

USING PHOTODYNAMIC THERAPY IN ROOT CANAL SYSTEM – A LITERATURE REVIEW

AJITHA P*

Department of , Saveetha Dental College, Chennai, Tamil Nadu, India. E-mail: ajitharijesh@gmail.com

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ABSTRACT

Microorganisms do play in pulpal and periapical infection. Success of endodontic treatment aims at effective eradication of bacteria from the root canal space. This, in turn, prevents further microbial recolonization. Persistent microbial colonies in the root canal lead to failure of the endodontic treatment. With the advent of photodynamic therapy (PDT), a novel invasive approach is aimed at complete disinfection of root canal with elimination of bacteria. Therefore, this paper aims to highlight the efficiency of PDT in endodontics by reviewing the literature published in journals

Keywords: Bacteria, *Enterococcus faecalis*, Microorganism, Photodynamic therapy, Root canal.

INTRODUCTION

Various microorganisms play an important role in pulpal and periapical infection. The reason for this failure is due persistence of microorganism causing infection by formation of biofilm [1,2]. Primary endodontic infections are associated with Gram-negative anaerobic rods whereas secondary endodontic infections are associated with Gram-positive bacteria with no apparent facultative anaerobes [3].

Persistent microbial infections and anatomical alterations of the root canal in the apical region due to its complexity do not disinfect the canal completely. Moreover, in secondary infection, the most commonly isolated bacteria are *Enterococcus faecalis* [4]. The success of treatment in such case needs an additional treatment of microbial elimination and disinfection.

Aiming to increase the efficiency of disinfection, photodynamic therapy (PDT) also known as photo activated disinfection or photo chemotherapy was developed [5] PDT is a non-invasive approach developed in recent years. This paper highlights the efficiency of PDT in endodontics by reviewing the literature published in journals.

HISTORY

Over 100 years back, first report showed the association between dye and light producing antimicrobial effect [6]. In the year 1900, Raab and von Tappeiner [7] found that red acridine absorb ambient light and produce toxic effect on protozoa.

Gordon Gould in the year 1957 introduced the term light amplification by stimulated emission of radiation (LASER) [8]. Helium neon laser was first invented by Ali Javan in 1960 [8]. Robert Hall invented diode laser in the year 1962 [8]. In the same year, EndreMester introduced low level laser therapy [9]. At present, it is known that various microorganisms can be eliminated by activating a nontoxic photosensitizing using a resonant light source [10].

PDT

Light-induced inactivation of microorganism is defined as PDT [11]. The use of photosensitizer (PS), that is, photo activated dye, at a specific wavelength gets activated by light in the presence of oxygen [12,13].

PS

The properties of PS are low cytotoxicity, photosensitivity, simplicity, reducibility, high stability, high affinity, and bacterial penetrability [14]. PS is a light sensitive non-toxic dye. PS when irradiated by light of suitable of wavelength, result in destruction of microorganisms 0.5–1.5

cm depth of penetration will be achieved when the PS absorbs light of a wavelength between the range of 630 and 700 nm. Cyanines are capable of absorbing light when irradiated at a wavelength of 600–805 nm. Phytotherapeutic agents absorb light at 550–700 nm. At a range of 620–650 nm hematoporphyrin derivatives absorb light. AP phenothiazine derivative such as Toluidine blue and Methylene blue which absorbs light at a wavelength of 620–700 nm [15]. In endodontics, the most commonly used PS is phenothiazine derivatives.

PS can be divided into three types based on antimicrobial purpose. The PS that strongly binds the microorganism, example chlorine. PS which weakly binds are Phenothiazine derivative and PS which does not bind is Rose Bengal [16]. It was stated that there was an increase in antibacterial efficiency when concentration of methylene blue and light energy fluence is increased [17].

Toluidine blue even in the absence of light interacts with lipopolysaccharide of Gram-negative bacteria [18]. Previous report stated that when exposed to a maximum absorption, destruction of microorganisms take place at a wavelength of 630 nm [19].

LIGHT SOURCE

The light of suitable wavelength should be used for effective treatment; therefore, LASER light should be preferred [4]. Every light source has a specific wavelength such as Helium-Neon lasers (633 nm), Gallium-Aluminum-Arsenide diode lasers (630–690, 830, or 906 nm), and argon lasers (488–514 nm) [4]. For effective microbial reduction, the most commonly used light sources are Helium Neon and diode laser [20].

At present, non-laser source of light such as light emitting diode is being used because it is less expensive, light weight, and flexible [4].

MECHANISM OF ACTION

On irradiation of light at a particular wavelength, there occurs transition of PS to excited singlet state from ground state. The PS then either return back to ground state with fluorescence emission or exist in high energy triplet state. At this stage, two types of reactions take place.

In first type of reaction, direct transfer of electron or hydrogen from PS produce electron or hydrogen removal from the substrate molecule to form free radical. This free radical reacts with oxygen resulting in highly reactive oxygen species leading to destruction of microorganism [21].

In second type of reaction, excited state oxygen gets released namely singlet oxygen causing rapid destruction of selected tissues. It is stated

that type 2 reactions are the most accepted pathway as the majority of the microbial cell undergo destruction [21].

COMPARATIVE STUDIES

Ng *et al.* [22] selected extracted teeth with pulp necrosis. The study was done comparing 6% sodium hypochlorite and PDT usage. The concentration of methylene blue used was 50 µg/mL and diode LASER at a wavelength of 665 nm connected to an optical fiber. The result showed PDT was able to eliminate 86.5% of microorganisms in the canal and only 49% microbial elimination when PDT was not used.

The previous reported that 2.5% sodium hypochlorite and PDT using 15 µg/mL Toluidine blue and diode LASER at a wavelength of 625 nm eliminate *E. faecalis* in single-rooted canals of freshly extracted teeth [23].

It was reported that of 0.01% of methylene blue, when activated at a wavelength of 660 nm produce large amount of singlet oxygen which resulted in reduction of microorganism [25]. Pagonis *et al.* [25] reported eradication of *E. faecalis* in experimentally infected root canals when irradiated using poly lactic-co-glycolic acid nanoparticles loaded with methylene blue (50 µg/mL).

In an extracted tooth survival rate of *E. faecalis* within the root canal is 0.1% when PDT is used along with 6% sodium hypochlorite. PDT or sodium hypochlorite when used separately showed survival rate of microorganisms to be 2.9% and 0.66%, respectively [26]. Endodontic treatment showed better results with the use of optic fiber when compared to LASER light directed into the access cavity against *E. faecalis* [27].

On comparing the efficacy of PDT in planktonic suspensions and mono-species biofilm *Pseudomonas aeruginosa* and *E. faecalis*, it was reported that there was increase in antibacterial efficiency when formulation of PS was modified [28].

Use of oxidant and an oxygen carrier along with methylene blue resulted in increased potential of photo-oxidation and generation of singlet oxygen of PDT, leading to the disruption of the biofilm matrix of *E. faecalis* in root canals [29].

It was reported that there was a substantial decrease in microbial count in primary endodontic infections with Toluidine blue O -mediated PAD [30].

The previous study reported effective elimination of biofilm formed by *E. faecalis* in polystyrene plate when microbial efflux pump inhibitor was added along with methylene blue [31]. The studies reported that PDT alone showed greater reduction in bacteria than PDT with 3–6% sodium hypochlorite, or conventional chemomechanical preparation. It was seen that both sodium hypochlorite and chemomechanical preparation when used alone showed better results in bacterial reduction [32,33].

Samiei *et al.* [34] concluded that 2.5% NaOCl was significantly better than that of PDT technique. In addition, 2.5% NaOCl was significantly better than 2% chlorhexidine (CHX). Bolhari *et al.* [35] reported that use of adjunctive antimicrobial PDT in combination with 2.0% CHX was an effective approach for reduction *E. faecalis* biofilm within the root canal space.

Shrestha *et al.* [36] reported that lipopolysaccharide and other inflammatory markers can be inactivated by combining PDT with

Table 1: Various studies done using photodynamic therapy and the percentage of bacterial elimination in root canal

Reference	Year	Study type	Microorganism	Bacteria ↓
Seal <i>et al.</i>	2002	<i>Ex vivo</i>	<i>Staphylococcus intermedius</i>	5log10
Bonsor <i>et al.</i>	2006	<i>In vivo</i>	<i>Staphylococcus intermedius</i> naturally infected teeth	96.7%
Bonsor <i>et al.</i>	2006	<i>In vivo</i>	Polymicrobial naturally infected teeth	91%
Williams <i>et al.</i>	2006	<i>In vivo</i>	<i>Fusobacterium nucleatum</i> , <i>Peptostreptococcus micros</i> , <i>Prevotella intermedia</i> , and <i>Staphylococcus intermedius</i>	99%
Silva Garcez <i>et al.</i>	2006	<i>Ex vivo/In vivo</i>	<i>Enterococcus faecalis</i>	99.2%
Soukos <i>et al.</i>	2006	<i>Ex vivo/In vivo</i>	<i>Porphyromonas gingivalis</i> , <i>Prevotella intermedia</i> , <i>Fusobacterium nucleatum</i> , <i>Peptostreptococcus micros</i> , <i>Porphyromonas endodontalis</i> , <i>Enterococcus faecalis</i>	97%
George and Kishen	2007	<i>In vitro/ex vivo</i>	<i>Aggregatibacter actinomycetemcomitans</i>	100/97%
Garcez <i>et al.</i>	2007	<i>ex vivo</i>	<i>Enterococcus faecalis</i>	98%
Foschi <i>et al.</i>	2007	<i>ex vivo</i>	<i>Pseudomonas aeruginosa</i> , <i>Proteus mirabilis</i>	77.5%
Fimple <i>et al.</i>	2008	<i>ex vivo</i>	<i>Enterococcus faecalis</i>	> 80%
Garcez <i>et al.</i>	2008	<i>In vivo</i>	<i>Porphyromonas gingivalis</i> , <i>Prevotella intermedia</i>	99.9%
Bergmans <i>et al.</i>	2008	<i>Ex vivo</i> 93.8/88.4	Polymicrobial naturally infected teeth	93.8/88.4
George and Kishen	2008	<i>In vitro/Ex vivo</i>	<i>Streptococcus anginosus</i> , <i>Enterococcus faecalis</i> , <i>Fusobacterium nucleatum</i>	100%
Fonseca <i>et al.</i>	2008	<i>Ex vivo</i>	<i>Enterococcus faecalis</i>	99.9%
Lim <i>et al.</i>	2009	<i>Ex vivo</i>	<i>Enterococcus faecalis</i>	99.99%
Pagonis <i>et al.</i>	2010	<i>In vitro/Ex vivo</i>	<i>Enterococcus faecalis</i>	84.8%
Souza <i>et al.</i>	2010	<i>Ex vivo</i>	<i>Enterococcus faecalis</i>	> 99.48%
Upadya and Kishen	2010	<i>In vitro</i>	<i>Enterococcus faecalis</i>	100/99%
Kishen <i>et al.</i>	2010	<i>In vitro</i>	<i>Enterococcus faecalis</i>	100%
Garcez <i>et al.</i>	2010	<i>In vitro</i>	Polymicrobial/naturally infected teeth	100%
Schlafer <i>et al.</i>	2010	<i>In vitro/ex vivo</i>	<i>Escherichia coli</i> , <i>Candida albicans</i> , <i>Enterococcus faecalis</i> , <i>Fusobacterium nucleatum</i>	99.75%
Rios <i>et al.</i>	2011	<i>ex vivo</i>	<i>Enterococcus faecalis</i>	99.9%
Nunes <i>et al.</i>	2011	<i>ex vivo</i>	<i>Enterococcus faecalis</i>	> 99.41%
Garcez <i>et al.</i>	2013	<i>ex vivo</i>	<i>Enterococcus faecalis</i>	99.99%
Cheng <i>et al.</i>	2012	<i>ex vivo</i>	<i>Enterococcus faecalis</i>	96.96%
Shrestha <i>et al.</i>	2012	<i>In vitro</i>	<i>Enterococcus faecalis</i>	100%
Shrestha and Kishen	2012	<i>In vitro/Ex vivo</i>	<i>Enterococcus faecalis</i>	27–98%
Bago <i>et al.</i>	2013	<i>Ex vivo</i>	<i>Enterococcus faecalis</i>	99.99 %

chitosan conjugated rose Bengal Nanoparticles. George and Kishen [37] reported that PDT cause damage of cell wall integrity, deoxyribonucleic acid, and bacterial membrane protein. During PDT, PS influences the degree of damage. The previous report has shown that diode laser along with Pyoktanin was effective in eradication of *E. faecalis* without having any toxicity to human dermal fibroblasts [38].

CONCLUSION

Use of PDT has potential advantage such as lack of scarring, highly selective tissue necrosis, significant reduction in bacteria, and precise directing the laser light using fiber optics. The most important advantage is that even after repeated exposures resistant to treatment do not occur. Thus, PDT is an important auxiliary tool for an effective disinfection of root canal.

REFERENCES

- Nair PN, Figdor D. Persistent periapical radiolucencies of root-filled human teeth, failed endodontic treatment and periapical scan. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999;87:617-27.
- Plotino G, Grande N, Mercade M. Photodynamic therapy in endodontics. *Int Endod J* 2018;52:760-74.
- Siqueira J. Aetiology of root canal treatment failure: Why well-treataed teeth can fail. *Int Endod J* 2001;34:1-10.
- Gomes BP, Gade Neto CR. Microbiological examination of infected dental root canals. *Oral Microbiol Immunol* 2004;19:71-6.
- Takasaki AA, Mizutani K, Scharz F, Sculean A, Wang CY, Koshy G, et al. Application of antimicrobial photodynamic therapy in periodontal and periimplant disease. *Periodontol* 2009;51:109-40.
- Ackroyd RK, Brown N, Reed M. The history of photo detection and photodynamic therapy. *Photochem Photobiol* 2001;74:656-69.
- Raab O. Über die wirkung fluoreszierender stoffe auf infusorien. *Z Biol* 1900;39:524-46.
- Weiner GP. Laser dentistry practice management. *Dent Clin North Am* 2004;48:1105-26.
- Mester EL, Selyei M, Szende B, Total GJ. The stimulating effect of low power laser rays on biological systems. *Laser Rev* 1968;1:3.
- De Oliveira BP, Camara AC. Photodynamic therapy in combating the causative micro organisms from endodontic infections. *Eur J Dent* 2014;8:424-30.
- Dougherty TJ, Henderson BW, Jori G, Kessel D, Korbelik M. Moan J, et al. Photodynamic therapy. *J Natl Cancer Ins* 1998;90:889-905.
- Mohammadi ZJ, Shalavi S, Kinoshita JI. Photodynamic therapy in endodontics. *J Contemp Dent Pract* 2017;18:534-8.
- Mohammadi ZJ, Shalavi S, Yari pour S, Sharifi F, Kinoshita JI. A review on triple antibiotic paste as a suitable material used in regenerative endodontics. *Iran Endod J* 2018;13:1.
- Konopka KE. Photodynamic therapy in dentistry. *J Dent Res* 2007;86:694-707.
- Meisal PK. Photodynamic therapy for periodontal diseases: State of the art. *J Photochem Photobiol B* 2005;79:159-70.
- Hamblin MR. Photodynamic therapy: A new antimicrobial approach to infectious disease? *Photochem Photobiol Sci* 2004;3:436-50.
- Fimple JL, Foschi F, Ruggiero K, Song X, Pagonis TC. Photodynamic treatment of endodontic polymicrobial infection. *J Endod* 2008;34:728-34.
- Usacheva MN, Biel MA. Comparison of the methylene blue and toluidine blue photobactericidal efficacy against gram-positive and gram-negative microorganisms. *Lasers Surg Med* 2001;29:165-73.
- Zeina BG, Purcell WM, Das B. Killing of cutaneous microbial species by photodynamic therapy. *Br J Dermatol* 2001;144:274-8.
- Soukos NS, Morris JT, Ruggiero K, Abernethy AD, Som S, Foschi F, et al. Photodynamic therapy for endodontic disinfection. *J Endod* 2006;32:979-84.
- Foote C. Definition of Type I and Type II photosensitized oxidation. *Photochem Photobiol* 1991;54:659.
- Ng RS, Papamanou DA, Song X, Patel C, Holewa C. Endodontic photodynamic therapy. *J Endod* 2011;37:217-22.
- Vaziri SK, Shahbazi R, Nasab AN, Naseri M. Comparison of the bactericidal efficacy of photodynamic therapy, 2.5% sodium hypochlorite, and 2% chlorhexidine against *Enterococcus faecalis* in root canals; an *in vitro* study. *Dent Res J* 2012;9:613.
- Komine CT. A small amount of singlet oxygen generated via excited methylene blue by photodynamic therapy induces the sterilization of *Enterococcus faecalis*. *J Endod* 2013;39:411-4.
- Pagonis TC, Fontana CR, Devalapally H, Ruggiero K, Song X. Nanoparticle-based endodontic antimicrobial photodynamic therapy. *J Endod* 2010;36:322-8.
- Rios AH, Glickman GN, Spears R, Schneiderman ED, Honeyman AL. Evaluation of photodynamic therapy using a light-emitting diode lamp against *Enterococcus faecalis* in extracted human teeth. *J Endod* 2011;37:856-9.
- Garcez AS, Rodriguez HM, Nunez SC, Sabino CP, Suzuki H. The use of optical fiber in endodontic photodynamic therapy. Is it really relevant? *Lasers Med Sci* 2013;28:79-85.
- Upadya MH, Kishen A. Influence of bacterial growth modes on the susceptibility to light-activated disinfection. *Int Endod J* 2010;43:978-87.
- George SK. Augmenting the antibiofilm efficacy of advanced noninvasive light activated disinfection with emulsified oxidizer and oxygen carrier. *J Endod* 2008;34:1119-23.
- Pourhajibagher M, Bahador A. An *in vivo* evaluation of microbial diversity before and after the photo-activated disinfection in primary endodontic infections: Traditional phenotypic and molecular approaches. *Photodiagn Photodynam Ther* 2018;22:19-25.
- Kishen AU, Tegos GP, Hamblin MR. Efflux pump inhibitor potentiates antimicrobial photodynamic inactivation of *Enterococcus faecalis* biofilm. *Photochem Photobiol* 2010;86:1343-9.
- Bouillaguet SW, Zapata O, Campo M, Lange N, Schrenzel J. Production of reactive oxygen species from photosensitizers activated with visible light sources available in dental offices. *Photomed Laser Surg* 2010;28:519-25.
- Foschi FF, Ruggiero K, Riahi R, Vera A, Doukas AG, Pagonis TC, et al. Photodynamic inactivation of *Enterococcus faecalis* in dental root canals *in vitro*. *Lasers Surg Med* 2007;39:782-7.
- Samiei MS, Abdollahi AA, Eskandarinezhad M, Negahdari R, Pakseresh Z. The antibacterial efficacy of photo-activated disinfection, chlorhexidine and sodium hypochlorite in infected root canals: An *in vitro* study. *Iran Endod J* 2016;11:179.
- Bolhari BP, Bazarjani F, Chiniforush N, Rad MR, Pirmoazen S, Bahador A. *Ex vivo* assessment of synergic effect of chlorhexidine for enhancing antimicrobial photodynamic therapy efficiency on expression patterns of biofilm-associated genes of *Enterococcus faecalis*. *Photodiagn Photodynam Ther* 2018;22:227-32.
- Shrestha AC, Kishen A. Photo activated polycationic bioactive chitosan nanoparticles inactivate bacterial endotoxins. *J Endod* 2015;41:686-91.
- George SK. Photo physical, photochemical, and photo biological characterization of methylene blue formulations for light-activated root canal disinfection. *J Biomed Opt* 2007;12:034029.
- Masuda YS, Horiike M, Kadokura H, Yamasaki T, Klokkevold PR, Takei HH, et al. Photodynamic therapy with pyoktanin blue and diode laser for elimination of *Enterococcus faecalis*. *In Vivo* 2018;32:707-12.