult population to seek dental treatment.[1] Even though most of the malalignment is a result of developmental origin, there are other causes that may contribute to malalignment in a fully developed dentition.[2] Periodontal disease is one such condition,[3,4] which initially presents as an inflammation of the gingival tissue initiated by polymicrobial plaque biofilm which left untreated can result in destruction of the periodontal ligament, cementum and alveolar bone. The reduced periodontal support may contribute to pathologic migration of the teeth resulting in malalignment which may further deteriorate the ongoing periodontal disease.[3,4]

Routinely, before delivering any orthodontic forces on the teeth, active periodontal disease should be controlled by periodontal therapy to avoid orthodontic forces becoming destructive to the periodontal tissues and teeth presenting as severe bone loss and root resorption.[5] On the other hand, in a healthy or periodontally treated dentition, commencement of orthodontic therapy may itself contribute to inadequate oral hygiene maintenance thus, initiating an inflammatory condition of gingiva.[6,7] The placement of fixed (brackets and bands) and removable devices (wires and elastics) act as retentive surfaces facilitating easy plaque accumulation and incomplete removal of etiologic agents during routine oral hygiene or periodontal therapy.[8] In this context periodontally diseased patients undergoing orthodontic therapy pose additional risk for disease recurrence or progression.[7] To resolve the inflammatory condition, conventional non-surgical/ mechanical periodontal therapies like scaling and root planing are routinely executed.[9] However in most of the cases this may not be adequate to completely reverse the inflammatory process due to the reduced accessibility to interdental and proximal tooth surfaces, thus requiring some adjunctive therapies that are less invasive and favorable for the ongoing orthodontic therapy.[9]

Adjunctive laser therapy has been advocated in management of gingival inflammation and periodontal pockets.[10,11] The beneficial effect of lasers in resolution of gingival inflammation and pocket is mainly through the photo biomodulation, microbial decontamination in areas difficult to access with conventional mechanical therapy and through the ablative effect of the lasers on the gingival wall of the periodontal pocket etc.[11] Additionally, the use of lasers with a photosensitive dye which is known as antimicrobial photodynamic therapy (aPDT) has shown to enhance the effect of laser periodontal therapy.[12] The interaction of dye with the laser energy in the presence of oxygen results in free radical formation that kills the pathogenic microflora within the subgingival environment.[12] This has the advantage of elimination of microbes in inaccessible areas, absence of resistance formation, broad spectrum of activity etc.[13,14] Thus use of photodynamic therapy in orthodontic patients might be beneficial, as it is noninvasive and can access difficult to reach areas like the interdental region with the presence of wires and brackets. Currently there is a lack of solid evidence that supports the biological plausibility of beneficial effects of photodynamic therapy in periodontally diseased subjects undergoing orthodontic therapy. Hence, this systematic review was designed to find the available evidence on the efficacy of photodynamic therapy as an adjunct to conventional mechanical debridement (scaling) in reduction of gingival inflammation of periodontally diseased subjects undergoing fixed orthodontic treatment.

MATERIALS AND METHODS

This systematic review follows the PRISMA checklist reporting tool for systematic review. The research question for the review was: Can adjunctive aPDT reduce gingival inflammation effectively in fixed orthodontic patients compared to scaling alone?

Based on the following research question, the PICO was formulated:

Population (P) - Gingivitis/ gingival enlargement in subjects undergoing fixed orthodontic treatment.

Intervention (I) - Scaling with Photodynamic therapy

Comparison (C) - Ultrasonic scaling

Outcomes (O) - Primary outcome: reduction of gingival inflammation (Gingival Index (GI), Bleeding on Probing (BOP)

Secondary outcome: Changes in periodontal microflora, gingival crevicular fluid (GCF) cytokine levels.

Search Strategy:

Comprehensive search was conducted in electronic databases like PubMed, Scopus and Google along with hand search in relevant journals published between 2013 till 2023. Unpublished data were also searched from repositories like ClinicalTrails.gov and thesis database. The search was limited to studies only published in the English language and the search terms used were listed in **Table 1.**

Table 1: Search strategy table.

DATABASES	KEYWORDS/MESH TERMS	TOTAL COUNT
PubMed	(((((((((orthodontics[MeSH Terms]) AND (attachment loss, periodontal[MeSH Terms])) AND (orthodontics)) OR (periodontium)) OR (fixed appliance)) OR (orthodontic appliance)) OR (orthodontic treatment)) AND (((((((low level laser therapy[MeSH Terms]) AND (photodynamic therapy[MeSH Terms])) AND (laser)) OR (photobiomodulation)) OR (low level laser therapy)) OR (LLLT)) OR (photodynamic therapy))) OR ((((((control) OR (conventional)) OR (baseline)) AND (pharmacological)) AND (non-surgical)) AND (therapeutic))) OR (((((((pain) OR (swelling)) OR (inflammation)) OR (inflammatory)) OR (pain perception)) AND (patient outcome)) AND (chemical)) AND (mediator)) Filters: Randomized Controlled Trial	**806**
Google Scholar	Periodontal AND Periodontitis AND Orthodontic treatment AND Laser AND Photodynamic Theory AND Scaling AND Gingival health AND Gingiva	**872**
Scopus	((((ALL=(orthodontics OR Fixed appliance OR orthodontic treatment)) AND ALL=(Periodontium OR gingivitis OR periodontal health)) AND ALL=(low level laser therapy OR photodynamic therapy OR laser OR photobiomodulation)) AND ALL=(control OR nonsurgical OR scaling OR ultrasonic OR periodontal therapy)) AND ALL=(pain perception OR patient outcome OR chemical OR inflammatory mediator OR inflammation)	**214**

Eligible Studies:

Clinical trials (Randomized Controlled Trials (RCTs), Non-Randomized Controlled Trials (NRCTs)) with 2 treatment groups (Scaling plus aPDT Vs Scaling alone) in treating gingivitis patients undergoing fixed orthodontic therapy were included. Retrospective studies, Prospective studies, case reports, case series and animal studies were excluded from the review.

Study selection:

Two reviewers (SH, TS) independently assessed all the titles and abstracts obtained from electronic search for relevancy to the systematic review. Inter-examiner agreement was assessed using Kappa Cohen's coefficient. Disagreements between the examiners were settled by taking opinion from a third examiner (AJ) for decision making. Articles were screened for duplicates using EndNote Software (Version X9; Clarivate Analytics, Philadelphia, Pa, USA). The sequence of selection of studies for the review is presented as a PRISMA flow diagram **(Figure 1)**.

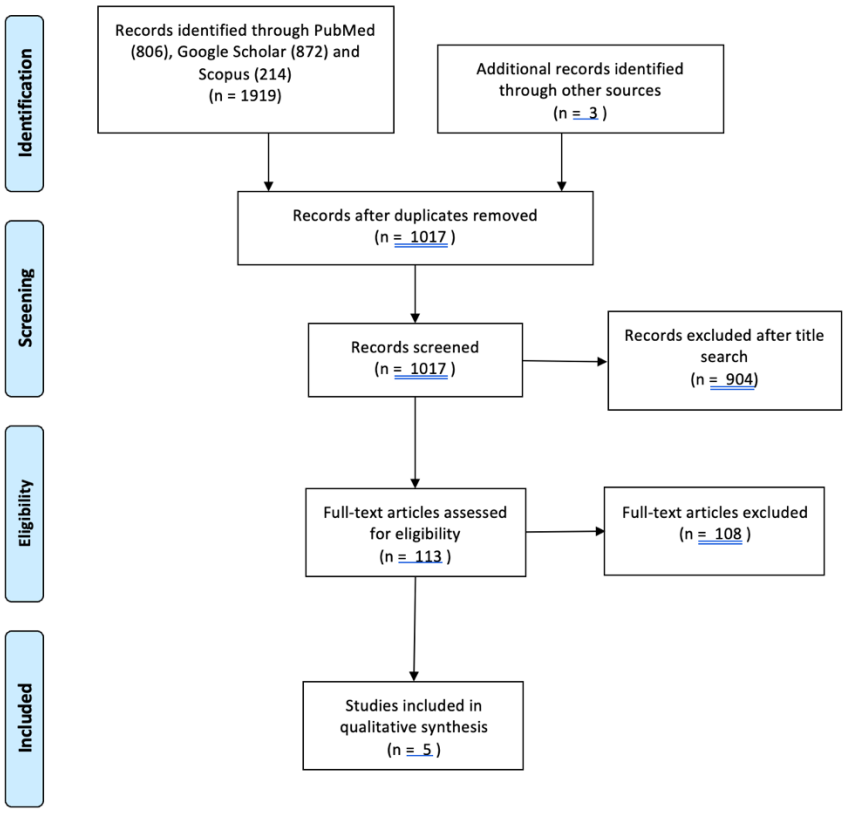

Figure 1: PRISMA flow diagram of included studies

Data extraction:

The above two examiners were also involved in the data extraction process independently. The following data were extracted from the included studies: background data (authors details, year of publication, study setting)

methodology (study design, grouping, randomization, allocation) intervention details (technical details, site of intervention, type of intervention) outcomes (clinical, microbiological, cytokine levels) follow-up schedule.

Risk of Bias assessment:

All the included studies were assessed by the same examiners for risk of bias for the qualitative assessment using Cochrane Collaboration's Risk of Bias 2 (ROB-2) tool for 3 randomized controlled clinical trials and Newcastle-Ottawa Scale tool for other 2 non randomized controlled clinical trials.

RESULTS

Study selection:

The electronic database search from PubMed Web of Science & Google Scholar resulted in identification of 1919 records related to the search terms. Further, other sources like hand search of grey literature added 3 more relevant records to the already identified articles. After excluding duplicates 1017 records were subjected to title assessment by the 2 examiners with an inter-examiner agreement of 0.95 (kappa). 904 records were excluded after title assessment with 113 potentially related records further assessed in depth based on the inclusion criteria to be included in the review process. Finally, only 5 articles satisfied the criteria and were included in qualitative synthesis of the systematic review. **(Figure 1)**

Characteristic of Included studies:

From the five clinical trials included in this systematic review, three were randomized clinical trials (RCTs) and two were non randomized controlled clinical trials (NRCTs) with parallel designs. Three of the studies were financially sponsored by the institute where the study was conducted, and the other two studies did not mention the data regarding funding. In total 160 patients with gingivitis/ gingival enlargement were treated in the study and there were 2 dropouts that were reported. Three of the included studies had a follow-up period of 4 weeks and the other two studies reporting 6 weeks and 9-month follow-up post therapy respectively. All the studies assessed the gingival inflammation status as the primary outcome. The secondary objective evaluated in all of the studies was the assessment of total bacterial count of periodontal pathogen Porphyromonas gingivalis (*P.g*). However, most of the studies also assessed the quantity of other bacteria like, Eikenella corrodens, Aggregatibacter actinomycetemcomitans, Capnocytophaga species, Campylobacter rectus, Tanerella forsythia, Treponema denticola etc as the CFU/ml. Additionally four of the included studies evaluated the gingival crevicular levels (GCF) of various pro and anti-inflammatory cytokines like IL-1beta, TNF alpha, IL-6, IL-10, IL-1ra, FGF-2. **(Table 2)**

Table 2: Characteristics of included studies

Article	Abellan R	Nazeh AA	Baeshen HA	Alshahrani A	Kamran MA
Study design	RCT with parallel design	RCCT with parallel design	RCCT with parallel design	Clinical trial with parallel design	Clinical trial with parallel design
Country	Spain	Saudi Arabia	Saudi Arabia	Saudi Arabia	Saudi Arabia
Participants	22 systemically healthy subjects	22 adolescent subjects	30 subjects, 15 in each group	26 adolescent (16 boys, 10 girls) mean age - 16.8 years	50 adolescent patients
Groups	**Group 1:** Scaling with **a**PDT (Photodynamic Therapy) **Group 2:** US (Ultrasonic scaler)	**Group US** - Ultrasonic group **Group aPDT** - Ultrasonic scaling with aPDT	**Group A** - Scaling (DS) + aPDT **Group B** - Scaling (DS) alone.	**Group FMPD** - debrided with Gracey curettes followed by ultrasonic scalers, use of CHX mouthwash for 14 days **Group PDT** - after FMPD, aPDT in preselected mandibular central incisors,	**Group A** - **a**PDT + FMS, **Group B** - FMS alone.
Investigation parameters	Clinical Assessment - PD, PI, GI. Microbial assessment - Presence of Aggregatibacter actinomycetemcomitans (A.a), Porphyromonas gingivalis (Pg),Prevotella intermedia (Pi), Micromonas micros (Mm), Fusobacterium nucleatum (Fn), Tannerella forsythia (Tf), Campylobactor rectus- Cr), Capnocytophaga sp (Csp), Eikenella Corrodens (Ec) (CFU/ml) Immunological assay: GCF levels of IL-1beta, IL-1ra, IL-6, IL-10, TNF alpha, FGF-2,	Clinical - Plaque score (PS) Bleeding on probing (BOP) Bacterial analysis - CFU/mL for P.gingivalis and T. forsythia (Day 0, 1 week and 4 weeks after treatment).	Clinical- Plaque score (PS) Bleeding on Probing (BOP) done at 6 sites in each tooth (except third molars). Pain - intensity for orthodontic therapy Visual Analogue scale (0 -10) (VAS) McGill Pain Questionnaire (MPQ) (mild to excruciating) GCF cytokine levels Levels of IL-6 and TNF alpha. Bacterial analysis Total counts (CFU/mL) of P.gingivalis and T. forsythia	Clinical - Hyperplastic Index (HI) - 0, 1, 2, 3. Plaque score (PS) - Dichotomous recording Bleeding on Probing (BOP) - Dichotomous recording. PD (Probing depth). Bacterial Analysis - Total bacterial counts of P.gingivalis, T. denticola, T forsythia (log CFU/mL). Immunological assessment - GCF sample - interleukin 1 (IL-1beta), interleukin 6 (IL-6).	Clinical - Full mouth plaque score (PS), BOP, PD. Microbial analysis- total bacterial counts of P.intermedia and P. gingivalis. Volume of GCF assessed. IL-6 and TNF alpha levels
Intervention	**Group 1:** PDT - methylene Blue - 0.005% (w/v) with hydroxymethyl cellulose as mucoadhesive agent (Periowave) - 3 mins application, Diode laser	**Group US**- Ultrasonic scaling in one session, OHI **Group aPDT**- methylene blue (0.0005%) mediated PDT, Diode laser (670 nm, energy fluency - 22J/cm2,	**Dental Scaling (DS)** - ultrasonic scaler **aPDT** - single session, Diode laser (Power -150 mW, 670nm, 22J/cm2, 1.1 W/cm2), methylene blue (0.005%) - 2 mins, laser irradiation	**Group FMPD** - Prophylactic use of chlorhexidine (CHX), selected areas debrided with Gracey curettes followed by ultrasonic scalers for at least 1 hour.	All patients underwent full mouth ultrasonic scaling **aPDT** - diode laser, 670nm, 22J/cm2 energy efficiency, 150 mW power output, 1.1W/cm2 power

	(Periowave(670nm) - 60 secs/ tooth, in continuous mode, power output - 190 mW, irradiance - 6.05 W/cm2, average fluence -67.06 J/cm2). **Group 2:** US - Ultrasonic scaling at 7 sessions.	power output - 150 mW) Duration of exposure - 1 minute into the gingival sulcus - around 6 sites of each tooth	for 1 min.	**Group aPDT** - after FMPD, Diode laser (670nm, energy fluency - 22 J/cm2, power output - 150 mW) with methylene blue (0.0005%), laser irradiation time - 1 minute at 6 sites per tooth.	density, 60 seconds exposure. methylene blue - 0.0005% (3 mins)
Duration of Orthodontic treatment	Non extraction orthodontic treatment for at least 12 months	Group US- 8.9 months Group aPDT - 10.1 months	Group A - 8.5 months Group B - 8.9 months	Fixed orthodontic therapy for a minimum of 6 months (mean - 8.3+1.9 months)	1.25 years
Reevaluation/ Follow-up	BL, 3, 6 and 9th month	1 week and 4 weeks from BL	1 week and 4 weeks from BL	2 weeks and 4 weeks after BL	3 weeks and 6 weeks.
Results	Failed to show any difference between the groups in clinical, microbial and cytokine levels assessment (p>0.05).	No statistically significant difference between the groups in BOP & PS (p>0.05) Between groups there was a significant reduction of both bacteria in PDT than in the US group (p<0.05).	No significant difference between groups in PS and PD. Significant better reduction of BOP in group B over Group A. Significant reduction of T. forsythia & P. gingivalis in Group A over B. No significant difference in pain scores between groups. No significant difference between groups.	No significant difference between groups in BOP & PS. Both HI & PD reduced significantly with the PDT group showing significantly higher reduction compared to FMPD(p<0.05). PDT showing higher reduction for T. forsythia & P. gingivalis compared to FMPD at all points and T. denticola only at 2-week followup. IL-6 (p<0.05) showed higher reduction in PDT compared to FMPD at 4th week alone (p<0.05). There was correlation between HI and levels of P. gingivalis and IL-6.	BOP showed higher reduction in PDT at 3rd and 6th week (p<0.05). Higher reduction of IL-6 at 3 weeks and TNF alpha at 6th week in the PDT group (p<0.05). PDT showed higher reduction of P.g & P.i at both 3rd and 6th week intervals (p<0.05).

RCT – Randomized clinical trial, RCCT – Randomized Controlled Clinical Trail, US – Ultrasonic scaling, aPDT – antimicrobial Photodynamic Therapy, CHX – Chlorhexidine, DS – Dental Scaling, FMS – Full mouth scaling, PI – Plaque Index, GI- Gingival index, BOP – Bleeding on Probing, PD – Probing Depth, HI – Healing Index, GCF – Gingival crevicular fluid, BL – Baseline.

Characteristic of the intervention:

In all the 5 included studies, the interventional group consisted of aPDT adjunct to scaling in patients undergoing fixed orthodontic therapy with gingival inflammation. Dental scaling was performed using ultrasonic scalers in all the included studies prior to the aPDT therapy. For the aPDT group, all the studies have reported the use of diode lasers in combination with methylene blue (MB) as the photosensitizer dye. However, the concentration of the MB varied between 0.0005% in 3 studies and 0.005% in 2 of the studies included. The MB dye pre-irradiation exposure time to gingival tissue was 3 minutes in three of the studies included. In one study, an exposure time of 2 minutes was found to be sufficient for achieving the same results as that of the study which used 3 minutes exposure time. However, the data regarding exposure time of the dye is not mentioned in 1 of the included study. Following the application of the dye for 3 minutes within the gingival sulcus, excess dye was removed, and laser irradiation was done. The lasers used for aPDT were diode lasers with a wavelength of 670 nm in all the included studies. The laser irradiation parameters utilized were more or less of closer range in all the studies included. The power output ranged from 150 mW in four studies and 190 mW in one of the studies. The energy fluence delivered with the laser tip was 22 J/cm2 in four of the studies and 67 J/cm2 in one of the studies. The energy density was 1.1 W/cm2 in 2 of the studies and 6.05 W/cm2 in one of the studies and not mentioned in the other 2 included studies. All the studies had unanimously exposed the laser for a period of 1 minute around each tooth in the gingival sulcus.

Risk of bias/ quality assessment:

Out of the 5 included studies, ROB-2 Tool was used for three RCTs. Newcastle Ottawa Scale was used for the remaining two NRCTs. Among the RCTs, one study had low risk of bias, two studies were showing some concerns. **(Figure 2)** Among the NRCTs, Two studies were of good quality with overall scores of 6 and 7 respectively. **(Table 3)** In the study by Abellan R et al [15] a low risk of bias was observed in randomization process, deviation from intended intervention, missing outcome data, measurement of outcome, selection of reported results. While Baeshan HA[16] et al and Nazeh AA et al [17] studies showed some concerns with respect to selection of the reported results and information on missing outcome data. Studies by Alshahrani A et al [18] and Kamran MA et al [19] had an overall score of 6 and 7 respectively due to inconsistencies in the assessment of outcomes, adequacies to follow up of cohorts and demonstration of outcome at the start of the study.

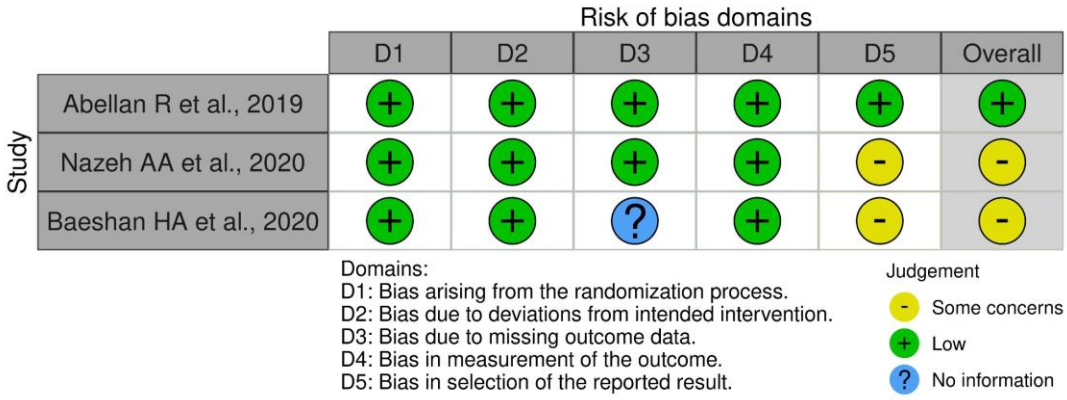

Figure 2: Risk of bias summary for RCTs using ROB-2 tool

Table 3: Newcastle-Ottawa scale for non-randomized controlled clinical trial

Question	Alshahrani A	Kamran MA
A) SELECTION		
1)Representativeness of the exposed cohort	*	*
2) Selection of the non-exposed cohort	*	*
3) Ascertainment of Exposure	*	*
4) Demonstration that outcome of interest was not present at start of study	*	
No. of stars in this domain	4	3
Quality	Good	Fair
B) COMPARABILITY		
1) Comparison of cohorts on basis of design/analysis	**	**
No. of stars in this domain	2	2
Quality	Good	Good
C) ASSESSMENT OF OUTCOMES		
1) Assessment of outcome	------	------
2) Was follow-up long enough for outcomes to occur	*	*
3) Adequacy of followup of cohorts	------	------
No. of stars in this domain	1	1
Quality	Poor	Poor
Total	7	6
Overall Quality	Good	Good

Effects of intervention:

Adjunctive use of aPDT in the selected population showed a mixed outcome in terms of resolution of gingival inflammation. Only one [19] out of the five studies included showed a significant reduction of gingival inflammation (GI/BOP) in the aPDT group compared to ultrasonic scaling. Another study by Abellan R et al [15] showed a similar trend with slightly more reduction of inflammation in the aPDT group, but without achieving any statistical significance. However, these were contradicting the Baeshan et al [16] study which reported greater reduction of inflammation in ultrasonic scaling (US) group compared to aPDT. The rest of the two studies had no significant difference between the scaling and the aPDT groups.[17,18] Apart from resolution of gingival inflammation Abellan R at al [15] also reported significant reduction of gingival enlargement in patients who underwent aPDT compared to scaling alone.

The aPDT resulted in significant reduction of most of the bacterial species assessed when compared to only scaling for a period of 3 - 6 weeks in all the included studies except for one study, [15] which reported no difference. Further, one of the studies also reported an increase in the bacterial count after 3 weeks in both the evaluated groups, however still showing a significantly higher reduction in the aPDT group over the scaling group.

The aPDT resulted in decrease of most of the proinflammatory cytokines levels at the 3rd and 6th week evaluation except for one study, [15] whereas there was no significant difference in IL-6 and TNF- alpha levels in both the groups. The levels of IL-1ra remained stable in both the groups while FGF-2 levels increased without any significant difference. One study also found a correlation between hyperplastic index (HI) with levels of P.g and IL-6 in fixed orthodontic patients with gingival enlargement. [18]

DISCUSSION

Malalignment is one of the contributing factors for accumulation of plaque biofilm and calculus formation on the teeth. When these patients undergo fixed orthodontic therapy the placement of fixed and removable devices on the tooth structure further compromises the oral hygiene of the patient as well as the thoroughness of the periodontal debridement by conventional mechanical therapy (scaling) due to inaccessibility to most of the regions. This results in chronic inflammatory gingival response to the accumulated biofilm that can even result in gingival enlargement further complicating the oral hygiene process. Thus, the use of adjunct therapies to scaling could be of benefit to these populations.

Recently two systematic reviews [26, 27] were reported similar to our study which assessed the effect of aPDT in reducing orthodontically induced gingival inflammation and concluded as effective when compared to scaling. Although, the study by Mirhashemi AH et al [26] evaluated the adjunctive effect of aPDT in management of gingival inflammation in orthodontic patients similar to our study, there were some concerns in the methodology of the SR, like missing information on the eligibility criteria for the included studies and absence of risk of bias assessment. The second SR by Shafaee H et al [27] evaluated the effect of two interventions (Low

level Laser therapy and aPDT) adjective to scaling in oral health and white spot lesions in fixed orthodontic population, which differed from our study, which focused only in addressing the adjunctive effect of aPDT to scaling. Further the studies included in the latter review also showed heterogeneity in terms of the number of treatment groups, the type of intervention, the use different photosensitizer other than methylene blue etc.

Gingival Inflammation:

The present systematic review (SR) included clinical trials which had evaluated aPDT as an adjunct to scaling for orthodontic patients with gingivitis/ gingival enlargement. The primary objective of all the studies included was the reduction of gingival inflammation which was based on clinical evaluation of the gingival tissue health status. Even though there is only one earlier reported SRs on this research question, an abundance of reports on the effect of aPDT adjunct to scaling and root planing (SRP) in periodontitis patients, [20,21] can be used to discuss the results obtained here. Several literature reports and meta-analyses have concluded that adjunctive use of aPDT results in significant reduction of PD and clinical attachment level gain (CAL) compared to conventional scaling in patients with periodontitis. [20,22] However, the mixed results in the present review with only 1 study showing significant reduction of gingival inflammation by aPDT[19] and the rest either reporting no significant difference [15,17,18] or better reduction in scaling group[16] might be due to the population included in these studies, which consisted of young individuals who were free of periodontitis.

Microbial colony count:

One of the other outcomes assessed by all the included studies was the microbial analysis using total CFU of periodontopathogens. All the studies reported a significant reduction in the total CFU of periodontal pathogens after aPDT compared to conventional scaling alone except for Abellan et al [15] where a similar trend was observed without a statistical significance. The later study had a follow-up period of 9 months whereas the rest of the studies had a follow-up period only till 4 weeks. [15] This longer time duration would have allowed the plaque microbial community to recolonize at the treated sites closer to the preoperative levels. However, the repeated applications of aPDT (4 sessions) and scaling in Abellan et al [15] could explain the reduced microbial count observed irrespective of its recurrence to baseline levels. The reduction of microbial counts is mainly attributed to the specific cytotoxicity of aPDT to the microbial cell walls which have absorbed the photosensitizer dye (methylene blue).[23] Further the presence of singlet oxygen molecules in the extracellular matrix of plaque biofilm can become highly reactive with laser light resulting in damage to the matrix, which is a significant advantage of aPDT compared to antibiotics and mechanical therapy.[23,24] In mechanical therapy (scaling) the reduction of microbial count is achieved by disruption and physical removal of the plaque biofilm that may itself become invasive to the gingival tissues.

GCF cytokine levels:

Additionally, four of the included studies evaluated the gingival crevicular fluid (GCF) levels of various pro and anti-inflammatory cytokines like IL-1beta, TNF alpha, IL-6, IL-10, IL-1ra, FGF-2. aPDT resulted in significant decrease in most of the proinflammatory cytokines levels at 3rd and 6th week evaluation except for one study where there was no significant difference in IL-6 and TNF- alpha levels in aPDT group compared to the scaling group.[15] The levels of IL-1ra remained stable in both the groups while FGF-2 levels increased without any significant difference.[15] One of the included study also found a correlation between hyperplastic index (HI) with levels of P.g and IL-6 in fixed orthodontic patients with gingival enlargement.[18] This decreased levels of cytokine post therapy is a result of reduction in the microbial counts from the mechanical as well as aPDT effect. Presence of microbes and their metabolites induces immune cells and other host tissue cells (fibroblast) to secrete inflammatory cytokine. In this context aPDT reduces the virulence of lipopolysaccharide (LPS) and other proteases of the microbial cells thereby reducing the inflammatory response [25] against these metabolites which may be the reason behind the significantly decreased levels of the cytokines in aPDT seen in these studies.

Since all the studies had subjects, only with a probing depth (PD) <3mm, most of the studies did not report any major changes in the probing depth after the intervention. Also, the follow-up evaluation ranged from 3 weeks to 6 weeks in 4 of the included studies and the remaining 1 study had a follow-up period of 9 months. There was no report of adverse reaction for aPDT application in any of the included studies reflecting the safety of the aPDT protocol used.

LIMITATIONS

Even though this review attempted to critically analyze all the evidence reported the evaluation of aPDT as an adjunct to scaling in reduction of gingival inflammation for fixed orthodontic treatment subjects, the results should be cautiously interpreted since it has limitations like heterogeneity of the follow-up periods, study population age, sample sizes, and single session of aPDT in all the studies except for one study. The number of randomized controlled clinical trials were less, and the other clinical trials included were found to have moderate to high risk of bias thus reducing the quality of evidence available.

CONCLUSIONS

Within the limitations of this systematic review, there is no clear evidence that aPDT adjunctive to scaling has a better effect in reducing gingival inflammation in fixed orthodontic patients. Future studies addressing this area should focus on well planned standardized, long term RCTs that will aid clinicians in making a more evidence - based decision.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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