Quest Journals
Journal of Medical and Dental Science Research
Volume 8~ Issue 6 (2021) pp: 11-14
ISSN(Online) : 2394-076X ISSN (Print):2394-0751
www.questjournals.org

Research Paper

Photodynamic Therapy as an Adjunct in Disinfection of Canal In Endodontics: A Review

Dr. Seema D. Pathak[1], Dr. Pradnya V. Bansode[2], Dr. M. B. Wavdhane[3], Dr. Rinky Hajong[4]

1. Professor, Department of Conservative Dentistry and Endodontics, GDC & Hospital, Aurangabad/ MUHS, INDIA
2. Professor & Head of the Department, Department of Conservative Dentistry and Endodontics, GDC & Hospital, Aurangabad/ MUHS, INDIA.
3. Associate Professor, Department of Conservative Dentistry and Endodontics, GDC & Hospital, Aurangabad/ MUHS, INDIA.
4. Post-Graduate Student, Department of Conservative Dentistry and Endodontics, GDC & Hospital, Aurangabad/ MUHS, INDIA
Corresponding Author: Dr. Rinky Hajong

ABSTRACT:
One of the main goals in root canal treatment is to eliminate the endodontic bacteria. Conventional chemo-mechanical debridement is considered as the basic treatment in root canal therapy, but adjunctive techniques such as antimicrobial photodynamic therapy (PDT) can also be helpful and is gaining attention. Different techniques have been developed to enhance root canal disinfection. Among these techniques, PDT has gained popular as it can improve the success rate. The concept of photodynamic inactivation requires microbial exposure to either exogenous or endogenous photosensitizer molecules, followed by visible light energy, typically wavelengths in the red/near infrared region that cause the excitation of the photosensitizers resulting in the production of singlet oxygen and other reactive oxygen species that react with intracellular components and consequently produce cell inactivation and death. It can also be applied as a supplement to chemo-mechanical treatment.

KEYWORDS*: Antimicrobial, Root canal disinfection, Endodontics, Photodynamic therapy.*

Received 02 June, 2021; Revised: 04 June, 2021; Accepted 16 June, 2021 © The author(s) 2021. Published with open access at www.questjournals.org

I. INTRODUCTION:

Bacteria are considered the main etiology of pulp and periapical lesions due to the production of toxins that irritate the pulp and peri radicular tissue.[1,2] The lack of suitable accessibility of the immune system to the root canal space can lead to an incomplete elimination of endodontic infection.[3] Therefore, root canal therapy is needed to eliminate infection and return the peri radicular tissue to full health. It is widely accepted that the main reason for endodontic treatment failure is the insufficient root canal micro-organisms eradication **(Siqueira et al., 2000)**. As residual species are not reachable to the host's immune system, propagation and re-colonization is highly possible, endorsing microbial spread inside root canal system, which leads to endodontic infections.[4]

The main microorganism in root canal treatment failure is **Enterococcus faecalis**, which is the most resistant form of bacteria that is reported in primary and secondary endodontic infection. Conventional antibacterial irrigants showed some cytotoxicity. To reduce these unfavorable side effects, Photodynamic endodontic disinfection has gained special attention. Photodynamic therapy (PDT) has been defined as "the light induced inactivation of cells, microorganisms, or molecules" Gursoy et al. (2013).

Antimicrobial photodynamic therapy (aPDT) is based on the application of a photosensitizer (PS), a light source, and oxygen for bacterial damage. After the application of a PS to the site of infection, the light source, which coincides with the peak absorption of the PS, is illuminated to produce singlet oxygen and free radicals, which results in bacterial cell damage. This technique is minimally invasive, non-resistant, and repeatable.[5]

HISTORY TERMINOLOGY:

PDT was discovered at the very beginning of the twentieth century, when a combination of non-toxic dyes exposed to visible light resulted in microorganism cell death. The concept of microbial cell death induced by interaction of light and chemicals was introduced by Oscar Raab, a medical student while working with Professor Herman Von Tappeiner in Munich. During the course of Raab's study, he demonstrated that the combination of light and dyes was much more effective in killing the microorganism **Paramecium**. Later his observations were investigated and experimented with a diversity of other uni & multicellular organisms.[6]

Different historical terminologies that had been used for Photodynamic Therapy--

- **Antimicrobial photodynamic therapy (APD) by Wainwright in 1998,**
- **Photodynamic inactivation (PDI) by O' Riordan et al. in 2006**,
- In the dental field, **Photo-activated disinfection (PAD) and Light-activated disinfection (LAD) by Bergmans et al. in 2008**
- **Photodynamic antimicrobial chemotherapy (PACT) by Takasaki et al. in 2009 and Photodynamic disinfection (PD) by Rossoni et al. 2010**

MECHANISM OF ACTION OF PDT

The mechanism of PDT can be explained in two stages that involves-

FIRST STEP

It includes the application and retention of an applied (PS) compound in target tissues.

SECOND STEP

- Followed by activation by exposure to visible light in an appropriate wavelength that is excitatory to this compound and that is applied though a light device, which can be directly driven to the target.
- Upon irradiation, the PhotoSensitizers undergoes transition from singlet low-energy level "ground state" to a higher-energy "triplet state".

There are two mechanisms by which in the presence of a substrate such as oxygen, the activation of the sensitizer drug to the triple-state can get into chemical reactions with biomolecules

Type I mechanism-

- It lead to the formation of free radicals by hydrogen or electrons transference.
- These reactive species, after the interaction with oxygen, might produce highly reactive oxygen species, such as peroxide or superoxide anions, which attack cellular targets
- Type I reactions could cause direct cellular damage by the action of free radicals

In type II mechanisms-

- An electronically excited and highly reactive state of oxygen is released, which is named singlet oxygen.
- Since type II reactions are mediated through singlet oxygen species, this is accepted as the major pathway in microbial cell destruction

BACTERICIDAL EFFECTS OF PHOTODYNAMIC THERAPY:

There is a fundamental difference in susceptibility to antimicrobial PDT between **Gram+** (positive) and **Gram-(negative)** bacteria. In general, **Gram+(positive)** bacteria are more susceptible than **Gram-(negative)** bacteria. It can be explained due to the relatively porous layer of peptidoglycan and lipoteichoic acid outside the cytoplasmic membrane of **gram**+(positive) species which allows the Photosensitizers to diffuse into sensitive sites.[7] Whereas, **Gram-**(negative)bacteria have an inner cytoplasmic membrane and an outer membrane, separated by a peptidoglycan containing periplasm that forms a physical and functional barrier between the cell and its environment preventing the diffusion of Photosensitizers.

Neutral or anionic PS molecules are effective in binding and inactivating Gram+(positive) bacteria. Whereas, in Gram-(negative) bacteria, these molecules bind only with the outer membrane and thus not being able to completely inactivate them after illumination.

To inactivate a bacterial cell, the PS must be absorbed by the cell membrane or be translocated to the cytoplasm, leading to inhibition of further DNA, RNA, and protein synthesis.[8]

II. PHOTOSENSITIZERS (PSs) & LIGHT SOURCES (LS)

Photosensitizers (PS), which were preferentially located at the bacterial cytoplasmic membrane, have been found to be very effective photo-antimicrobial agents. The first PS used in endodontic field was toluidine blue (TBO). However, Methylene blue (MB) as a photosensitizer has been used more commonly in PDT for targeting endodontic bacteria. The hydrophilicity of MB, along with its low molecular weight and positive charge, allows it to cross outer membrane of Gram-negative bacteria through porin channels. MB predominantly

interacts with anionic macromolecule lipopolysaccharide, resulting in generation of MB dimers, which participate in the photosensitization process. The desired properties of an optimal PhotoSensitizers include favorable photophysical, chemical, and biological characteristics such as low cytotoxicity, short-time photosensitivity, absorption peaks in the low-loss transmission window of biological tissues, simplicity in formulation, reproducibility, high stability and high affinity, and penetration into bacterial cells rather than healthy tissues (selectivity). Although the photochemical principle for cancer and antimicrobial PDT is the same, there are important differences in the structures of PSs and cellular targets. For cancer treatment, porphyrins, chlorins, phthalocyanines, and bacterio chlorins are the indicated PSs, for their tumor location and low toxicity in the absence of light in mammalian cells[9]. To eradicate microorganisms, the most studied PSs belong to the groups halogenated xanthenes, phenothiazines, acridines, and conjugated chlorins.

Hamblin and Hasan have mentioned that PSs for antimicrobial purposes can be divided into three groups:

1. Those that strongly bind and penetrate the microorganisms (e.g., chlorin e6),
2. Those that bind weakly [i.e., toluidine blue (TB) and methylene blue (MB)],
3. Those that do not demonstrate binding (i.e., rose bengal).

The outer membrane damage plays an important role in bacterial cells differently from mammalian cells. The main targets for PDT are lysosomes, mitochondria, and plasma membranes.[10]

PS activation has been accomplished by using various LSs, such as argon lasers, Nd:YAG, gold, or copper vapor lasers, all complex and expensive equipment. Diode lasers have now become the most used because of their low cost and portability. Other LSs, such as light-emitting diodes (LED) or conventional halogen light, have also been used with good results. The use of intracanal optical fibers (ICFs) has also been studied as a way to increase the effectiveness of PDT. Calibration of the LS should be correct. The resonance between the LS wavelength and the selected PS should be monitored. PS has zero or very low cytotoxicity in total absence of light and this indicates antimicrobial PDT efficacy results strictly from combination between PS and light source.

Pre-irradiation time (PIT) and irradiation dose

Pre-irradiation time (PIT) corresponds to the time elapsed between the PhotoSensitizers application and its activation by light. This time is necessary to allow PhotoSensitizers uptake by the target before irradiation, as it is expected to bind or even translocate the target cell membrane. According to Wainwright, a PhotoSensitizer which is taken up slowly by the microorganism will only cause cell wall photo damage at first, whereas nucleic acid strand breakage will be evident only after longer incubation times.[11]

The ***Pre-irradiation time*** is a key factor in PDT, as it permits the PhotoSensitizers to penetrate through the dentine and to exert its antibacterial effect and it helps to keep the PhotoSensitizers inside the bacteria, allowing more light absorption (Usacheva et al. 2001; Figueiredo et al. 2014). The total energy applied by the Light Source to the Photosensitizers may also interfere with the chemical reactions and ROS release, changing the outcome of PDT.

OPTIMIZATION OF PDT EFFICACY

- Current research is also focused on increasing the anti-biofilm efficacy of PDT by combining the photodynamic effects with bioactive micro and nanoparticles like rose bengal–functionalized chitosan nanoparticles (CSRBnps) [12]
- In order to improve the uptake of PS by microorganisms using the PDT approach, these molecules have been loaded in a drug delivery system for widely different purposes (Ding et al. 2016, Junqueira et al. 2016).

III. CONCLUSION

With the advancement in endodontics, still there are many cases that result in failure of the endodontic treatment due to microbial factors. Such challenges have motivated many researchers in recent years is to develop new technologies to eliminate these persistent microorganisms. PDT is a minimally invasive approach that has been demonstrated to be an adjunct to conventional root canal treatment in eliminating microorganisms that remain viable in the root canal system. The technique of aPDT can be applied alongside conventional chemo mechanical techniques to improve the reduction in the number of endodontic bacteria, or the behavior of the bacteria by altering the virulence factors, which can reduce their ability to form biofilms.

REFERENCES

[1]. S.Friedman, "Considerations and concepts of case selection in the management of post-treatment endodontic disease (treatment failure),"EndodonticTopics,vol.1,no.1,pp.54–78,2002.

[2]. U.Sjogren,D.Figdor,S.Persson ,and G.Sundqvist,"Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis," International EndodonticJournal,vol.30,no.5,pp.297–306,1997.

[3]. T. Waltimo, M. Trope, M. Haapasalo, and D. Ørstavik, "Clinical efficacy of treatment procedures in endodontic infection control and one year follow-up of periapical healing," Journal of Endodontics, vol.31,no.12,pp.863–866,2005.

[4]. J. F. Siqueira Jr., M. C. Ara´ujo, P. F. Garcia, R. C. Fraga, and C.J.Dantas,"Histological evaluation of the effectiveness of five instrumentation techniques for cleaning the apical third of root canals,"JournalofEndodontics,vol.23,no.8,pp.499–502,1997.
[5]. S. Stojicic, H. Amorim, Y. Shen, and M. Haapasalo, "Ex vivo killing of Enterococcus faecalis and mixed plaque bacteria in planktonic and biofilm culture by modified photoactivated disinfection, "International EndodonticJournal,vol.46,no.7,pp. 649–659,2013. [6] Y.-G. Qiang, C. M. N. Yow, and Z. Huang, "Combination of photodynamictherapy and immune modulation:currentstatus and future trends," Medicinal Research Reviews, vol. 28, no. 4, pp.632–644,2008.
[6]. L.C.DePaz,"Redefining the persistent infection in root canals: possible role of biofilm communities," Journal of Endodontics, vol.33,no.6,pp.652–662,2007.
[7]. J. W. Costerton, K. J. Cheng, G. G. Geesey et al., "Bacterial biofilm in nature and disease,"Annual Review of Microbiology, vol.41,pp.435–464,1987.
[8]. G. Svensater, B. Sjogreen, and I. R. Hamilton, "Multiple stress responses in Streptococcus mutans and the induction of general and stress-specific proteins," Microbiology, vol. 146, no. 1, pp. 107–117,2000.
[9]. K. Lewis, "Persister cells and the riddle of biofilm survival," Biochemistry, vol.70, no.2, pp.267–274,2005.
[10]. G.H.W.BowdenandI .R.Hamilton,"Survival of oral bacteria," Critical Review in Oral Biology & Medicine,vol.9,no.1,pp.54–85,1998.
[11]. A.Kishenand M. Haapasalo,"Biofilm models and methods of biofilm assessment, "EndodonticTopics,vol.22,no.1,pp.58–78, 2010.