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A review of antimicrobial photodynamic therapy (aPDT) in periodontitis

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Abstract
Introduction: Periodontitis is an inflammatory disease caused by a multitude of pathogens, that eventually affects the entirety of all periodontal tissues and may lead to tooth mobility or even tooth loss. The destruction of said tissues occurs via 2 pathways: a direct pathway (defense mechanisms belonging to the pathogens) and an indirect pathway (the host's immune system). Therapy is complex and requires strict follow-ups in order to prevent relapse. **Aim:** Our objective was to determine whether or not aPDT can be considered to be an effective adjunctive approach to the current standard initial treatment method when dealing with periodontitis (scaling/root planing). **Methods:** We performed an electronical search of the PubMed and ScienceDirect data bases starting from January 2014 and up to May 2019. Eligibility criteria included English-language systematic reviews and randomized clinical trials which evaluated the efficiency of aPDT, and that had been carried out on human subjects with permanent dentition. We excluded studies and reviews that were focused on the microbiology and/or immunology in photodynamic therapy and also those that used other LASER treatment modalities than aPDT. **Results:** Current literature displays many opinions regarding periodontal therapy with adjunctive aPDT, but it seems to be mainly regarded as a safe, effective and easy-to-use approach. **Conclusion:** aPDT seems to be efficient in the treatment of periodontitis when carried out additionally to classical scaling/root planing. Residual pockets seem to respond well to aPDT, as opposed to subsequent debridement flap elevation and its consequences on hard and soft tissues. However, further studies with a stricter treatment protocol and subsequent follow-ups are required in order to obtain a firmer conclusion.

Key words: *periodontitis LASER, periodontitis aPDT, periodontitis photodynamic therapy,*

Introduction

Periodontitis is defined as an inflammatory disease caused by various pathogenic microorganisms, which leads to the destruction of all periodontal tissues: gingiva, periodontal ligaments, alveolar bone and cementum. The destruction occurs not only due to the direct damage caused by the pathogens, but also due to the indirect destruction produced by the host's immune response. Therapy must be multidisciplinary and the main goal is to reduce inflammation.

When left untreated, periodontitis may not only lead to tooth mobility and eventually tooth loss, but it can also cause other systemic diseases. Being a chronic oral infection, periodontitis represents a continuous source for subsequent co-morbidities and even mortality in respective patients. Examples include cardiovascular diseases, cerebrovascular diseases, respiratory diseases and low birth weight (1, 2).

Conventional approach is based on the removal of hard deposits and plaque from the root surface by subgingival scaling and root planing, thus leading to a reduction of the bacterial load in the periodontal pocket. Frequent associated consequences to this maneuver are bleeding, pain, swelling and overall patient discomfort, all of which have a negative impact on the postoperative quality-of-life (QoL) factor.

The use of LASERs has evolved since the first LASER was introduced in 1985. Research in hard and soft tissue LASERs is continuously advancing through the discovery of newer wavelengths. Nowadays, science has come a long way and has been developing increasingly modern devices with the aim to improve hemostasis, patient comfort, healing and provide less postoperative swelling and pain (3).

There are many LASERs commercially available that advertise to be able to achieve all of these positive features.

It is already known that photodynamic LASER therapy is unable to remove subgingival calculus on its own. The principle of soft tissue LASER therapy is based on the reduction of bacterial population and removal of necrotic epithelial tissue (3). In antimicrobial photodynamic LASER assisted procedures (also known as “aPDT”), LASER energy is absorbed by the chromophores within the diseased periodontal pocket and transformed into photothermic energy. Pathogens contain different amounts of wavelength-specific chromophores and, according to these, require different LASER parameters in order to be neutralised.

Laser wavelengths can be classified into soft and hard tissue LASER types. Soft tissue LASERs are the CO_2, Nd:YAG and diode LASERs, while Erbium-based wavelengths produce effects both on soft, as well as on hard tissues.

Among the LASER types applied in periodontology are the CO_2-LASER (very efficient in cutting and vaporizing soft tissues), the diode LASERs (efficient in cutting, decreasing bacterial loads in periodontal pockets and hemostasis), Erbium-based LASERs (effective in cavity preparations and caries removal, as well as the removal of soft and hard deposits from root surfaces, furcations and infrabony defects) and Nd:YAG LASERs (which have an affinity to chromophores similar to that of the diode LASERs, thus leading to good bacterial reduction).

Antimicrobial photodynamic therapy relies on three components: photosensitizer, light in a spectrum that is appropriate to activate the photosensitizer, and oxygen. The photosensitizer is transferred from its basic singlet state into an activated singlet state after irradiation with a specific wavelength. This reaction pathway is recognized as the major course of microorganism destruction. As far as the photosensitizer is concerned, Methylene blue and Toluidine blue O seem to have the strongest bactericidal effect among medical photosensitizers (4). They are the most commonly used and are very efficient in killing Gram-positive and Gram-negative periodontopathic bacteria, but also the influenza virus, Helicobacter pylori and Candida albicans after they are activated by light (5). Thus, it can be stated that aPDT is a fairly novel antimicrobial approach with less complications and side effects when compared to conventional antibiotic therapy, one of which's well known side effects is bacterial resistance. Thus, LASER-assisted therapy seems to be a very desirable approach in contemporary dentistry, which helps keep treatment at a minimally invasive level.

The question that arises is if aPDT is effective as an adjunctive approach to the current standard treatment method of periodontitis cases. Therefore, our objective in this systematic review was to assess the efficiency of photodynamic therapy when treating periodontitis in a combined fashion: standard scaling/root planing with additional aPDT.

Methods

Search strategy and selection criteria

We performed an electronical search of the PubMed and ScienceDirect data bases starting from January 2014 and up to May 2019. Our aim in this systematic review was to assess the clinical outcomes of aPDT when used as an adjunctive to scaling and root planning in periodontal treatment. The following eligibility criteria was established: systematic reviews and randomized clinical trials which evaluated the efficiency of aPDT. Our search was limited to the last 5 years (January 2014 - May 2019) and only took studies in human population with permanent teeth into account. Also, only articles that were published in English were included. The search protocols on the different databases were similarly constructed, respective to each site’s individual search engine design. The following key word constructions were used: periodontitis LASER, periodontitis aPDT, periodontitis photodynamic therapy. We did not include studies and reviews that investigated the effects of the photodynamic therapy from a microbiological or immunological point of view. Moreover, all studies that used LASER treatment modalities other than aPDT were also not included in this review (mainly those using CO_2, Nd:YAG and Erbium-based LASERs).

Study selection and data extraction

Initially, 10 articles were found on ScienceDirect and 93 articles on PubMed. After excluding all articles that did not meet our inclusion criteria, a total of 23 articles remained. All articles were either systematic reviews or randomized clinical. After applying the above mentioned exclusion criteria, 8 articles about aPDT remained, 7 of which were systematic reviews and 1 was a randomized clinical trial. In the aforementioned 7 articles there were 47 studies involved.

Data extracted from the included studies contained: general information about the publication (year, author), number of patients taken into consideration, treatment-related information (type of LASER used and its characteristics, treatment duration, number of meetings) and clinical outcomes (Table 1).

Results

Current literature contains a wide range of results concerning treatment options in periodontitis. aPDT is mainly regarded as being a safe and easy-to-use approach.

The review of Fahim Vohra et al. (6) showed that aPDT was effective as an adjunct approach to SRP (i.e., scaling and root planing) in aggressive periodontitis – now considered to be an outdated diagnostic - in generally healthy patients. More randomized clinical trials with properly defined control groups are needed to assess the best parameters for adjunctive aPDT application.

The review of Dong Xue (7) showed a significant improvement in PD (i.e., probing depth) and CAL (i.e., clinical attachment level) gain after the usage of SRP with aPDT in non-smoking patients. However, more trials with clearer treatment protocols and similar study designs are recommended to reduce bias.

The review of Zohaib Akram et al. (8) showed that it was debatable whether or not aPDT was effective. Due to the reduced sample size and high heterogeneity of the studies, it is necessary to be cautious with the interpretation of the outcomes and further trials are needed to obtain a more convincing conclusion.

The article of M. Meimandi et al. (9) contained 16 studies, out of which 9 were included in this review. 5 out of these 9 clinical trials showed a significantly better outcome of periodontal parameters after SRP with aPDT (10-14), while 1 study showed short-term efficiency (15). The other 3 studies (16-18) showed no significant difference regarding the clinical outcomes when SRP was combined with aPDT or in comparison with SRP alone. In most of the studies, bleeding on probing (BoP) was improved after additional LASER application. Further studies with higher homogeneity and clearer treatment protocols are needed to firmly conclude efficiency.

The systematic review of E. Souza et al. (19) concluded that further clinical trials which include aggressive periodontitis patients are needed and that the follow-up should be carried out on a time frame longer than 6 months. Also, a strict treatment protocol should be set in order to reach stronger evidence regarding aPDT efficiency. Identifying a most effective number of necessary applications/sessions could contribute to clarifying treatments protocols.

The systematic review of Dong Xue et al. (20) concluded the following: 4 studies (21- 24) showed a positive outcome for the adjunctive use of aPDT, while 2 studies (25, 26) showed no additional benefits for adjunctive aPDT. The clinical trials show a significant improvement of the clinical parameters after SRP with adjunctive aPDT when smokers are not involved.

The study of Betsy and Joseph et al. (27) determined aPDT to be efficient as an adjunctive therapy to SRP. It showed improvements in the gingival index and gingival bleeding index after 1 month of treatment, and also an enhancement of PD and CAL after 3 and 6 months, respectively, after aPDT.

Conclusions

Regarding all conclusions of the presented studies, it can be stated that aPDT is efficient when carried additionally to standard SRP, especially regarding gingival bleeding. Also, residual pockets might be alternatively treated with aPDT (as opposed to subsequent SRP/debridement flap elevation, which may lead to increased hard/gingival tissue loss). Furthermore, patients with HIV and chronic periodontal infections might have additional benefits when adjunctive aPDT is used.

In the case of the disease formerly classified as “aggressive periodontitis”, aPDT cannot replace the antibiotic adjunctive treatment, a fact confirmed by better clinical outcomes when antibiotics rather than aPDT were used additionally to SRP. In most of the studies, adjunctive aPDT demonstrated better outcomes in PD, CAL gain and gingival bleeding. However, aPDT efficiency seems to be compromised in smokers. It has no reported side effects. If side effects appear, they seem to be related to allergic reactions to the photosensitiser.

All outcomes have to be interpreted with great caution due to the heterogeneity among the studies. More studies with a strict treatment protocol are needed to strengthen the current positive conclusion, as well as to assess the best treatment parameters for establishing a future firm therapeutic protocol.

Conflicts of Interest

The authors declare that they have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Table 1. General information about the studies included in this article.

Author/Date	Concept/theoretical model	Context/Setting/Sample	Control groups
Fahim Vohra & Zohaib Akram/2015 (6)	Systematic Review	5 studies - aPDT performed adjunct to SRP; 2 studies – aPDT alone	SRP alone and SRP + ABX
Dong Xue & Ying Zhao/2016 (7)	Systematic Review & Meta-analysis	4 studies – SRP + aPDT, non-smoker and smoker	Only SRP
Zohaib Akram & Tahira Hyder/2017 (8)	Systematic Review & Meta-analysis	SRP + aPDT	SRP + ABX
Mansour Meimandi & mohammed Reza Talebi Ardakani/2017 (9)	Literature Review	[1] PDT, SRP + aPDT, [2] SRP + aPDT, [3] SRP + aPDT, [4] SRP + aPDT, [5] SRP + aPDT, [6] SRP + aPDT, [7] SRP + aPDT, [8] SRP + aPDT, [9] aPDT; aPDT + PS, [10] SRP + aPDT (HIV), [11] SRP + aPDT, [12] SRP + aPDT, [13] SRP + aPDT, [14] SRP + aPDT, [15] 1x TB + aPDT, [16] SRP + PS; SRP + aPDT.	- SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - SRP, - No aPDT, - SRP.
Emmanuel Souza & Ana Claudia Madeiros/2015 (19)	Systematic Review & Meta-analysis	SRP + aPDT	SRP
Betsy Joseph & Chandra Sekhar Prasanth/2014 (26)	Randomized Clinical Trial	SRP + aPDT	SRP
Dong Xue, Lu Tang/2017 (20)	Systematic Review & Meta-analysis	SRP + aPDT	SRP

References

1. Arigbede AO, Babatope BO, Bamidele MK. [Internet]. Advances in pediatrics. U.S. National Library of Medicine; 2012 [cited 2018Jul4]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3590713/
2. Roman A, Soanca A, Petrutiu SA, Condor D, Cioban C. Parodontologie 2 Ghid de tratament. Ed.Med. Univ. Iuliu Hatieganu 2018.
3. Coleton S. The Use of Lasers in Periodontal Therapy. Alpha Omegan. 2008;101(4):181–7.
4. Wilson M, Dobson J, Sarkar S. Sensitization of periodontopathogenic bacteria to killing by light from a low-power laser. Oral Microbiol Immunol. 1993: 8: 182–187.
5. Wiebe CB, Putnins EE. The Periodontal Disease Classification System of the ... [Internet]. 2000 [cited 2018Jul3]. Available from: https://www.bing.com/cr?IG=94E349692BD643D3B1726278F7A9CD4C&CID=12B0F7FD23FA607E1BDFFBDC2207612B
6. Vohra F, Akram Z, Hasnur S, Devi R, Ghanem A, Sergis K, et al. Photodiagnosis and Photodynamic Therapy Role of antimicrobial photodynamic therapy in the treatment of aggressive periodontitis : A systematic review. Photodiagnosis Photodyn Ther [Internet]. Elsevier B.V.; 2016;13:139–47. Available from: http://dx.doi.org/10.1016/j.pdpdt.2015.06.010
7. Xue D, Zhao Y. Photodiagnosis and Photodynamic Therapy Clinical effectiveness of adjunctive antimicrobial photodynamic therapy for residual pockets during supportive periodontal therapy : A systematic review and meta-analysis. Photodiagnosis Photodyn Ther [Internet]. Elsevier B.V.; 2017;17:127–33. Available from: http://dx.doi.org/10.1016/j.pdpdt.2016.11.011
8. Akram Z, Hyder T, Al-hamoudi N, Binshabaib MS, Alharthi SS, Hanif A. Photodiagnosis and Photodynamic Therapy E ffi cacy of photodynamic therapy versus antibiotics as an adjunct to scaling and root planing in the treatment of periodontitis : A systematic review and. Photodiagnosis Photodyn Ther [Internet]. Elsevier. 2017;19(May):86–92. Available from: http://dx.doi.org/10.1016/j.pdpdt.2017.05.007
9. Meimandi M, Reza M, Ardakani T, Nejad AE, Yousefnejad P. The Effect of Photodynamic

Therapy in the Treatment of Chronic Periodontitis : A Review of Literature. Laser Appl Med Sci Res Cent [Internet]. 2017;8(Suppl 1):S7–11. Available from: http://dx.doi.org/10.15171/jlms.2017.s2
10. Aykol G, Baser U, Maden I, et al. The effect of low- level LASER therapy as an adjunct to non-surgical periodontal treatment. J Periodontol. 2011;82(3):481-488. doi:10.1902/ jop.2010.100195.
11. Cappuyns I, Cionea N, Wick P, Giannopoulou C, Mombelli A. Treatment of residual pockets with photodynamic therapy, diode LASER, or deep scaling. A randomized split- mouth controlled clinical trial. Lasers Med Sci. 2012;27(5):979-986. doi:10.1007/s10103-011-1027-6.
12. Noro Filho GA, Casarin RC, Casti MZ, Giovani EM. PDT in non- surgical treatment of periodontitis in HIV patients:a split–mouth, randomized clinical trial. Lasers Surg Med. 2012;44(4):296-302. doi:10.1002/lsm.22016.
13. Berakdar M, Callaway A, Fakhrddin M, Rob A,Willershausen B. Comparison between scaling–root planning and SRP/photodynamic therapy: six–month study. Head Face Med. 2012;8:12.
14. Giannelli M, Formigli L, Lorenzini L, Bani D. Combined photoablative and photodynamic diode LASER therapy as an adjunct to non-surgical periodontal treatment
15. Lui J, Corbet EF, Jin L. Combined photodynamic and low -level LASER therapies as an adjunct to non-surgical treatment of chronic periodontitis. J Periodontol Res. 2011;46:89-96.
16. Polansky R, Haas M, Heschl A, Wimmer G. Clinical effectiveness of photodynamic therapy in treatment of periodontitis. J Clin Periodontol. 2009;36:575-580.
17. Ruhling A, Fanghanel J, Hushmand M, et al. Photodynamic therapy of persistent pockets in maintenance patients - a clinical study. Clin Oral Investig. 2010;14(6):637-644. doi:10.1007/s00784-009-0347-4.
18. Balata ML, Andrade IP, Santos DB, et al. Photodynamic therapy associated with full-mouth ultrasonic debridement in the treatment of severe chronic periodontitis:a randomized–controlled clinical trial. J Appl Oral Sci. 2013;21(12):208-214. doi:10.1590/1678-7757201302366.
19. Souza E, Medeiros AC, Gurgel BC, Sarmento C. Antimicrobial photodynamic therapy in the treatment of aggressive periodontitis : a systematic review and meta-analysis. 2015;
20. Xue AD, Tang L, Bai Y, Ding Q, Wang P, Zhao Y. Clinical efficacy of photodynamic therapy adjunctive to scaling and root planing in the treatment of chronic periodontitis : a systematic review and meta-analysis. Photodiagnosis Photodyn Ther [Internet]. Elsevier B.V.; 2017; Available from: http://dx.doi.org/10.1016/j.pdpdt.2017.01.183
21. Christodoulides N, Nikoldakis D, Chondros P, et al. Photodynamic therapy as an adjunct to non-surgical periodontal treatment a randomized controlled clinical trial. J Periodontol 2008;79(9):1638-44.doi:10.1902/jop.2008.070652.
22. H.A. Alwaeli, S.N. Al-Khateeb, A. Al-Sadi, Long-term clinical effect of adjunctive antimicrobial photodynamic therapy in periodontal treatment: a randomized clinical trial, Lasers Med. Sci. 30 (2013): 801–807.
23. S. Malgikar, S. Reddy, P. Babu, et al., A randomized controlled clinical trial on efficacy of photodynamic therapy as an adjunct to nonsurgical treatment of chronic periodontitis, J. Dent. Lasers 9 (2015) :75–79.
24. R. Birang, M. Shahaboui, S. Kiani, et al., Effect of nonsurgical periodontal treatment combined with diode LASER or photodynamic therapy on chronic periodontitis: a randomized controlled split-mouth clinical trial, Lasers Med. Sci. 6 (2015) :112–119.
25. S.H. Bassir, N. Moslemi, R. Jamali, et al., Photoactivated disinfection using light-emitting diode as an adjunct in the management of chronic periodontitis: a pilot double-blind split-mouth randomized clinical trial, J. Clin. Periodontol. 40 (2013) :65–72.
26. A.C. Queiroz, F.A. Suaid, P.F.D. Andrade, et al., Adjunctive effect of antimicrobial photodynamic therapy to nonsurgical periodontal treatment in smokers: a randomized clinical trial, Lasers Med. Sci. 30 (2015) :617–625.
27. Betsy J, Prasanth CS, Baiju KV, Prasanthila J, Subhash N. Efficacy of antimicrobial photodynamic therapy in the management of chronic periodontitis: a randomized controlled clinical trial - Betsy - 2014 - Journal of Clinical Periodontology - Wiley Online Library [Internet]. Journal of Clinical Periodontology. John Wiley & Sons, Ltd (10.1111); 2014 [cited 2019May16]. Available from: https://onlinelibrary.wiley.com/doi/10.1111/jcpe.12249