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Systematic Review

Efficacy of antimicrobial photodynamic therapy versus antibiotics as an adjunct to scaling and root planing for the treatment of aggressive periodontitis: a systematic review

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ABSTRACT

Treating aggressive periodontitis (AgP) is quite challenging. Conventional treatment for aggressive periodontitis involves systemic antibiotics (AB) with scaling and root planing (SRP). However, antimicrobial photodynamic therapy (aPDT) presents a promising alternative due to its targeted action and reduced side effects. This suggests the need to analyse and compare both treatments to determine the best approach for effective management of AgP. A systematic literature searches in three databases: PubMed, Google Scholar, and Cochrane, and a hand search of relevant scientific journals was performed. The eligible studies included randomized controlled trials (RCTs) with parallel-group design, comparing aPDT to AB as adjuncts to SRP for treating AgP. Studies published in English language between January 2003 and December 2023 were included. Studies were assessed for quality using the Cochrane risk-of-bias tool for randomized trials version 2 (RoB 2) and were classified as high-quality studies. Five RCTs meeting eligibility criteria were selected and underwent qualitative analysis. The clinical parameters assessed in studies were Pocket Probing Depth (PPD), Bleeding on Probing (BOP), and Clinical Attachment Level (CAL). Two studies reported significant improvements in all parameters with both therapies, three studies indicated a greater reduction in clinical parameters in the AB group compared to aPDT. Adjunctive use of AB with SRP results in significant clinical outcomes compared to SRP and aPDT. According to the studies of this systematic review 4-5 applications of aPDT with an interval of 7 days, and a follow-up period of 6 months are beneficial in treating AgP.

Keywords: Aggressive periodontitis, Antibiotics, Antimicrobial photodynamic therapy, Scaling and root planing

INTRODUCTION

The classification system of periodontal diseases and conditions (1999) introduced aggressive periodontitis (AgP), replacing terms like "early-onset periodontitis (EOP)" and its subtypes.[1] AgP is characterized by rapid bone and connective tissue deterioration, often not correlated with levels of gingival inflammation or plaque accumulation. Additionally, it commonly exhibits a familial predisposition. Apart from genetic susceptibility, the presence of pathogens possessing particular virulence traits seems to play a crucial role in the pathogenesis of the disease by impeding the host's defenses.[2] It exhibits a microbiological profile predominantly composed of Aggregatibacter actinomycetemcomitans in the subgingival plaque biofilm.[3] This microorganism disrupts the balance in the host's immunoinflammatory response through its structural components, leading to elevated production of tissue inflammatory cytokines, for instance interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF)-α.[4] Aggressive periodontitis typically presents in two forms: localized (LAP) and generalized (GAP), categorized based on the distribution of affected teeth assessed clinically and radiographically.[5] Predominantly

affecting young individuals, its prevalence ranges from 1% to 15%, significantly impacting function, aesthetics, and overall quality of life, emphasizing the necessity for prompt and effective disease management.[6]

Nonsurgical periodontal therapy, including scaling and root planing (SRP), aims to disrupt bacterial biofilm, reducing periodontal pathogen load. While longitudinal studies support its efficacy in chronic periodontitis (CP), addressing aggressive periodontitis (AgP) is challenging due to its tissue-invading capacity.[7] Mechanical therapy alone may not fully eliminate pathogens like A.a., necessitating adjunctive systemic antibiotics, resulting in significant clinical improvements but posing risks of adverse effects and bacterial resistance. To mitigate these concerns, novel antimicrobial protocols are being explored.[8-10] Antimicrobial photodynamic therapy (aPDT) is emerging as a promising adjuvant to scaling and root planning (SRP) in treating aggressive periodontitis (AgP). Utilizing light-induced cell inactivation, aPDT combines visible light, typically from a diode laser, with a photosensitizer to selectively eradicate bacteria and their by-products. This targeted approach offers a non-invasive method for antimicrobial treatment, holding potential for effective management of AgP.[11]

Systematic reviews evaluating the effects of PDT and systemic antibiotics for the treatment of aggressive periodontitis are available in literature individually, however, currently there is no data on the systematic review which has been done to compare both the treatment modalities.

Thus, the present systematic review aimed to analyse and compare the clinical outcomes of aPDT / systemic antibiotics as an adjunct to scaling and root planing in the treatment of aggressive periodontitis.

METHODS

The protocol for systematic review has been accepted by Prospero and the Registration ID is CRD42023433991. The comprehensive data search of the scientific literature was performed through the following databases: PubMed, Google Scholar, and Cochrane between 1st January 2003 and December 31st 2023 in English language. Cross references and grey literature were checked for relevant articles. The search strategy utilized a combination of keywords, MeSH terms, and Entry terms, including "systemic antibiotics," "antimicrobial agents," "anti-bacterial agents," "antibacterial agents," "aggressive periodontitis," "photodynamic therapy," "photochemotherapies," and "photochemotherapy." Hand-searching of articles was done when the full texts of the relevant studies were not available through the electronic database.

Inclusion criteria

The studies were considered eligible if they met the following criteria: randomized controlled clinical trials (RCTs) with a parallel-group design; patients diagnosed with aggressive periodontitis according to the 2017 classification of periodontal and peri-implant diseases and conditions criteria, undergoing scaling and root planing (SRP). The RCTs involving a comparison between antimicrobial photodynamic therapy (aPDT) and antibiotics as adjuncts to scaling and root planing for aggressive periodontitis. Only RCTs published between 2003 and 2023 were deemed eligible; additionally, RCTs published in English literature were included.

Exclusion criteria

All in-vitro, animal studies, non-randomized studies, observational studies and retrospective studies were excluded. Studies conducted on patients with systemic diseases; pregnant or lactating women; or individuals with habits such as tobacco product usage, smoking, or alcohol consumption were not included. Studies conducted on patients who underwent antimicrobial therapy within the preceding 6-12 months were also excluded.

Study selection process and data collection

At each stage of the study screening, 2 researchers namely (AG and SVK) independently screened the titles and abstracts obtained by search strategy and included them if they met the inclusion criteria. Full-text of relevant articles that met the inclusion criteria were then reviewed and any uncertainty or disagreements were resolved by discussion. For inclusion of articles for the systematic review, the quality assessment of each article was done by two researchers (AG and SVK) independently and later it was cross checked. The search yielded 5 articles for inclusion in systematic review

A standardized data extraction sheet in Microsoft Excel was prepared for the qualified studies with the help of an expert and discussion was done in case of any disagreement. The following criteria were predetermined for extracting data: The mean difference, standard deviation for all the parameters were assessed. All the variables were mentioned in the selected articles for Primary outcome and secondary outcomes. The individual data collected by the two reviewers (AG and SVK) were combined at the last and any disagreement was resolved by discussion

Quality assessment

The methodological quality of all the included studies was assessed using the Cochrane risk-of-bias tool for randomized trials version 2 (RoB 2) for assessing the risk of bias in RCTs. The major aim of quality assessment was to determine the potential for selection bias [eligibility criteria, sampling strategy, sample size, primary outcome (reduction in pocket probing depth [PPD]) and secondary outcomes (reduction in bleeding on probing [BOP], gain in clinical attachment level [CAL]). The risk of bias in individual studies were assessed.

Objectives of the study, the population under the study, the setting in which the study was conducted, eligibility criteria for including or excluding the participants, sampling strategy used, mention of calculating sample size for the study based on previous study, primary and secondary outcome measurement for the treatment of aggressive periodontitis.

A study was classified as high-quality study, moderate quality study and as low-quality study.

RESULTS

Literature search and screening

The electronic and manual searches identified 66 articles from 3 databases (i.e., PubMed, google scholar, Cochrane) and 01 from the cross-references. Of the 66 articles obtained, 31 articles were duplicates and were excluded. Further, title screening was done for 35 articles and 12 articles were excluded after review of titles. Abstract screening was done according to the inclusion and exclusion criteria that had been set by the authors. 14 articles were excluded because they did not comply with the inclusion criteria. The remaining 09 studies had their full text read. Finally, a total of 05 articles were selected which met the inclusion criteria and answered the main focused question which was to assess the efficacy of antimicrobial photodynamic therapy (aPDT) in comparison to antibiotics as an adjunct to scaling and root planing for the treatment of aggressive periodontitis. The absence of a meta-analysis was attributed to the data's heterogeneity. The article screening process is depicted in Figure 1.

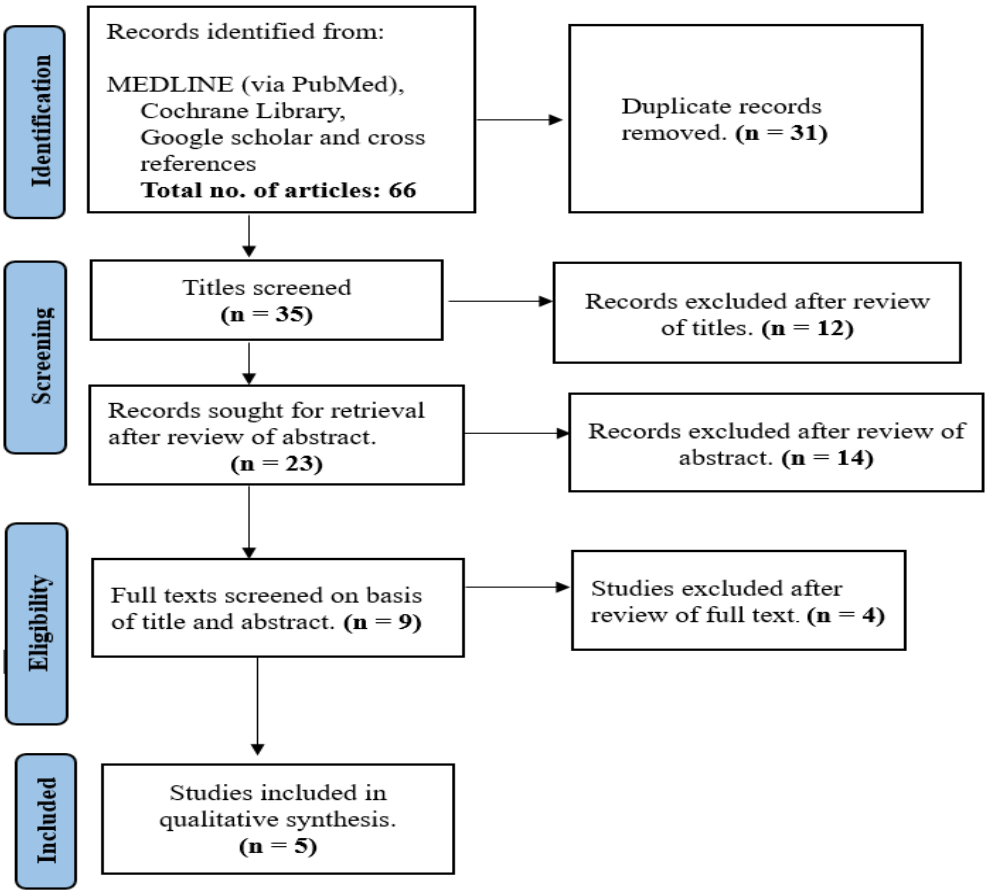

Figure 1: PRISMA flow chart.

Study and patient characteristics

A total of 05 eligible articles were included in this review that evaluated the efficacy of antimicrobial photodynamic therapy (aPDT) versus antibiotics as an adjunct to scaling and root planing for the treatment of aggressive periodontitis.

All the participants having aggressive periodontitis were considered for the study. A total of 146 patients were included. The age group of individuals incorporated in the studies that were included in this review was in the range of 18-55 years.

All the included studies in this review had a parallel group design with two arms: a test group i.e., aPDT as an adjunct to scaling and root planning; and a control group i.e., systemic antibiotics as an adjunct to scaling and root planning.

Table 1 showing data extraction sheet of all included studies.

Table 1: Data extraction sheet of all included studies.

Author (year)	Geographical location	Study design	Sample size (Intervention/ control)	Age (years)	Intervention				Control			Dropouts intervention/ control
					Dye used	Time of dye application (min)	Wavelength & power of laser used	Time of laser tip application (min)	No. of applications	Antibiotic Prescribed	Frequency of drug administered	No. of days drug prescribed	
Skaleric et al[20] (2022)	Slovenia	RCT	20 (10/10)	18-38	Phenothiazine chloride	3	670 nm 75 mW	1	Two (Day 1,8)	Amoxicillin 500 mg Metronidazole 400 mg	Three times	7	intervention=1 (at 9th and 12th month) ctrl=1 (12th month)
Al-Khureif et al[21] (2019)	Saudi Arabia	RCT	18 (9/9)	≤35	Phenothiazine chloride	1	670 nm 75 mW	1	Four (Day 1, 3, 7, 14)	Amoxicillin 500 mg Metronidazole 500 mg	Three times	7	intervention=0 ctrl=1(6th month)
Andere et al[16] (2018)	Brazil	RCT	36 (18/18)	<35	Methylene blue	1	660 nm 60 mW	1	One (Day 1)	clarithromycin 500 mg	Two times	3	0
Arweiler et al[7] (2014)	Poland	RCT	36 (18/18)	23-55	Phenothiazine chloride	3	660 nm	1	Two (Day 1,7)	Amoxicillin 375 mg Metronidazole 250 mg	Three times	7	intervention=1 ctrl=0
Arweiler et al[23] (2012)	Poland	RCT	36 (18/18)	23-55	Phenothiazine chloride	3	660 nm	1	Two (Day 1,7)	Amoxicillin 375 mg Metronidazole 250 mg	Three times	7	intervention=1 ctrl=0

Table 2: Summary of primary outcomes.

S. no.	Author (year)	Primary outcome				
		PPD	Test		Control	
			Mean	SD	Mean	SD
1	Skaleric et al[20] (2022)	Baseline	3.68	1.88	3.51	1.84
		3 months	2.77	1.06	2.54	0.83
		6 months	2.85	1.16	2.47	0.76
		9 months	2.86	1.05	2.46	0.71
		12 months	2.58	0.89	2.40	0.82
2	Al-Khureif et al[21] (2019)	Baseline	5.44	0.39	5.61	0.35
		3 months	3.23	0.68	3.71	0.76
		6 months	2.74	0.46	2.95	0.45
3	Andere et al[16] (2018)	Baseline	7.2	1.2	6.8	2.64
		3 months	4.4	0.9	3.7	0.8
		6 months	4.6	0.9	3.7	0.7
4	Arweiler et al[23] (2014)	Baseline	5.1	0.5	5.0	0.8
		6 months	3.9	0.8	3.0	0.6
5	Arweiler et al[7] (2012)	Baseline	5.1	0.5	5.0	0.8
		3 months	4.0	0.8	3.2	0.4

Table 3: Summary of secondary outcomes.

S. no.	Author (year)	Secondary outcome									
		BOP	Test		Control		CAL	Test		Control	
			Mean	SD	Mean	SD		Mean	SD	Mean	SD
1	Skaleric et al[20] (2022)	Baseline	45.7%	-	42.3%	-	Baseline	3.88	2.15	3.70	1.91
		3 months	10.6%		8.5%		3 months	3.06	1.43	2.80	1.09
		6 months	6.7%		8.3%		6 months	3.13	1.47	2.80	1.08
		9 months	6.6%		8.8%		9 months	3.23	1.36	2.84	1.15
		12 months	5.4%		5.2%		12 months	2.94	1.40	2.73	1.10
2	Al-Khureif et al[21] (2019)	Baseline	45.72	7.6	36.83	9.5	Baseline	5.69	0.84	5.74	0.89
		3 months	23.61	5.1	19.68	7.3	3 months	3.27	1.18	4.06	1.07
		6 months	15.48	4.9	17.91	6.8	6 months	3.00	0.94	3.15	1.04
3	Andere et al[16] (2018)	Baseline	100%	-	100 %	-	Baseline	7.3	1.2	7.5	2.8
		3 months	33.3%		11.1%		3 months	4.8	1.7	4.4	1.6
		6 months	33.3%		16.6%		6 months	4.9	1.4	4.5	1.5
4	Arweiler[23] et al (2014)	Baseline	70.4	22.4	85.7	15.9	Baseline	5.7	0.8	5.5	1.1
		6 months	48.8	22.2	32.6	21.0	6 months	4.7	1.1	3.6	0.9
5	Arweiler et al[7] (2012)	Baseline	70.4	22.4	85.7	15.9	Baseline	5.7	0.8	5.5	1.1
		3 months	37.7	21.3	34.6	22.8	3 months	4.7	1.1	3.9	1.0

All the selected studies addressed the primary outcome, pocket probing depth (PPD), and along with secondary outcomes bleeding on probing (BOP) and clinical attachment level (CAL). Table 2 and 3 showing summary of primary and secondary outcomes.

Quality assessment

Risk of bias within each study was assessed, and were categorized into high, medium and, low risk. All trials demonstrated a low risk of bias across several domains that were evaluated. Summary of the judgements of the risk of bias are shown for each domain in each of the included studies (Figure 2). In all the studies included in this systematic review, a low risk of bias was observed across all assessed domains. Each of the five studies demonstrated a low risk in every domain evaluated, indicating a high overall quality of the included studies. Overall, the studies included in this review were classified as high-quality studies.

The results from all individual studies are summarized in Table 2 and 3.

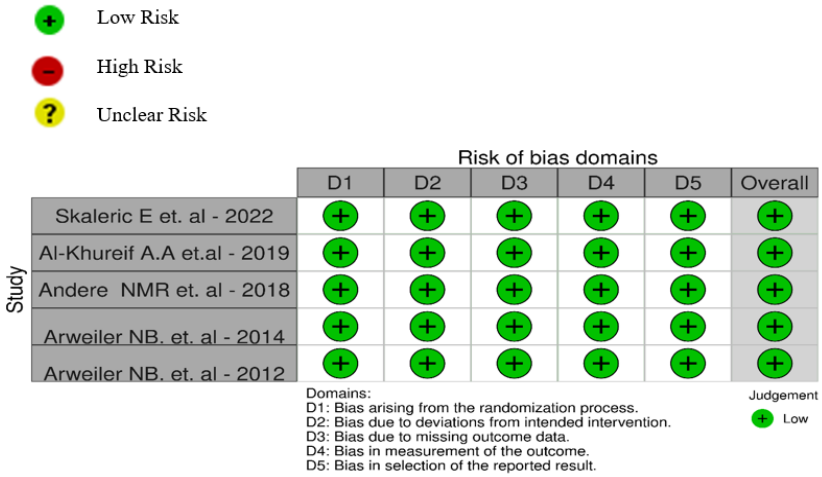

Figure 2: Summary of risk of bias: review authors' judgments about each risk of bias item for each included studies.

DISCUSSION

Periodontitis, characterized by chronic inflammation initiated by microorganisms in the dental biofilm, involves complex microbe-host-clinical interactions.[12] Aggressive periodontitis, particularly affecting adolescents and young adults, poses challenges for conventional treatment like scaling and root planing (SRP), necessitating adjunctive systemic antibiotics.[6,13,14] However, uncertainty remains regarding the optimal antibiotic regimen, especially among Aggregatibacter species which may be resistant to certain antibiotics like imidazole and tetracyclines.[15]

Multiple studies have emphasized the benefits of using antibiotics such as clarithromycin, 1620 a combination of amoxicillin and metronidazole,9 or azithromycin.[17] These antibiotics have shown efficacy in reducing A.a. and P.g. levels and improving clinical outcomes, including reduced pocket probing depth (PPD), increased clinical attachment level (CAL), and reduced inflammation (e.g., decreased bleeding on probing). However, concerns over systemic antibiotic use have emerged due to issues like biofilm-associated antibiotic resistance, the development of antibiotic resistance, and potential side effects like gastrointestinal disorders.[18] Consequently, alternative antimicrobial approaches have been explored. Antimicrobial photodynamic therapy (aPDT) has emerged as a promising alternative for eliminating subgingival microbial species and enhancing root surface disinfection. It offers several advantages, including ease of application, no need for anesthesia, rapid bacteria eradication (in less than 60 seconds), absence of bacterial resistance induction, and minimal harm to host tissues.[19]

This systematic review aimed to evaluate the efficacy of antimicrobial photodynamic therapy (aPDT) in comparison to systemic antibiotics as an adjunct to scaling and root planing for the treatment of aggressive periodontitis. Primary outcomes focused on pocket probing depth (PPD), with secondary outcomes including bleeding on probing (BOP) and clinical attachment level (CAL). Five eligible randomized controlled trials (RCTs) were identified through a comprehensive literature search. Among the five studies included in the present systematic review, there was a significant improvement in all clinical parameters from the baseline to the postoperative endpoint in the intra-group comparisons. Skaleric et al and Al-Khureif et al, reported significant improvements in both the antimicrobial photodynamic therapy (aPDT) and systemic antibiotics groups.[20,21] On the contrary, Andere et al, Arweiler et al, found that SRP with systemic antibiotics resulted in more substantial improvements compared to aPDT at 3- and 6-month follow-ups.[22,23,27]

Skaleric et al study was one of the first studies comparing the prolonged outcomes of aPDT and antibiotic therapy as adjuncts to conventional non-surgical treatment for aggressive periodontitis.[20] Notably, it was one of the few to administer two sessions of aPDT following non-surgical therapy, revealing comparable clinical outcomes to antibiotic adjuncts and suggesting aPDT's potential as an alternative to systemic antibiotics, thus minimizing associated side effects and antibiotic resistance risks. This contrasts with numerous other studies that solely employed a single application of aPDT, which resulted in an even greater improvement in clinical parameters than a single episode of aPDT alone.

Al-Khureif et al study highlighted aPDT's significant enhancement of clinical periodontal parameters, attributed to its localized administration of photosensitizers.[24,25] This targeted approach potentially facilitated deeper penetration into periodontal pockets, effectively eliminating infectious agents where conventional methods might be less effective.[26] Moreover, the multiple applications of photosensitizer post-debridement contributed to a delay in the bacterial recolonization, countering the typical resurgence observed post-treatment after three weeks, thus indicating aPDT's preventive potential against bacterial recurrence.[27]

Andere et al conducted a study comparing the outcomes of aPDT and clarithromycin (CLM), finding statistically significant benefits with clarithromycin at 6 months, suggesting the superiority of systemic antibiotics over aPDT.[22] This potential disparity could be attributed to the specific aPDT protocol used in the study, which involved a single application. While studies indicate that combining amoxicillin (AMX) and metronidazole (MET) with periodontal therapy provides superior clinical benefits compared to mechanical therapy alone, concerns regarding bacterial resistance exist.[16,28] Alternatively, CLM offers broad antimicrobial coverage against A.a. and improved treatment compliance with a shorter regimen of just 3 days. Although patients in the aPDT group experienced a significant reduction in PPD at 3 months post a single aPDT application, this effect did not persist after 6 months, suggesting limited long-term efficacy. While aPDT shows short-term benefits, its extended effectiveness as an adjunct to SRP for AgP patients remains uncertain, and the study lacks sufficient evidence to support its superiority over antibiotic treatment, particularly with only a single application. Arweiler et al in their studies conducted in 2012 and 2014 respectively, emphasized the statistically significant improvements observed in the clinical parameters, particularly the reduction of PPD and the improvement in CAL with the antibiotic group.[7,23] Their findings suggested a preference for treating AgP using SRP combined with antibiotics rather than SRP along with aPDT. However, the adverse effects associated with antibiotics often cause patients to discontinue or reject this form of treatment, prompting the search for alternative therapies. In this study, even two applications of aPDT failed to produce substantial clinical improvements compared to antibiotics. This indicates a requirement for repeated sessions of aPDT applications, as seen in Al-Khureif et al to achieve favourable outcomes.[21]

The systematic review findings suggest that systemic antibiotics alongside SRP had a greater impact on clinical outcomes post-therapy compared to SRP combined with aPDT, as observed in studies by Andere et al and Arweiler.[7,22,23] This difference could be attributed to the specific aPDT application protocols used. Researchers propose repeated applications of aPDT to enhance clinical outcomes, supported by Lulic et al.'s study, which demonstrated improved outcomes with five sessions of aPDT in chronic periodontitis patients. This protocol resulted in significant reductions in PPD and an increase in CAL when applied to AgP patients receiving aPDT as an adjunct to SRP.[29]

An essential factor to consider when interpreting these findings is the absence of reported bacterial resistance against aPDT in existing literature. Consequently, its repetitive use alongside mechanical debridement might emerge as a promising option worth exploring in the future.30 This prospect holds significant clinical relevance, particularly in light of documented rises in bacterial resistance against antibiotics. Furthermore, all studies incorporated in this systematic review have affirmed the safety of aPDT. In contrast, Andere et al reported gastrointestinal discomfort in two patients following the use of antibiotics.[22]

Based on the current data, it is evident that both treatments led to statistically significant clinical improvements. However, the systemic use of antibiotics as an adjunct to SRP showed greater clinical improvements compared to aPDT. The results also imply that while aPDT could be a promising therapeutic concept in periodontal treatment for AgP patients, its potential benefits require more than two applications and an extended follow-up period.

The systematic literature search reported the presence of a limited number of randomized controlled trials till today assessing aPDT versus antibiotics as an adjunct for AgP therapy.

Limitations

The primary limitation was due to the scarcity of eligible studies for comprehensive analysis of periodontal outcomes, as well as the varied durations of participant follow-up among the selected studies. Heterogeneity in the parameters of photodynamic therapy and antibiotic approaches precluded meta-analysis. Hence, there is a need for methodologically well-designed, long-term randomized controlled clinical trials with standardized laser application parameters and extended follow-up periods, to establish guidelines for the use of aPDT in managing AgP. Future research could explore the influence of confounding factors such as genetic susceptibility and lifestyle habits on treatment efficacy.

CONCLUSION

The combined use of antibiotics as an adjunct to SRP resulted in significantly improved clinical outcomes compared to SRP and aPDT. This study advances our understanding by highlighting the superior efficacy of antibiotics as an adjunctive therapy in enhancing periodontal treatment outcomes, thereby providing a stronger evidence for clinical decision-making for the treatment of aggressive periodontitis.

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