

Photodynamic Therapy- A new paradigm in periodontics!!!

Amit Mani¹, Shubhangi Mani², Raju Anarthe³, Sanket Brahmhatt⁴, Rajiv Saini⁵, Prachi Shukla⁶

Abstract:

The advancement in science and technology in the medical field amends a path for embedding new treatment modalities to the challenges presented by the viable diseases. The emergence of resistant microorganisms and a shift in the microflora after extended use limit the use of antimicrobials. This created the foundation for our modern use of chemotherapy and emergence of photodynamic therapy. The oral cavity is especially suitable for photodynamic antimicrobial chemotherapy (PACT) because it is relatively accessible to illumination. Photodynamic therapy (PDT) was discovered over 100 years ago by its ability to kill various microorganisms when the appropriate dye and light were combined in the presence of oxygen. However it is only in relatively recent times that PDT has been studied as a treatment for various types of localized infections. This resurgence of interest has been partly motivated by the alarming increase in drug resistance amongst bacteria and other pathogens. Many periodontal pathogenic bacteria are susceptible to low-power lasers in the presence of dyes, such as methylene blue, toluidine blue O, malachite green, and indocyanine green. aPDT uses these light-activated photosensitizer that is incorporated selectively by bacteria and absorbs a low-power laser/light with an appropriate wavelength to induce singlet oxygen and free radicals, which are toxic to bacteria. This review will focus on the clinical applications of antimicrobial PDT.

Keywords: *Periodontal treatment, photodynamic therapy, photosensitizer, wound healing*

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Introduction

Periodontal disease caused by dental plaque is characterized by the clinical signs of inflammation and loss of periodontal tissue support. The mechanical removal of this biofilm and adjunctive use of antibacterial disinfectants and antibiotics have been the conventional methods of periodontal therapy.^[1] But the removal of plaque and the reduction in the number of infectious organisms can be impaired in sites with difficult access. The possibility of development of resistance to antibiotics

by the target organism has led to the development of a new antimicrobial concept with fewer complications. Hence the aroused the need for newer, better and less complicated technique. Photodynamic therapy (PDT) is a very promising treatment method. PDT consists of light irradiation (red light or ultraviolet light for diagnostic purposes) and special chemical compound, which is called photosensitizer. It is very important that the applied doses of light and photosensitizer are too small to achieve therapeutic effects when given separately. The combined use of light and photo sensitizer in special configurations may ensure therapeutic effects.^[2]

Concepts of PDT

PDT is based on the principle that a photoactivable substance (the photosensitizer) binds to the target cell and can be activated by light of a suitable wavelength.^[3] During this process, free radicals are formed (among them singlet oxygen), which then produce an effect that is toxic to the cell. To have a specific toxic effect on bacterial cells, the respective photosensitizer needs to

¹Professor, ³ Reader, ⁴ Postgraduate student, ⁵ Reader, Dept. of Periodontology, Rural Dental College, Loni, Maharashtra, India

² Professor, Dept. of Orthodontics, Rural Dental College, Loni, Maharashtra, India

⁶ Private Dental Practitioner, USA

Corresponding author:

Dr. Sanket Brahmhatt,
Postgraduate student, Dept. of Periodontology, Rural Dental College,
Loni, Maharashtra, Mobile No: +919860088708
E-mail: dr.sanketvb@gmail.com

have selectivity for prokaryotic cells. Although several authors have reported the possibility of a lethal photosensitization of bacteria in vivo and in vitro, others have pointed out that Gram negative bacterial species, due to their special cell wall, are largely resistant to PDT.^[4] By irradiation with light in the visible range of the spectrum the dye (photosensitizer) is excited to its triplet state, the energy of which is transferred to molecular oxygen. The product formed is the highly reactive singlet oxygen capable of reacting with biological systems and destroying them. Only the first excited state with energy of 94 kJ/mol (22kcal/mol) above the ground state is important, the second excited state does not react.^[5]

Components of PDT

PDT has three key components: association of light with a suitable photosensitizer (photosensitive dye) in the presence of tissue molecular oxygen. When photosensitizer is irradiated with light of a specific wavelength, it gets activated from ground-state to a highly energized triplet state

A) Dyes/ Photosensitizers

- Tricyclic dyes (methylene blue, toluidine blue O, and acridine orange) (2) Phthalocyanines (aluminum disulfonated phthalocyanine and cationic Zn(II) phthalocyanine)
- Chlorines: Chlorine e6, stannous (IV) chlorine e6, chlorine e6-2.5 N-methyl-d-glucamine (BLC1010), polylysine and polyethyleneimine conjugates of chlorine e6
- Porphyrines: Hematoporphyrin HCl, photofrin, and 5-aminolevulinic acid (5-ALA), benzoporphyrin derivative (BPD)
- Xanthenes: Erythrocine
- Monoterpene: Azulene^[6]

B) Light Source

We have three light systems for the therapy:

- Diode laser systems: They are easy to handle, portable, and cost-effective.
- Non-coherent light sources: Preferred for treatment of larger areas and include tungsten filament, quartz halogen, xenon arc, metal halide, and phosphor-coated sodium lamps.

- Non-laser light sources include light-emitting diodes (LEDs). They are economical, light weight, and highly flexible.^[7]

Mechanism of action -

The photosensitizer can react with biomolecules in two different pathways - type I and II.^[8] Type I reaction involves electron - transfer reactions between the excited state of the photosensitizer and an organic substrate molecule of the cells, producing free radicals. These free radical species are generally highly reactive and interact with endogenous molecular oxygen to produce highly reactive oxygen species, such as superoxide, hydroxyl radicals, and hydrogen peroxide, which are harmful to cell membrane integrity, causing irreparable biological damage. In type II reaction, the triplet state photosensitizer reacts with oxygen to produce an electronically excited and highly reactive state of oxygen, known as singlet oxygen (1O_2) which can interact with a large number of biological substrates inducing oxidative damage on the cell membrane and cell wall. Microorganisms that are killed by singlet oxygen include viruses, bacteria, and fungi. Singlet oxygen has a short lifetime in biological systems and a very short radius of action (0.02 mm). Hence, the reaction takes place within a limited space, leading to a localized response; thus making it ideal for application to localized sites without affecting distant cells or organs. Thus, the type II reaction is accepted as the major pathway in microbial cell damage.^[9] (Figure 1)

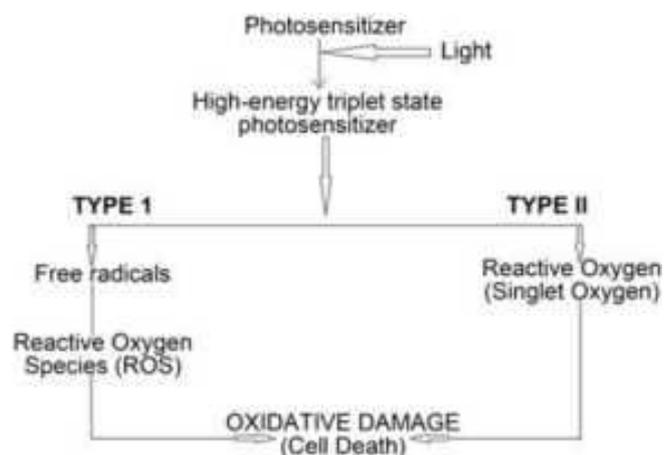


Figure 1: Mechanism of PDT

Applications in Periodontics-

PDT can be considered as an adjunctive to conventional mechanical therapy. The technical simplicity and effective bacterial eradication are the two reasons why photodynamic

therapy is extensively studied in periodontics. Antimicrobial PDT not only kills the bacteria, but may also lead to the detoxification of endotoxins such as lipopolysaccharide. These lipopolysaccharides treated by PDT do not stimulate the production of pro-inflammatory cytokines by mononuclear cells. Thus, PDT inactivates endotoxins by decreasing their biological activity.^[10] It has been demonstrated that bacteria associated with periodontal disease can be killed through photosensitization with toulidine blue O by irradiating with helium - neon soft laser.^[11] In an animal study, it was found that PDT was useful in reducing the redness, bleeding on probing, and *Porphyromonas gingivalis*.^[12] On interpreting the data from the various controlled clinical studies, it becomes obvious that in patients with chronic periodontitis, aggressive periodontitis and peri implantitis, the adjunctive use of PDT to scaling and root planning may result in greater clinical attachment level gains, reduction in bleeding on probing and probing pocket depths. PDT has advantage such as reducing the treatment time, no need for anesthesia, destruction of bacteria, inactivation of endotoxins, and unlikely development of resistance by the target bacteria and no damage to the adjacent host tissues.^[13] The use of PDT in furcation involvement shows some advantages over use of conventional antimicrobials, reduced need for flap procedures and shorter treatment time with lack of microflora disturbance in other sites of oral cavity. Thus PDT may be an effective alternative for control of bone loss.

Limitations of PDT

Possible limitations include the following:

- The initial investment for some devices must be considered, as well as required supplies and maintenance
- No biopsy material is yielded
- Technological innovations, training, and continuing education are essential
- There may be clinician and hospital resistance to a new approach
- Cost of the setting can be prohibitive
- The previous lack of inexpensive and convenient light sources
- FDA clearance for different lights and dyes ^[14]

Despite all these limitations, the existing photosensitizers and light sources have achieved significant clinical success.

Conclusion:

In spite of different results and suggestions from various researchers, the present review showed that use of PDT may help improve periodontal outcomes. Therefore, it could become a new method for antibacterial treatment and may be used as an adjunct to or as conventional therapy for the treatment of periodontal and peri-implant diseases. Based on the knowledge presented here in, there is promising, albeit preliminary, information regarding the benefits of PDT use on periodontal treatment outcomes. However, the majority of systematic reviews conclude that the inclusion of PDT as an adjunct to nonsurgical periodontal treatment seems to be therapeutically useful. Further studies of PDT are needed for establishing this as a beneficial adjunct treatment for periodontitis.

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