

Anti-microbial Photo Dynamic Therapy (aPDT) in Endodontics: A Literature Review

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Abstract Elimination of root canal pathogens is one of the main objectives for successful outcome of root canal treatment. Conventional chemo-mechanical debridement is not always successful in removing all bacteria. Adjunctive use of antimicrobial photodynamic therapy (aPDT) can be used as a practical approach for successful elimination of all these bacteria. The aim of this review was to assess scientific literature that used various photosensitizers for bacterial reduction using aPDT methods. A search of the PubMed and Cochrane data bases using appropriate terms and keywords related to antimicrobial photodynamic therapy in endodontic disinfection was conducted. A hand search also was conducted in the preceding 5 years of several journals. Full texts of the selected articles were obtained and analyzed. A total of 177 articles published were identified at first stage of data extraction. After final screening, 41 articles were included in this review. This review summarizes the usage principles of aPDT and outlines the applications of aPDT in root canal disinfection procedures. It was concluded that aPDT should be used in conjunction with the conventional chemo mechanical debridement and disinfection of root canal system. It is critical to note that selection of photosensitizer dye, its correct delivery within the prepared root canal system, laser application with correct type of tips are predictors for successful outcome of this protocol of root canal disinfection.

Keywords: *Root canal disinfection, photodynamic therapy, E-faecalis*

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1. Introduction

Endodontic treatment outcome is dependent on the presence and absence of microbes inside the root canal system [1]. Failure of root canal treatment is attributed to various causes from persistence of bacteria after treatment to micro leakage from coronal restorations in cases of late failures [2]. Variations and complexities of the root canal system, in addition to composition of dentin, are the main challenges to disinfect the root canal system [3]. There are different antimicrobials that are common in practice [4]; however, anatomical variations and un-instrumented areas of the canal can reduce their effectiveness considerably.

To enhance the root canal disinfection properties of ordinary irrigants, using Anti-microbial photo dynamic therapy (aPDT) protocol is proposed. High power lasers due to their heat based destruction of microbes aided in developing the methods that are useful in root canals disinfection [5,6,7,8]. There are concerns of some undesirable effects on surface of radicular dentin that include carbonization and cratering with some lasers types e.g. Nd:YAG and carbon dioxide lasers, and this warrants following strict protocols to minimize these effects during use of these lasers for root canal disinfection [9].

2. Search methodology and Study Selection

A search was done of the PubMed and Cochrane databases using appropriate Medical Subject Headings terms and keywords related to use and application of aPDT in root canal disinfection. The following combination of MeSH terms and keywords were used: "anti-microbial photodynamic therapy" OR "photodynamic" OR "light activated disinfection" OR "photodynamic therapy" OR "photo-activated disinfection" AND "endodontics" OR "photodynamic therapy endodontics" OR "anti-microbial light activated disinfection root canal" OR "anti-microbial light activated disinfection endodontic" OR "photo-activated disinfection endodontics." No time limit was applied. One hundred seventy-seven articles published were identified. After removal of duplication and full text screening of all the studies 41 articles were selected. From each study information was gathered for this review.

3. Disinfection by Photochemical Process

A light of an appropriate wavelength is used to irradiate molecules of photosensitizer dyes, this promotes the target molecule to a high energy state also called triplet state that transfers its energy to oxygen molecule, which results in

reactive oxygen species (ROS) and singlet oxygen. Because resistance to ROS and singlet oxygen is extremely rare, hence it initiates the destruction of bacteria within the root canal system [7,9,10].

Two pathways are recognized for bactericidal mechanisms of aPDT [11]. The Type I pathway comprised of electron transfer reactions from photosensitizer triplet state that result in formation of free radicals. This reaction in bacterial environment produces hydroxyl radicals which combine to give rise to hydrogen peroxide and results in cytotoxicity. These reactions cause bacterial cell membrane lysis. Due to damage to other cell wall and cell membrane structures e.g. lipids and peptides, membrane enzymes and receptors are inactivated.

Type II pathway comprised of transfer of energy from photosensitizer to molecule of oxygen, which produces the singlet oxygen in an excited state. This can result in prompt oxidation of many bacterial molecules such as proteins, nucleic acids and lipids finally resulting in cytotoxicity. Because of short half-life of singlet oxygen, a localized response is predicted. Singlet oxygen not only reacts with molecules of cell wall and cell membrane architecture but also with ROS it results in DNA strand destruction, nuclear damage and mitochondrial disruption [11,12].

4. Antimicrobial Photo Dynamic Therapy (aPDT)

aPDT can be defined as “a method of disinfecting or sterilizing a hard tissue or soft tissue site by topically applying a photosensitizing compound to the site, and then irradiating this with laser light at a wavelength absorbed by the photosensitizing compound, so as to destroy microbes at the site” [13]. The damaging effects to bacteria are not associated with considerable alterations in temperature, hence not damaging to human vital tissues to an extent that can cause irreversible damage [14,15].

In aPDT, it is ensured that ROS and singlet oxygen are applied only to bacterial structures and not to human cells by selective distribution using a dye which only binds to microbes. It is essential that wavelength of laser light should be matched with the optical absorption properties of the photosensitizer dye.

5. Root Canal System in Diseased State

Obligate anaerobes are dominant species in the root canal microflora of necrosed teeth and a diseased periapex [16,17]. Because of absence of catalase, gram negative and strict anaerobes are more vulnerable to toxic effects of oxygen compounds. In contrast, Gram positive bacteria are more resistant to photosensitizing effects. The microflora of previously failed endodontic treatment is different from the primary root canal infections. Gram positive bacteria that includes *Enterococcus faecalis* are more frequently isolated in cases of refractory endodontic infections as compared to cases of primary endodontic treatment [1,18,19,20,21]. This bacterium if becomes inhabitant to root canal system is very difficult to remove with use of ordinary antimicrobial agents and root canal

irrigants [22,23,24]. Hence, in root filled teeth this bacterium can remain viable on behalf of nourishment from tissue fluids [25].

6. Photosensitizing Dyes

Tolonium chloride is found effective against clinically relevant Gram positive and Gram-negative bacteria [10,26]. Hence, in root canal system highly predictable and consistent bactericidal action of tolonium chloride is seen than other photosensitizer dyes [27,28]. All photosensitizing dyes are used in low concentration (0.001-0.01 %w/v) in aqueous solutions. [29,30]. This relative low concentration does not cause any tissue irritation and dentinal discoloration [31]. Photosensitizing liquid contains salts for optimum tonicity, buffers to ensure reliable aPDT effectiveness in different situations, preservatives, antioxidants and surfactants which has surface wetting effects [32]. The pH effects on penetration and binding of photosensitizers [33]. At higher pH levels, there is better penetration of dye into the bacteria as opposed to acidic environments, thus alkaline pH environments have trends to enhance photosensitization effects that also include enhanced cytotoxicity of singlet oxygen and increased life of excited molecular state in photosensitizing dye as compared to low energy inert state [34,35]. As far as safety to human tissues are concerned there are several studies including direct laboratory evidence [36] and animal study evidence [33,37] that aPDT procedures are safe to use with photosensitizing dyes including most commonly used photosensitizers for root canal disinfection procedure tolonium chloride and caries detection dye methylene blue [33,37,38,39,40,41].

Recently use of curcumin as a photosensitizer has gained attention. Peak absorption of curcumin occurs at around 450 nm, this is similar to LED devices [42]. Thus, it is necessary to connect the fiber optic to LED for optimum outcome of aPDT. Additionally, the fiber optic should be placed inside the canal. Results of different studies are in favor of irradiation by LED when curcumin was used as photosensitizer [43,44].

7. aPDT in Endodontics

aPDT is two stage process, this involves delivery of photosensitizer dye at first stage and then application of laser light, this produces a toxic photochemistry, leading to microbial destruction [45,46,47]. Successful eradication of various clinically relevant microbes notably *S. mutans* and *E. faecalis* have been reported using aPDT approach, with effective destruction of 97-99.9% of planktonic bacterial loads [48,49]. *S. intermedius* were killed also similarly completely within the root canal system [50]. aPDT can be used as an adjunct to usually performed mechanical root canal preparation and chemical disinfection procedures [24,51]. The combination of conventional mechanical root canal preparation and disinfection methods with aPDT resulted in greater reduction (>98%) of microbial loads clinically [27]. In another study, Garcez *et al.* [52] found that aPDT in combination with usual root canal treatment eliminated

completely antibiotic resistant species in teeth with necrosed pulps infected with microflora resistant to previous antibiotic treatment. It is also found that use of optical fiber for addition of aPDT within the root canal system is better than application of laser light directed at access cavity [53]. In a recent study, radial firing tip is found to be superior method of application of aPDT and significantly more viable *E. faecalis* were removed within the prepared root canals when compared to bare end fiber tips [54]. In a recent study Kasic S. et al. compared efficacy of three different lasers (Nd:YAG, Er:YAG and Er,Cr:YSGG) in root canal disinfection and found that Er,Cr:YSGG as most efficient tool in eradication of *E. faecalis* and *C. albicans* biofilms [47].

8. Method of Use

It is important that photosensitizing dye should be placed in contact with the radicular dentine free from blood or saliva, for a short time period e.g. 30 seconds to allow binding of microbes with the photosensitizer and hence becoming photosensitive. Slight agitation of dye solution will eliminate any trapped air and contact with bacteria will be more predictable [12]. For enhanced effects a radial firing tip with optimum emission pattern of light should be used [54]. This will also result in even distribution of light and eradication of bacteria up to a depth of 1mm ensuring effective disinfection of root canal system even in cases of persistent infection where microbes like *E. faecalis* may penetrate up to a depth of 150 μm [55,56].

9. Conclusion

Results of recent studies are encouraging to use of aPDT as an adjunct to the usual root canal preparation and irrigation techniques. This is particularly important in cases of previously failed endodontic treatment and refractory infections which are resistant to antibiotic therapy. Because bacterial biofilm is extremely difficult to remove with usual endodontic therapy, aPDT should be considered as practical approach in such cases due to its predictably successful outcome.

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