

Photodynamic Therapy - A Review

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Abstract: Development of resistance against antibiotics and side effects of the drugs has urged to search for alternatives; to eliminate the micro-organisms from the root canal system. Failure in root canal therapy has been accounted for insufficient removal of the micro-organisms, which has been attributed to the intricate nature of dental anatomy, which in turn strongly limits the effect of mechanical debridement. Moreover, the lateral canals and apical ramifications are inaccessible to root canal instrumentation. Methods of root canal disinfection that supports the chemo-mechanical debridement have a strong bactericidal effect, but the commonly used irrigants, such as sodium hypochlorite or chlorhexidine digluconate do not always eradicate the entire microbial flora. Currently, Photoactivated disinfection (PAD) has been proposed as an alternate adjunct to conventional endodontic disinfection.

Key words: Photodynamic • Disinfection • Photosensitizer

INTRODUCTION

The success of endodontic treatment is to thoroughly clean and shape the root canal system, which is enable to seal the canal with microbial free tight filling. The literature review stated the success rate of 85%, but periapical radiolucency were prevalent in 15 - 20% of all the root canal treated teeth [1]. Failure in endodontic therapy has been accounted for insufficient removal of the micro-organisms from the root canal system. Currently endo pathogens have developed a variety of strategies to survive in adverse conditions [2]. Therefore, the main goal of endodontic therapy is to eliminate the bacterial infection from the root canal space and allow healing of the periapical infection. Elimination of micro-organism from the infected root canal system is a complex task. Although the bulk of infective micro-organisms are removed through chemo-mechanical debridement procedure, residual bacteria are still readily detectable in approximately one-third of the teeth at the time of obturation [3]. This has been attributed to the complexity of the root canal system that make complete debridement of the bacteria almost impossible even when conventional or automated methods of endodontic instrumentation and irrigation are performed. Thus debridement of the root

canal space is critical and the need for better root canal disinfection is clear and compelling. Currently, the use of photodynamic therapy (PDT) has become an alternate method for root canal disinfection.

The word photodynamic means the applications of dynamics of photons of light on the biological molecules. German physician Friedreich Mayer performed the first study, which was first called as photo-radiation therapy with porphyrins (1913) in humans. It is also know as photo-radiation or phototherapy which involves the use of a photoactive dye that is activated by exposing it to a specific light source in the presence of oxygen [4]. The PDT was first developed at the beginning of 20th century in Munich when Oscar Rab and his professor, Herman noticed the effects of photosensitivity. It is an emerging treatment modality that employs the photochemical interaction of 3 components: light, photosensitizer (PS) and oxygen. It became popular after the invention of laser, which allowed the production of monochromatic light that could be easily coupled into optical fibres. This optical fibre enable the light can to be directed easily to the desired region.

PDT has been used for the treatment of non-malignant and malignant diseases from head to toe. It is a disease site-specific treatment modality. In the recent

years various novel antimicrobial approaches to disinfect root canals have been proposed that include the use of high power lasers as well as PDT [5-7]. It is a new antimicrobial strategy that involves the combination of non toxic PS and a harmless visible light source. The excited PS reacts with the molecular oxygen to produce highly reactive oxygen species, which cause injury and death of micro-organisms. It has the advantage of dual selectivity in that the PS can be targeted to its destination cells and in addition the illumination can be spatially directed to the lesions. It is stated that the PS, which possess a pronounced cationic energy can charge rapidly, which in turn bind and penetrate in to the bacterial cells and therefore have a high degree of selectivity for killing micro-organisms when compared to host mammalian cells [8].

Principle: It is based on the principle that when the PS is excited by light source of suitable wavelength, it is activated from the ground level to the triplet state and produce free radicals, which have a site-specific toxic effect to the cells. Longer the life time of the triplet state, enables the excited PS to interact more with the surrounding molecules which leads to the formation of cytotoxic products. These products usually cannot migrate more than > 0.02 mm after its formation and thus it is ideal for local application, since and hence it avoids damage to the distant molecules, cells and organelles [9]. Several studies have shown that PDT is lethal to most of the bacteria except for some gram-negative bacteria because they have a special cell wall due to which PDT is less effective [10].

Reaction: There are two types of reaction by which the triplet state PS can react with the biomolecules

Type I Pathway: It involves electron transfer reaction directly from the PS producing ions or electrons/hydrogen removal with the participation of a substrate molecule to produce free radical ions that rapidly react with oxygen to produce highly reactive oxygen species such as super oxide, hydrogen peroxide, hydroxyl radicals and lipid derived radicals.

Type II Pathway: It produces electronically excited and highly reactive state of oxygen known as singlet oxygen, which can oxidize many biological molecules such as proteins, nucleic acids and lipids and lead to cytotoxicity. In PDT, it is difficult to exactly delineate between the two reactions mechanisms. The mechanism of damage is by

contribution of both the reactions which in turn depends on oxygen tension and photosensitizer concentration.

Procedure: The PS agent is administered into the tissue followed by its activation with light of a specific wavelength. The wavelength of light range between 600-800nm and is called 'therapeutic window'. In this range the energy of each photon is high enough to excite the photosensitizer and yet it is low enough so that the light has sufficient penetration into the tissue. It consists of two stages; initially the PS is accumulated in the target tissue following topical or systemic administration. Then in the second stage, the PS is exposed to light at absorption spectrum of the PS agent. This activated agent transfers energy to the molecular oxygen generating reactive oxygen species (ROS) [9,10]. These ROS cause subsequent oxidization of lipids, amino acids and proteins which in turn induces necrosis and apoptosis of the cells [11]. In addition, ROS indirectly stimulate the transcription and release of inflammatory mediators. Oxidization of the cell constituents by ROS damages the plasma membrane and the cell organelles with a subsequent alteration in permeability and transport functions between the intra and extra-cellular media. The two basic mechanisms that accounts for the lethal damage are:

- DNA damage.
- Damage to the cytoplasmic membrane allowing leakage of cellular contents or inactivation of membrane transport system and enzymes

The three major component of this PDT are:

Photosensitizer: Various photosensitizing agents are available and the most commonly used PS in dentistry are

- Tolonium chloride - peak absorption, 633 nm
- Methylene blue - peak absorption, 670 nm
- Rose Bengal - peak absorption, 550 nm
- Aluminium disulphonated phthalocyanine - peak absorption, 675 nm
- Porphyrin conjugates, polysine conjugates and chlorine conjugate are with different peak absorption.

The most widely available photosensitizer are 5-aminolevulinic acid (ALA) and its lipophilic derivative methyl-aminolevulinate (MAL). Some new second generation synthetic sensitizing drugs are derived from benzoporphyrins, phthalocyanines, chlorines and

porphyrins [5,12]. They can be either systemic or topical PS depending on the type of agent, it may be injected intravenously, applied topically, or ingested orally.

The Ideal Characteristics of a PS Include:

- Chemical purity non-toxic.
- Ability to target the tissue, cost-effective, easily available.
- Short interval between administration of the drug and peak accumulation in the tissue.
- Short half life.
- Rapid elimination from normal tissue.
- Activation at wavelength at which penetration in to the target tissue is very good.
- Ability to produce a large amount of cytotoxic products.

Light: PDT require light source to activate the PS agent at a specific wavelength and the light source available for PDT belongs to three major groups

- Broad spectrum lamps
- Light emitting diode lamps
- Lasers.

Most of the PS are activated by red light ranging between 630 - 700 nm. PDT added to endodontic treatment lead to an enhanced decrease of bacterial load and may be an appropriate approach for the treatment of oral infection. Antimicrobial PDT offers an efficient non-toxic means of destroying micro-organisms remaining inside the root canal system after using conventional endodontic chemo-mechanical therapy. Thus PDT can be used as an adjuvant to conventional endodontic treatment. Its application has an adjunctive benefit besides mechanical treatment at sites with difficult access [13-15]. Thus it increases the patient comfort and decrease treatment time.

Uses: It is used to disinfect

- All types of carious lesions.
- Fissures before sealing
- Periopockets / mucosal disease.
- Site of peri-implantitis.
- Viral / fungal disease
- Oral biofilm such as plaque.

Safety:

- Does not cause any deleterious thermal effects to adjacent tissues.
- Neither the dye nor the reactive oxygen produced are toxic to the patient.
- Adjacent human cells are not affected are not affected during the treatment procedure [16].
- Until today, no resistant bacterial strains were developed to photoactive agent.
- No mutagenic or geneotoxic effects.
- Increased healing process

CONCLUSION

Application of PDT in dentistry is gaining more rapid attention as treatment for oral cancer, bacterial or fungal infection and diagnosis of malignant transformation of oral lesions. It is used effectively to kill gram negative or gram positive bacteria, fungi, viruses and various bacteria that are present in complex biofilm.

Limitations: The therapy sometimes develops burning, tingling or prickling pain restricted to the site of illumination. It can lead to hyper or hypo-pigmentation occasionally. Thus PDT represent a novel approach in the management of various oro-dental infective conditions. It includes preservation of functionality, good patient acceptance, good cosmetic result, willingness by the patient to repeat the treatment and low invasiveness. It is unlikely for the bacteria to develop resistance to the photodynamic action as has been reported by the conventional antimicrobial treatment [17]. PDT approaches to kill bacteria is clearly a rapidly emerging alternative to current antimicrobial regimen.

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