Antimicrobial Photodynamic Therapy as an Adjunct to Nonsurgical Periodontal Therapy

Denise M. Bowen, RDH, MS

The purpose of Linking Research to Clinical Practice is to present evidence based information to clinical dental hygienists so that they can make informed decisions regarding patient treatment and recommendations. Each issue will feature a different topic area of importance to clinical dental hygienists with A BOTTOM LINE to translate the research findings into clinical application.

The Bottom Line

Adjunctive photodynamic therapy (PDT or aPDT) is a low-power laser (diode laser, 660 to 810 nm) used in combination with a photosensitizing agent for antimicrobial purposes in the nonsurgical treatment of periodontitis. Mechanical therapy, including periodontal debridement or scaling and root planing, has been shown to effectively reduce periodontal pathogens, inflammation, bleeding and probing depths, and to increase clinical attachment levels. The effectiveness of mechanical nonsurgical periodontal therapy (NSPT), aimed at the reduction or elimination of periodontal pathogens and conditions which harbor them, is diminished in the presence of difficult access including deep pockets, furcation defects and root concavities. Many periodontal pathogens are susceptible to low-power lasers in the presence of photosensitive dyes, for example, methylene blue, toluidine blue or phenothiazine chloride. These light-activated photosensitizers are cytotoxic to microorganisms associated with periodontal disease, resulting in cell death. Thus, aPDT has been suggested as an antimicrobial adjunct to NSPT. The term phototherapy differs from aPDT, as phototherapy refers to the use of lasers in conjunction with mechanical periodontal treatment to perform soft tissue debridement or curettage as well as to reduce periodontal pathogens in the periodontal pocket.

Based on the findings of these 2 studies, the ensuing conclusions regarding aPDT can be drawn:

- Although additional research is needed to strengthen the evidence and make a clinical recommendation for aPDT use, there is some evidence to support the use of aPDT as an adjunct to scaling and root planing (SRP), but not as a monotherapy, in the treatment of chronic and aggressive periodontitis (AgP).
- The findings of these articles regarding aPDT support the findings of a systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts conducted and published by a panel of experts convened by the American Dental Association Council on Scientific Affairs.[1]
  - There was a low level of evidence supporting the non-PDT DL (809 to 980 nm) based on a small gain in clinical attachment loss (CAL) (0.21 mm) compared with SRP alone, although the ADA found a moderate level evidence supported the use of the PDT DL in conjunction with a photosensitizing agent (0.53 mm gain in CAL).
- Studies regarding use of lasers in NSPT show significant heterogeneity in techniques used including power settings, laser wavelengths, length of exposures, fiber diameter, and number of applications. Standardized parameters for use are needed for research and practice.
- Clinicians need to consider the initial investment for required laser devices as well as the cost of photosensitizing agents and maintenance. These factors should be weighed against the low level of evidence supporting the use of aPDT for the treatment of periodontitis in practice.

Al Habashneh R, Asa'ad FA, Khader Y. Photodynamic therapy in periodontal and peri-implant diseases. *Quintessence Int*. 2015;46(8):677-690.

Abstract: In recent years, photodynamic therapy (PDT) using a combination of photosensitizer and laser light source has been used in periodontal therapy. The aim of this review is to provide an overview of the current status and use of PDT.

Data Sources: A review of pertinent literature was carried out in PubMed to determine the current position of PDT applications in periodontal and peri-implant diseases.

Conclusions: In spite of different results and suggestions from various researchers, the present review showed that use of PDT may help improve

periodontal outcomes. Therefore, it could become a new method for antibacterial treatment and may be used as an adjunct to or as conventional therapy for the treatment of periodontal and peri-implant diseases. Based on the results presented herein, there is promising, albeit preliminary, information regarding the benefits of PDT use on periodontal treatment outcomes. However, the conclusions are a reflection of a relatively small sample size and therefore need to be demonstrated in the general population.

Clinical Relevance: Periodontal diseases and peri-implantitis are among the specific targets where PDT can be applied.

Commentary

In this article, Al Habashneh et al reported the results of a review of the literature designed to evaluate the current status and use of PDT as an adjunct to SRP during initial nonsurgical and supportive periodontal therapy for periodontitis and peri-implantitis. The review is not a systematic review, so it cannot be considered the highest level of evidence available. The authors explain a meta-analysis would have been misleading because differences in published studies related to populations, methods, interventions and types of indices used to measure outcomes. A meta-analysis is a research approach which statistically combines results of several individual studies to increase the power of the results and strengthen the conclusions. When data collected in different studies are not similar, this approach is precluded. The next highest level of evidence; however, is the systematic review, an approach that involves a detailed and comprehensive plan and search strategy derived in advance to answer a specific research question, with the goal of reducing bias by identifying, appraising and synthesizing all relevant studies on a particular topic. The systematic review can be conducted without taking the next step of meta-analysis. A narrative literature review, such as this one, is mainly descriptive and does not involve the same level of systematic search of the literature. Nonetheless, this review of the literature is informative and provides an overview of pertinent literature gathered through a search of PubMed regarding PDT in initial NSPT and maintenance therapy.

PDT has been shown to kill periodontal pathogens such as *Porphyromonas gingivalis*, *Fusobacterium nucleatum* and *Aggregatibacter actinomycetemcomitans* (previously *Actinobacillus actinomycetemcomitans*) to name a few, within dental biofilm. Although many studies have shown effects in vitro, this article is focused on the clinical effects of PDT in vivo. The findings presented in the literature review by Al Habashneh et al showed agreement regarding the fact that PDT must be used in conjunction with mechanical periodontal therapy and not as a monotherapy to provide clinical benefits. Results of the in vivo studies indicated that PDT kills periodontal pathogens when used in conjunction with NSPT; however, findings regarding bleeding on probing, pocket depths and clinical attachment levels following PDT as an adjunct to SRP were mixed. The authors presented a summary of findings of many randomized controlled trials (RCTs) using these parameters. All RCTs included in the review used a split-mouth design. Despite the mixed results of these published RCTs, as well as differing conclusions drawn on the basis of the systematic reviews and meta-analyses discussed by these authors, they concluded that the evidence indicates PDT in conjunction with NSPT may improve periodontal outcomes for healthy patients with chronic periodontitis. The authors indicated, however, more research is needed to determine effectiveness of PDT in medically compromised patients and aggressive periodontitis, as well as in treatment of peri-implant disease and during supportive periodontal therapy. The exact protocol for using PDT as an effective adjunct to periodontal therapy also needs to be defined and standardized. However, according this review by Al Habashneh et al, PDT is safe to use given that the patient and clinicians wear protective glasses for protection of the eyes from inadvertent irradiation.

Readers are cautioned to consider conclusions of narrative literature reviews in relation to stronger evidence presented in reports of meta-analyses, systematic reviews and RCTs. However, the findings of this literature review are supported by the findings of a 2015 systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of SRP with or without adjuncts conducted and published by a panel of experts convened by the American Dental Association Council on Scientific Affairs.[1] That review found that a moderate level evidence supported the use of the PDT diode laser (0.53 mm gain in CAL) beyond root planing alone.

Vohra R, Akram Z, Safii SH, et al. Role of antimicrobial photodynamic therapy in the treatment of aggressive periodontitis: A systematic review. *Photodiagnosis Photodyn Ther*. 2015. pii: S1572-1000(15)30001-6.

Abstract: The aim was to assess the efficacy of antimicrobial photodynamic therapy (aPDT) in the treatment of aggressive periodontitis (AgP).

Methods: The addressed focused question was "Is aPDT effective in the treatment of AgP?" MED-LINE/PubMed, EMBASE, Scopus, ISI Web of knowledge and Google-Scholar databases were searched from 1977 till May 2015 using combinations of the following keywords: antimicrobial; photochemotherapy; photodynamic therapy; photosensitizing agents; AgP; scaling and root-planing (SRP). Reviews, case reports, commentaries, and articles published in lan-

guages other than English were excluded.

Results: Seven studies were included. In 5 studies, aPDT was performed as an adjunct to SRP. Laser wave-lengths and duration of irradiation ranged between 660–690 nm and 60–120 s, respectively. Laser power output as reported in 2 studies was 75 mW. One study showed significant improvement in periodontal parameters for subjects receiving aPDT as an adjunct to SRP as compared to treatment with SRP alone at follow up. However, comparable periodontal parameters were reported when aPDT as an adjunct to SRP was compared to SRP alone in the treatment of AgP in one study. One study showed comparable outcomes when aPDT was compared to SRP in the treatment of AgP. In two studies, adjunctive antibiotic administration to SRP showed significantly better outcomes when compared to application of adjunctive use of aPDT to SRP.

Conclusion: aPDT is effective as an adjunct to SRP for the management of AgP, however, further randomized clinical trials with well-defined control groups are needed in this regard.

Commentary

This study was a systematic review and meta-analysis conducted to assess the efficacy of adjunctive photodynamic therapy, or aPDT (PDT), laser therapy for patients with AgP. AgP is a rapidly progressive form of periodontitis that generally is found without congruent systemic diseases or dental deposits, such as biofilm and calculus. Although SRP is a common nonsurgical treatment approach for AgP, its effectiveness is limited in deeper pockets and areas of difficult access. Systemic antibiotics have been studied with some evidence supporting their use as an adjunct to SRP, although risks of resistant strains and side effects present concerns. Thus, aPDT has been studied as an adjunct to SRP to reduce the bacterial load.

The authors described the specific system for the literature review including databases searched (Cochrane CENTRAL and MEDLINE PubMed), search terms used and criteria for inclusion of quality studies designed to address a specific questions. Following the systematic review, data from the 7 articles included in the systematic review were statistically combined in a meta-analysis. Thus, the findings of this study provide the highest level of evidence available regarding using aPDT in the treatment of AgP.

Similar to the literature review previously discussed, all of the seven RCTs included in this systematic review used a split-mouth design. Comparisons made in split mouth designs involve using a different intervention on each half of the mouth in the same patient, in this case SRP plus aPDT versus SRP. The advantages of this design include controlling for individual variations between subjects and allowing for lower numbers of subjects in the clinical trial without a loss of statistical power. Results, however, might be affected by differences in disease patterns on one side of the mouth versus the other unless randomized or controlled. Effects of the 2 treatments may also carry over from one side of the mouth to the other. A split-mouth design should only be used when it is known that no such crossover exists, and it has been assumed that there is none for laser therapy. The methods outlined for aPDT use in the studies included differed in terms of power output, wavelengths used, fiber diameter, time of exposure and number of applications. This heterogeneity is less than ideal for the combination of data from all 7 studies in the meta-analysis. The lack of a defined protocol for aPDT also is a disadvantage to practitioners using the antimicrobial laser therapy as the evidence regarding effectiveness is not based on a given procedure that has been determined to be safe and efficacious. However, this review concluded more than 1 application is needed to sustain an antimicrobial effect for 12 weeks.

Outcomes and comparisons with other nonsurgical periodontal therapies used for AgP varied in the seven studies included in this systematic review. Findings indicated that aPDT as a monotherapy was comparable to SRP, and aPDT plus SRP was either comparable or better in reducing bleeding and pocket depths and increasing CAL. The 2 studies comparing SRP with adjunctive systemic antibiotics or aPDT showed more favorable outcomes for the antibiotics. All 3 studies that measured microbial patterns, found significant reductions in periodontal pathogens with aPDT use, especially *Aggregatibacter actinomycetemcomitans*. Mixed results were found in the studies that measured gingival crevicular fluid for inflammatory markers associated with immune response.

The authors concluded the evidence supports aPDT as an effective adjunct to SRP in treatment of AgP. However, more RCTs with specific control groups, standardized protocols, and comparisons with localized application of antibiotics are needed to interpret the efficacy of aPDT plus SRP in patients with AgP.

Summary

Dental hygienists are preventive professionals responsible for providing NSPT to address treatment needs of patients with periodontitis. Among other laser therapies, aPDT has been studied as an adjunct to SRP based on reported benefits in reducing periodontal pathogens in areas where SRP is less effective due to access challenges. The authors of these 2 articles concluded that evidence presented supports this laser therapy application for treatment of chronic periodontitis and AgP, despite mixed results

of studies conducted to date. Although aPDT may show some promise in outcomes such as periodontal disease parameters and reducing periodontal pathogens in periodontitis, standard protocols for use in practice and research are needed. Robust, parallel studies are needed with consideration given to adequate controls and treatment comparisons.

Denise M. Bowen, RDH, MS, is Professor Emeritus in Dental Hygiene at Idaho State University. She has served as a consultant to dental industry, as well as numerous government, university and private organizations and presently is a member of the National Advisory Panel for the National Center for Dental Hygiene Research in the U.S. She has served as Chair of the American Dental Hygienists' Association Council on Research and Chair of the Research Committee for the Institute for Oral Health and has received national awards for excellence in dental hygiene. Professor Bowen is widely known through her published articles and textbook chapters and dynamic continuing education programs related to nonsurgical periodontal therapy, preventive oral self-care, research methodology, and dental hygiene education.

References

1. Smiley CJ, Tracy, SL, Abt E, et al. Systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts. *J Am Dent Assoc*. 2015;146(7):508-524