



Photodynamic Therapy in Endodontics

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ABSTRACT

Commonly used irrigants do not always eradicate the entire microbial flora in infected root canals. Therefore, several other strategies, such as photodynamic therapy (PDT) have been developed. Photoactivated disinfection is based on the interaction of a photosensitive antibacterial agent and a light source. It uses a nontoxic dye named photosensitizer (PS) and low-intensity visible light. In oxygen presentation, these combine to produce some cytotoxic species. The PS molecules attach to bacteria membrane. Irradiation with a specific wavelength of the light may lead to the production of singlet oxygen, resulting in rupture of the microbial cell wall. There are several applications for PDT in dentistry. A successful periodontal treatment is based on elimination of bacteria from the infected area. Phenothiazinium PSs have been shown to be highly effective and safe for this purpose. However, scaling/root planing should be performed before the PDT. While performing the PDT, PS should be first injected in the periodontal pocket and allowed to pigment. Then, the special fiber should be inserted 1 mm short of the pocket base and lased. Photodynamic therapy has also been used to disinfect caries dentin before restoration, disinfecting oral tissues before or during surgical procedures, treating denture stomatitis, and treating oral candidiasis in immunocompromised patients. Photodynamic therapy can be used in combination with mechanical instrumentation and chemical antimicrobial agents, such as sodium hypochlorite, too. The purpose of this study was to review historical

perspective, mechanism of action, and applications of PDT in dentistry and especially in endodontics was reviewed. Furthermore, the effects of PDT on dentin bonding and endotoxin are discussed.

Clinical significance: Photodynamic therapy has been advocated to increase the disinfection level of the root canal system.

Keywords: Chlorhexidine, *Enterococcus faecalis*, Photodynamic therapy, Sodium hypochlorite.

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INTRODUCTION

The essential effect of microorganisms on the development of pulpoperiapical lesions has been demonstrated in numerous animal and human studies. Due to the complex anatomy of the root canal system, elimination of microorganisms from infected root canal systems is a complicated task.¹⁻³

Chemical irrigation in endodontic treatment prepares a suitable bactericidal effect,^{4,5} however, commonly used irrigation solutions, such as chlorhexidine and sodium hypochlorite (NaOCl) and intracanal medicaments, such as calcium hydroxide cannot completely eradicate the entire microorganisms in infected canals.⁶

To increase the disinfection level of the root canal system, several other strategies, such as photodynamic therapy (PDT) have been developed.

HISTORICAL PERSPECTIVES

The earliest recorded therapies that exploited photosensitizer (PS) and light source can be found in ancient Indian and Egyptian sources. This, for example, included usage of topically applied plant substances to induce some photoreactions in the patient's skin and cause repigmentation in vitiligo.⁷

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Development of modern PDT was due to scientific progress in cancer biology and photobiology sciences and also development of modern photonic equipment, such as light emitting diodes and lasers.⁸ First, in 1981, photodynamic chemical therapy was introduced. Photodynamic therapy received even greater interest as a result of forming the International Photodynamic Association in 1986. The process and devices used today for PDT treatment were developed in the 1990s.

MECHANISM OF ACTION

Photoactivated disinfection (PAD) is based on the interaction of a photosensitive antibacterial agent and a light source. It uses a nontoxic dye [named photosensitizer PS] and low-intensity visible light. In oxygen presentation, these combine to produce some cytotoxic species. The PS molecules attach to bacteria membrane.^{9,10} Irradiation with a specific wavelength of the light may lead to production of singlet oxygen that results in rupture of the microbial cell wall.¹¹⁻¹³

Photosensitizers

Photosensitizer is a light-sensitive chemical that possesses low toxicity in the absence of light. Usage of PSs to photosensitization of infected tissues may allow uptake into the bacterial cells, and irradiation of the photosensitized tissues may result in destruction of both infected tissue and bacteria. The light should be used at a special wavelength, which relates to absorption wavelength of the PS being applied. Selectivity of PS toward bacteria over mammalian cells and effective removal of the causative bacteria are key points in successful usage of PDT to treat localized infection.^{14,15}

The most common PSs are phenothiazine, cyanine, phytotherapeutic agents, hematoporphyrin derivatives, and xanthene derivatives.¹⁶⁻¹⁸ Phenothiazine dyes have been claimed to have intense absorption in 620 to 660 nm wavelength and so be useful in PDT.¹⁹

Toluidine blue O and methylene blue are the most frequently used PSs. Sarkar and Wilson²⁰ demonstrated that toluidine blue O is effective against oral bacteria. Usacheva et al²¹ revealed that even in the absence of light, toluidine blue O interacts with lipopolysaccharides (LPS) of Gram-negative bacteria. However, Zeina et al²² showed that when exposed to a wavelength of 630 nm, it has a maximum level of absorption and good photodynamic properties for destroying different microorganisms. According to Chan and Lai,²³ methylene blue shows maximal absorbance when exposed to a wavelength of 660 nm. Soares et al^{24,25} and Fernandes et al²⁶ showed that toluidine blue O was preferred as a PS because it can easily pass through cell membrane.²⁷ These suitable

properties are shared by another dye, methylene blue,²⁸ however, toluidine blue O can interact with LPS of Gram-negative bacteria better than methylene blue.²¹

PHOTODYNAMIC THERAPY IN DENTISTRY

There are several applications for PDT in dentistry. A successful periodontal treatment is based on elimination of bacteria from the infected area. Phenothiazinium PSs have been shown to be highly effective and safe for this purpose.²⁹ However, scaling/root planing should be performed before the PDT. While performing the PDT, PS should be first injected in the periodontal pocket and allowed to pigment for 120 seconds. Then, the special fiber should be inserted 1 mm short of the pocket base and lased.³⁰

Photodynamic therapy has also been used to disinfect caries dentin before restoration, disinfecting oral tissues before or during surgical procedures, treating denture stomatitis, and treating oral candidiasis in immunocompromised patients.^{31,32}

With regard to bacteria involved in dental caries, Burns et al³³ showed that toluidine chloride (25 g/mL) used with 632.8 nm laser energy reduced the viability of *Streptococcus mutans*, *Streptococcus sobrinus*, *Lactobacillus casei*, and *Actinomyces viscosus*. This finding was confirmed by some other studies. Wilson³⁴ determined whether *Streptococcus sanguis* could be destroyed using a light-activated antibacterial agent. No significant decrease in the viable count was found when either the aluminum disulfonated phthalocyanine (AIPcS2) or the laser light was used alone. There was a light dose-related decrease in the viable counts of irradiated AIPcS2-treated biofilms. According to Williams et al,³⁵ current clinical protocols for PAD treatment of carious dentin include the use of a 0.8 mm diameter spherical isotopic diffuser to give even irradiation of the cavity floor.

EFFECT ON BOND STRENGTH

An *in vitro* study evaluated the effect of the PAD system on the bond strength of AH Plus, Sealapex, and MTA Fillapex root canal sealers using the push-out test design. Findings revealed that AH Plus and MTA Fillapex sealers had greater bond strength compared with Sealapex root canal sealers. It was also revealed that the PAD system adversely affected the bond strength of the MTA Fillapex root canal sealer to dentin.³⁶

EFFECT ON ENDODONTIC MICROBIOTA

Photodynamic therapy can be used in combination with mechanical instrumentation and chemical antimicrobial agents, such as NaOCl and hydrogen peroxide. Garcez et al³⁷ showed that endodontic treatment alone reduced 90% of bacteria, whereas PDT alone reduced it by 95%.

The combination of these two reduced bacteria by 98%. In another study, Garcez et al³⁸ showed that endodontic treatment alone may produce a significant decrease in microbial count, whereas using the combination of endodontic treatment with PDT all teeth were bacteria-free. Garcez et al³⁹ also demonstrated that usage of PDT added to endodontic treatment of infected canals with the optical fiber may be better than when the laser is used directed at the cavity.

Meire et al⁴⁰ compared the antimicrobial efficacy of neodymium-doped yttrium aluminum garnet (YAG), erbium-doped YAG (Er:YAG), two commercial antimicrobial PDT (aPDT) systems, and revealed that NaOCl is the most effective, while Er:YAG laser also resulted in high reductions of bacteria. Both aPDT systems resulted in a weak reduction of bacteria.

George and Kishen^{41,42} showed that PDT destroyed the integrity of cell wall, deoxyribonucleic acid, and membrane proteins of bacteria. Damage degree was influenced by PS solvent employed during PDT. Soukos et al⁴³ used methylene blue as PS and concluded complete elimination of all bacteria except *Enterococcus faecalis*. William et al⁴⁴ also showed that PAD can kill endodontic microorganisms at significant levels.

EFFECT ON ENDOTOXIN

Endotoxin is a part of the cell wall of Gram-negative bacteria, composed of lipids, polysaccharides, and proteins and referred to as Lipopolysaccharides (LPS).⁴⁵ When free to act, endotoxins cause no cell pathosis, but they can stimulate competent cells to release some chemical mediators.⁴⁶ Macrophages have been considered as the main target.^{46,47}

Endotoxins can act on neutrophils, macrophages, and fibroblasts, leading to release of a large number of inflammatory mediators, such as tumor necrosis factor, alpha-interferon, interleukin (IL)-1, IL-5, IL-8, and prostaglandins.⁴⁵

Shrestha et al⁴⁸ showed that antibacterial PDT with chitosan-conjugated rose Bengal nanoparticles can result in inactivation of LPS and subsequent reduction of all inflammatory markers.

PHOTOACTIVATED DISINFECTION IN REGENERATIVE ENDODONTICS

In a case report, Johns et al⁴⁹ described a new protocol for pulp revascularization with canal disinfection using a combination of a low-power laser light and PS solution. After the irrigation of the infected root canal using NaOCl and drying with paper points, PDT used to disinfect the canal, and platelet-rich fibrin was applied to revitalize the pulp. Then, canal was sealed with mineral trioxide aggregate, and permanent restoration was inserted. Follow-up

radiograph showed root lengthening, continued thickening of the canal walls, and apical closure.

BIOLOGICAL RESPONSE TO PHOTODYNAMIC THERAPY

The biological response to PDT is influenced by dye concentration, preirradiation period, environmental pH, light source, presence of exudates, and energy dose. One minute is considered to be sufficient to achieve cellular uptake of toluidine blue O, and 5 minutes to achieve that of methylene blue.^{50,51}

Bhatti et al⁵² demonstrated a dose-dependent relationship between concentration of toluidine blue O and its lethal effect. However, others showed that low concentrations of toluidine blue O produced optimal killing of *Cryptococcus gattii*.^{24,53} Some other studies also found that increase in concentration of methylene blue may cause a decrease in number of colonies recovered after the irradiation.^{54,55}

CONCLUSION

Several strategies, such as using intracanal medicaments, e.g., calcium hydroxide, irrigation solutions, e.g., NaOCl and chlorhexidine, and PDT have been advocated to increase the disinfection level of the root canal system.⁵⁶⁻⁵⁸

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