(e) ISSN Online: 2321-9599
(p) ISSN Print: 2348-6805

REVIEW ARTICLE

Phytodynamic Therapy in Dental Perspective: A Review

Neha Pal[1], Kapil Ahuja[2], Rohit Pannu[3], Neetu Aggarwal[4], Vikas Berwal[5]

[1,2]M.D.S. Oral Surgery, M S Ramaiah Dental College and Hospital, Bangalore, Karnataka, India
[3]M.D.S. Conservative Dentistry and Endodontics, Private Practitioner, Bhiwani, Haryana, India
[4]MDS Oral and Maxillofacial Surgery, Goa Dental College and Hospital, Bambolim, Goa, India
[5]Department of Oral and maxillofacial Surgery, PGI Rohtak, Haryana, India

ABSTRACT:
Photodynamic therapy is an innovative technology that utilizes two non-toxic components, a photo-activating liquid and an LED light source to preferentially mark and destroy cariogenic bacteria and periodontal pathogens. The interaction between photosensitizer (PS) and light with adequate wavelength provides a wide effect spectrum. Photodynamic therapy (PDT), also known as photoactivated disinfection/ photochemotherapy/ photoradiation therapy/ phototherapy, has the potential to be a good alternative to the routine disinfection protocol.
Keywords- Photodynamic therapy, Phototsensitizer, Cytotoxic, Disinfection, Irradiation, Reactive Oxygen species..

Corresponding author: Dr. Rohit Pannu, H.No. 3037, New Housing Board, Sector – 13, Bhiwani (Haryana), India.

This article may be cited as: Pal N, Ahuja K, Pannu R, Aggarwal N, Berwal V. Phytodynamic Therapy in Dental Perspective: A Review. J Adv Med Dent Scie Res 2017;5(10):38-41.

Access this article online	
Quick Response Code	Website: www.jamdsr.com
	DOI: 10.21276/jamdsr.2017.5.10.10

INTRODUCTION

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 presence, these combine to produce some cytotoxic species. The PS molecules attach to bacterial membrane.[1] Photo-Activated Disinfection involves three components: light, a photosensitizer, and oxygen. A photosensitizer or its metabolic precursor is administered to the patient. Upon irradiation with light of a specific wavelength, the photosensitizer undergoes a transition from a low-energy ground state to an excited singlet state. Subsequently, the photosensitizer may decay back to its ground state, with emission of fluorescence, or may undergo a transition to a higher energy triplet state. The triplet state reacts with endogenous oxygen to produce singlet oxygen and other radical species, causing a rapid and selective destruction of the target tissue.[2] Shrestha et. al.[3] showed that antibacterial PDT with chitosan-conjugated rose Bengal nanoparticles can result in inactivation of LPS and subsequent reduction of all inflammatory markers.

Various terms are used for PDT such as photoactivated chemotherapy (PACT), photodynamic disinfection (PDD), light-activated disinfection (LAD), and photoactivated disinfection (PAD) in different studies and literature.[4] The success rate of photodynamic therapy depends on the type, dose, incubation time, and localization of the PS, the availability of oxygen, the wavelength of light (nm), the light power density and the light energy fluency.[5]

History

The concept of treatment with light and photoactive compounds can be traced back over 6000 years to the ancient Egyptians who used light-sensitive substances (psoralens) by crushing leaves of plants related to parsley with sunlight to treat sunburns. Reference to the use of a plant extract for the restoration of skin pigmentation was made in 1400 BC and phototoxic effects of psoralens were described in 1250 AD.[6] But the actual breakthrough came by Finsen's pioneering research in 1901 in which he showed that skin tuberculosis could be successfully treated with natural and artificial ultraviolet light.The essential involvement of light and oxygen in the process was shortly thereafter demonstrated by Tappeiner,[7] who coined the term 'photodynamic'. Haxthausen and Hausmann in 1908 were the first to suggest that hematoporphyrin was a photodynamic photosensitizer. In 1960, Theodore Maiman, a scientist with the Hughes Aircraft Corporation, developed the first working laser device which emitted a deep red colored beam from a ruby crystal (Coluzzi, 2004). Wilson et al. (1993) proved the effect of cyanide photosensitizer on Gram-negative and Gram-positive species. Ackrayd (1999) used aminolevulinic acid-induced PDT for treatment of adenocarcinoma.

Mechanism of action

Photosensitization is a treatment that involves the interaction of two non-toxic factors, such as a photo-active compound (tolonium chloride) and a directly applied visible light (LED illumination at 635nm).[8]Photo-Activated Disinfection requires a source of light that activates the photosensitizer by exposure to low-power visible light at a specific wavelength.

The light source for PAD can be divided into three main categories namely:[9]
1) broad spectrum lamps,
2) Light emitting diode lamps (LED) and
3) lasers.
Most photosensitizers are activated by red light between 630 and 700 nm, corresponding to a light penetration depth from 0.5 cm (at 630 nm) to 1.5 cm (at ~ 700 nm).[10]

The ideal characteristics of a PS include:[2]
1) Chemical purity& non-toxic.
2) Ability to target the tissue, cost-effective, easily available.
3) Short interval between administration of the drug and peak accumulation in the tissue.
4) Short half-life.
5) Activation at wavelength at which penetration into the target tissue is very good.
6) Ability to produce a large amount of cytotoxic products.

The most common PSs are phenothiazine, cyanine, phytotherapic agents, hematoporphyrin derivatives and xanthene derivatives.[11]Phenothiazine dyes have been claimed to have intense absorption in 620 - 660 nm wavelength and so be useful in PDT.[12]According to Chan and Lai,[13] methylene blue shows maximal absorbance when exposed to a wavelength of 660 nm. Soares et. al.[14] and Fernandes et. al.[15] showed that toluidine blue O was preferred as a PS because it can easily pass through cell membrane.
The transfer of electrons in activated PS can be done in two pathways including transfer to the neighboring molecule (type-1 reaction) or to oxygen (type-2 reaction) to produce reactive oxygen species (ROS), typically singlet oxygen. Although, the two pathways can have a role on bacterial killing, type 2 by producing highly reactive singlet oxygen is detected as the main pathway in killing bacteria.[16]

Two mechanisms have a major role in lethal damage administered by PDT,[17]
1) DNA damage,
2) Damage to cytoplasmic membrane and cellular contents or inactivation of membrane transport systems and enzymes.

Bacterial cells are typically composed of a variety of cytoplasm materials enclosed by a cell wall. Many "traditional" anti-microbial substances must enter and accumulate inside the bacterium in order to destroy their targets. Since this process requires a transport mechanism through the cell wall, it gives the bacteria an opportunity to build up a resistance by modifying the transport mechanism required by the drug. This also applies to photo-activated drugs that must accumulate within the cell.[18]Certain photoactive agents are taken up by bacteria preferentially, with the agent residing in the proximity of or becoming attached to the cell wall. Some may even enter microorganisms. All bacteria have the potential to be targeted, though some combinations between certain sensitizers and certain organisms are more successful than others. Healthy human tissue will not be affected.PAD techniques, use low power lasers to elicit a photochemical reaction in a photosensitizer, which in turn exerts a lethal effect on particular cells such as bacteria. PAD is basically a lethal laser photosensitization. Photosensitizers alone in the right doses are not toxic to bacteria. Low power (diode) laser energy in itself is, again, not particularly lethal to bacteria but is useful for photochemical activation of oxygen-releasing dyes. Singlet oxygen, a protoplasmic poison released from dyes, causes lethal membrane, organ and DNA damage to microorganisms.[2]

Applications in dentistry

Photodynamic therapy has also been used to disinfect carious dentin before restoration, disinfecting oral tissues before or during surgical procedures, treating denture stomatitis, and treating oral candidiasis in immune-compromised patients.[19]

Endodontic treatment

Photodynamic therapy can be used in combination with mechanical instrumentation and chemical antimicrobial agents, such as NaOCl and hydrogen peroxide. Garcezet. al.[20] showed that endodontic treatment alone reduced90% of bacteria, whereas PDT alone reduced it by 95%, the combination of these two techniques reduced bacteria by 98%. PDT has shown to be effective against Gram positive as well as Gram-negative endodontic pathogens like Enterococcus faecalis, Streptococcus intermedius, Fusobacterium nucleotum, Pepto streptococcus micros, Prevotella intermedia.[21]Garcez et. al.[22] demonstrated that usage of PDT added to endodontictreatment of infected canals with the optical fiber may bebetter than when the laser is used directed at the cavity. In a case report, Johns et. al.[23] described a new protocol for pulp revascularization with canal disinfection using a combination of a low-power laser light and PS solution.

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.[24]

Dental Caries

With regard to bacteria involved in dental caries, Burns et. al.[25] showed that tolonium chloride (25 g/mL) used with 632.8 nm laser energy reduced the viability of Streptococcus mutans, Streptococcus sobrinus, Lactobacillus casei, and Actinomyces viscosus.The technique involves applying a photo-active solution that is absorbed selectively by cariogenic bacteria to the operative surfaces. This sensitizes them to the application of visible illumination which causes cytotoxic bacterial reactions that result in selective destruction of the target microorganism.[26]

Periodontal therapy

Scaling and root planning can remove the calculus and plaque but has little effect on the acidogenic and aciduric bacteria that is the cause of these deposits and the ensuing periodontal disease that has been associated with numerous systemic health problems. Research has indicated that PAD mechanism functions to combat the bacteria that are largely responsible for periodontitis like porphyromonas gingivalis, Actinobacillus actinomycetem comitans, Fusobacterium nucleatum, Streptococcus sanguinis, Bacteroides forsythus, Campylobacter rectus and Eikenella corrodens.[27]

Other applications of PAD

Photodynamic Antimicrobial Chemotherapy (PACT) represents an alternative antibacterial, antifungal and antiviral treatment for drug resistant micro-organisms. It is unlikely that bacteria would develop resistance to the cytotoxic action of singlet oxygen or free radicals. Applications of PAD are growing rapidly in the treatment of oral cancer, bacterial, fungal infections and diagnosis of malignant transformation.[2]Limitations of this treatment which should be taken into account are the low-oxygenated environment and the diffusion ability of the PS and light to be used.[19]

CONCLUSION

With Photodynamic therapy, the remaining tooth surfaces are disinfected and thus are far more likely to remineralize effectively. Photo-activated disinfection offers a heightened level of disinfection during and after operative and periodontal procedures. Despite being an effective auxiliary tool to antimicrobial therapy, further studies needed in order to determine appropriate parameters for photosensitizer concentration, energy dosage used, time of irradiation, and exposure.

REFERENCES:-

1. Dai T, Huang YY, Hamblin MR. Photodynamic therapy for localized infections – state of the art. Photodiagnosis Photodyn Ther 2009;6(3-4):170-188.
2. Konopka K and TGoslinski. Photodynamic Therapy in Dentistry. J Dent Res. 2007;86:694-707.
3. Shrestha A, Cordova M, Kishen A. Photoactivated polycationic bioactive chitosan nanoparticles inactivate bacterial endotoxins. J Endod 2015;41(5):686-691.
4. Parker S. The use of diffuse laser photonic energy and indocyanine green photosensitizer as an adjunct to periodontal therapy. Br Dent J. 2013; 215(4):167-171.
5. Chrepa V, Kotsakis GA, Pagonis TC, Hargreaves KM. The effect of photodynamic therapy in root canal disinfection: a systematic review. J Endod. 2014;40:891-898.
6. Llano J, Raber J, Eriksson LA. Theoretical study of phototoxicreactions of psoralens. J Photochem Photobio A: Chem. 2003; 154: 235-43.
7. Von Tappeiner H. Zurkenntis der lichtwirkenden (fluoreszierenden) stoffe. Dtsch Med Wochen, 1904; 1: 579-80.
8. Calin MA, Parasca SV.Light Sources for Photodynamic Inactivation of Bacteria. Lasers Med Sci. 2009; 24(3): 453-460.
9. Salva KA. Photodynamic therapy: unapproved uses, dosages or indications. Clin Dermatol. 2002;20(5):571-581.
10. Komerik N, MacRobert AJ. Photodynamic therapy as an alternative antimicrobial modality for oral infections. J Environ Pathol Toxicol Oncol. 2006; 25: 487-504.
11. Wainwright M. Photodynamic antimicrobial chemotherapy (PACT). J Antimicrob Chemother 1998;42(1):13-28.
12. Wainwright M, Giddens RM. Phenothiazinium photosensitisers: choice in synthesis and application. Dyes Pigm 2003:57(3):245-257.
13. Chan Y, Lai CH. Bactericidal effects of different laser wavelengths on periodontopathic germs in photodynamic therapy. Lasers Med Sci 2003;18(1):51-55.
14. Soares BM, Alves OA, Ferreira MV, Amorim JC, Sousa GR, Silveira Lde B, Prates RA, Avila TV, Baltazar Lde M, de Souza Dda G, et al. Cryptococcus gattii: in vitro susceptibility to photodynamic inactivation. Photochem Photobiol 2011 ;87(2):357-364.
15. Fernandes LA, de Almeida JM, Theodoro LH, Bosco AF, Nagata MJ, Martins TM, Okamoto T, Garcia VG. Treatment of experimental periodontal disease by photodynamic therapy in immunosuppressed rats. J Clin Periodontol 2009 ;36(3):219-228.
16. Sharman WM, Allen CM, Van Lier JE. Photodynamic therapeutics: Basic principles and clinical applications. Drug Discov Today. 1999;4(11):507-517.
17. Xiu-jun Fu, Yong Fang, Min Yao. Antimicrobial photodynamic therapy for methicillin-resistant Staphylococcus aureusinfection. Biomed Res Int. 2013;2013:159157.
18. Winckler K. Special Section: Focus on anti-microbial photodynamic therapy (PDT). Journal of photochemistry and Photobiology B: Biology. 2007; 86: 43-44.
19. Gursoy H, Ozcakir-Tomruk C, Tanalp J, Yilmaz S. Photodynamic therapy in dentistry: a literature review. Clin Oral Investig 2013;17(4):1113-1125.
20. Garcez AS, Nuñez SC, Hamblim MR, Suzuki H, Ribeiro MS. Photodynamic therapy associated with conventional

endodontic treatment in patients with antibiotic-resistant microflora: a preliminary report. J Endod 2010 ;36(9):1463-1466.
21. Fimple JL, Fontana CR, Foschi F, et al. Photodynamic treatmentof endodontic polymicrobial infection in vitro. J Endod. 2008; 34: 728-34.
22. Garcez AS, Núñez SC, Baptista MS, Daghastanli NA, Itri R,Hamblin MR, Ribeiro MS. Antimicrobial mechanisms behind photodynamic effect in the presence of hydrogen peroxide. Photochem Photobiol Sci 2011 ;10(4):483-490.
23. Johns DA, Shivashankar VY, Krishnamma S, Johns M. Use of photoactivated disinfection and platelet-rich fibrin in regenerative endodontics. J Conserv Dent 2014 Sep;17(5): 487-490.
24. Ok E, Ertas H, Saygili G, Gok T. Effect of photoactivated disinfection on bond strength of root canal filling. J Endod 2013 ;39(11):1428-1430.
25. Burns T, Wilson M, Pearson GJ. Effect of dentin and collagen on the lethal photosensitization of Streptococcus mutans. Caries Res 1995;29(3):192-197.
26. Sibata CH, Colussi VC, Oleinick NL, Kinsella TJ. Photodynamic Therapy in Oncology. Expert Opin Pharmacother. 2001; 917-927.
27. Zanin ICJ, Lobo MM, et. al. Photosensitization of in vitro Biofilms by Toluidine Blue O combined with a light-emitting Diode., Eur J Oral Sci., 2006; 114: 64-69.

Source of support: Nil **Conflict of interest:** None declared