Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 09, pp.58268-58271, September, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

PHOTODYNAMIC THERAPY A NEW TREATMENT APPROACH IN PERIODONTITIS PATIENTS – A REVIEW

***Dr. Bhuvaneswarri, J., Dr. Sajid. T. Hussain, Dr. Ramya, V. and Dr. Preethepaddmanabhan**

Department of Periodontics, Sree Balaji Dental College & Hospital, Velachery Main Road, Pallikaranai, Chennai - 600 100, Tamilnadu, India

ARTICLE INFO

Article History:
Received 27th June, 2017
Received in revised form
15th July, 2017
Accepted 17th August, 2017
Published online 30th September, 2017

Key words:
Photodynamic Therapy,
Periodontitis,
Laser,
Photo Sensitizers.

ABSTRACT

Photodynamic therapy (PDT) employs a non-toxic dye, termed a photosensitizer (PS), and low intensity visible light which, in the presence of oxygen, combine to produce cytotoxic species. PDT has the advantage of dual selectivity, in that the PS can be targeted to its destination cell or tissue and, in addition, the illumination can be spatially directed to the lesion. PDT has previously been used to kill pathogenic microorganisms in vitro, but its use to treat infections in animal models or patients has not, as yet, been much developed. It is known that Gram-(−) bacteria are resistant to PDT with many commonly used PS that will readily lead to phototoxicity in Gram-(+) species, and that PS bearing a cationic charge or the use of agents that increase the permeability of the outer membrane will increase the efficacy of killing Gram-(−) organisms. Treatment of localized infections with PDT requires selectivity of the PS for microbes over host cells, delivery of the PS into the infected area and the ability to effectively illuminate the lesion.

Citation: Dr. Bhuvaneswarri, J., Dr. Sajid. T. Hussain, Dr. Ramya, V. and Dr. Preethepaddmanabhan, 2017. "Photodynamic therapy a new treatment approach in periodontitis patients – a review ", *International Journal of Current Research*, 9, (09), 58268-58271.

INTRODUCTION

PDT could be used as an alternative to conventional therapeutic methods. It essentially involves use of light activated drugs to kill periodontal pathogen. It also enhances reparative process, is anti-inflammatory in action and used in killing of tumour cells (Phillippe Bidault, 2007).

HISTORICAL BACKGROUND

The term "photodynamic therapy" was established as early as 1900 by Rabb. It was initially investigated for the treatment of malignancy because chemotherapeutic drugs could be given to patients systemically in an essentially inert form and then activated by administering light, usually laser, at the tumor site, thereby killing the tumour cells without making patient ill from chemotherapy (Osterberg, 1979).

RATIONALE

Use of photodynamic therapy in periodontics is chiefly based on its antibacterial action and to a lesser extent because of its anti-inflammatory action. Briefly, plaque is the main factor in periodontal disease.

Corresponding author: **Dr. Bhuvaneswarri, J.,**
Reader, Department of periodontics, Sree Balaji Dental College & Hospital, Velachery Main Road, Pallikaranai, Chennai - 600 100, Tamilnadu, India.

All treatment modalities (mechanical or chemical) are targeted towards its elimination or maintaining it in a nonpathogenic state. From health to disease shift in microbiota observed is from gram positive and gram negative, cocci to rods (later spirochetes), nonmotile to motile, facultative anaerobes to obligate anaerobes, fermenting to proteolytic species (Osterberg, 1979). Major offenders are generally gram negative anaerobes. Treatment is targeted toward P. gingivalis, P.intermedia, Aggregatibacter actinomycetemcomitans, Capnocytophaga and F.nucleatum. They form a biofilm closely associated with tooth surface and causes inflammatory changes in adjacent epithelium and connective tissue. They can invade into the host tissue, that is, gingival connective tissue and thereby become inaccessible for nonsurgical mechanical therapy. These bacteria which have penetrated into the tissue respond to antibiotics given either locally or systemically. There presence in the tissue serve as reservoir for recolonization. Photodynamic therapy acts by causing photodamage to intracellular organelles of bacteria also preventing release of various inflammatory mediators. It is a recent approach of great importance as bacterial species are gradually developing resistant to various antibiotics. As the term indicates photodynamic therapy is a therapeutic modality which uses photons (that is, light energy) to bring about some changes, which will help diseased tissue to reverse back to healthy state.

It brings about changes in cells (host or bacterial) at cellular organelle level. It is the use of laser system with associated dye known as photosensitizers. It differs from direct use of lasers as it acts through a chemical substance (photosensitizer) which when activated causes photodamage to target cells while in lasers treatment they act directly on target tissue/cells and destroy it by its heating action (Thomaes, 1996).

COMPONENTS

Photodynamis therapy consists of two components:-

- a photosensitiser (chemical/drug) which can penetrate into the tissue and binds with the target cell and is photoactivable.
- laser component of a particular wavelength which can activate a photosensitiser and initiate the reaction. It can be delivered to target site by non invasive fibrooptic applicator.

Effective therapy depends on number of factors like

- drug concentration
- period of maintenance of drug within tissue
- sufficient tissue in tissue for biologic response
- wavelength of laser system (in nm)
- intensity of radiation (J/cm2)
- exposure time required for drug to be activated (in sec)
- maintenance of etiologic agent
- pH of the environment, presence of exudates, gingival crevicular fluid
- affinity of drug to particular target cell
- mode of drug application (irrigation / slow released gel)

Photosensitizer (Natalie *et al*., 1994)

Photosensitizer is a photoactivable substance that binds to the target cell and can be activated by light of suitable wavelength. E.g. methylene blue, toluidine blue O, cyanide photosensitizer, porphyrin containing photosensitizer (chloride 6, BLC1010 AND BLC1014).

Methylene blue

It is a phenothiazide dye and has been in medical practice for more than 100 yrs. It has very low tissue toxicity. It possesses antibacterial activity without additional light exposure. Although isolated use of drug does not present a significant lethal action. It is active against yeast, viruses, cariogenic bacteria and periodontopathogens. Methylene blue is a cationic drug. Therefore, its metabolism and absorption by bacteria may be influenced by local release of exotoxins by periodontopathogenic bacteria. It's absorption is improved by its association with a laser which may modify the bacterial cell membrane, thus allowing greater absorption of the drug and consequently interfering with bacterial viability. Methylene blue with low level laser therapy causes reduction in active bone resorption associated with periodontal disease. Methylene blue has a strong absorption at wavelength larger than 620 nm, where light penetration into tissue is optimal. According to Wilson, methylene blue at concentrations of 78 µm using energy density 22 J/cm2 showed reduction in F.nucleatum and no phototoxic effect on A.actinomycetemcomitans and P.gingivalis.

Other uses of methylene blue include ifosfamide encephalopathy, methaemoglobinemia, urolithiasis, cyanide poisoning. 0.5% methylene blue is used to stain barett's oesophagus and bronchial lesions.

Toluidine Blue O (Shackley, 1999)

- It is widely used in local, oral and parenteral diagnosis and treatment.
- It has no carcinogenic potential in humans.
- According to Wilson, when used in case of 81.7 µm and energy density of 22 J/cm2 there is reduction in number of P.gingivalis, A.actinomycetemcomitans and F.nucleatum. In that study He-Ne light source was used.
- Use of toluidine blue O at a range of concentration 12.5, 25, 50 and 100 µg/ml could give bluish tinge to teeth. These stains can be removed by EDTA irrigation. Studies in which paste form is used no bluish tinge was observed.
- Methylene blue and toluidine blue O may react with polysaccharides from gram negative bacteria and cause damage to these substances in the presence of light or not.
- Studies point out that gram negative bacteria due to their special cell wall are largely resistant to photodynamic therapy. However, Wilson proved effect of a cyanide photosensitizer on gram positive and gram negative species.
- Nitzan *et al* showed limited activity of porphyrin containing photosensitizers towards gram negative bacteria.
- Attempts are being made to increase permeability of gram negative bacterial membrane to photosensitizer by using membrane active substance or by synthesizing special positively charged photosensitizers that bind more easily with bacterial membrane.
- Photosensitizers with porphyrin skeleton e.g. chloride 6, BLC1010, BLC1014, were assessed for their bactericidal action.
- BLC1010 AND BLC1014 were designed to achieve a better binding of photosensitizer to bacterial cell wall and/or to increase the water solubility of photosensitizer.
- Pfizner *et al* (2004) found that the inactivation of P.gingivalis, F.nucleatum and Capnocytophaga occurs using chloride 6, BLC1010 and BLC1014 at wavelength 662 nm while A.actinomycetemcomitans and E.corrodens respond minimally.
- Success of photodynamic therapy depends on photosensitizer used e.g. chloride causes marked decrease in P.gingivalis, BLC1010 causes lesser decrease while BLC 1014 causes marked decrease in F.nucleatum.
- All three were able to kill anaerobic periodontopathogenic species. BLC1014 showed the least effect with regard to bacterial spectrum affected.
- Photosensitizer can be in form of irrigant, gel, paste, in form of solution applied with help of applicator from base of pocket coronally.

Principle of action (Shackley, 1999; Katie O'Riordan, 2002; Killoy, 2002)

Photodynamic therapy is based on the principle that a photoactivable substance or photosensitizer binds to the target cell and can be activated by light of suitable wavelength. This causes the initiation of series of photochemical reaction and thereby releasing free radicals (singlet oxygen).

This produces toxic effects on cell. When associated with low level lasers reparative processes are activated by biomodulation of tissues that occur at intracellular level. As it can penetrate epithelium and connective tissue it can kill pathogens in tissues, thereby reducing inflammation (Killoy, 2002).

Antibacterial Action (Killoy, 2002)

- Photodynamic therapy can kill various periopathogens. E.g. P.gingivalis, P.intermedia, A.actinomycetemcomitans and F.nucleatum.
- Lethal photosensitization of these microorganisms must involve changes in membrane, changes in plasma membrane proteins and DNA damage. These actions are mediated by release of singlet oxygen.
- Photosensitizing agents interact with the outer wall of surface of several types of bacteria and yeast cells to increase their permeability and allow a significant amount of photosensitizer to accumulate at the level of cytoplasmic membrane.
- To have a specific toxic effect on bacterial cells, the photosensitizers need to have selectivity for the prokaryotic cells.

Reparative action (Killoy, 2002; Konopka1, 2007; Muller, 2007)

Photodynamic therapy may favor repair process when it is associated with low level laser therapy as it may cause.

- increase mitochondrial respiratory chain and ATP synthesis favor repair process
- induces cell proliferation
- promote production of nucleic acid
- increase collagen synthesis
- increase activity of leukocytes
- causes release of various growth factors
- because of its bactericidal effect reparative processes are enhanced.

Destruction of cancer cells

Photodynamic therapy was developed initially for treatment of malignancy. The drug is given systemically but activated by lasers only in cancer/ tumour region resulting in localized action of drug, thereby preventing systemic side effects. Photodynamic therapy was first approved by FDA in 1999 to treat precancerous skin lesions of face or scalp.

Reduction in Inflammatory Process (Konopka1, 2007; Muller, 2007)

Sigush *et al*. (2005) showed significant reduction in periodontal inflammatory signs of redness and bleeding on probing using photodynamic therapy. Reduction in bacterial load (etiologic agent) especially motiles and spirochetes causes reduction in inflammation. Decreased P.gingivalis is associated with reduction in bleeding on probing. Low level lasers reduces gingival inflammation after nonsurgical treatment and there was reduction or decline in gingival index and probing pocket depth. Gingival crevicular fluid volume also fell after use of low level laser treatment as laser irradiation reduced PGE2 and reduced MMP-8.Decreased MMP-8 signifies reduced neutrophils. In vitro irradiation of peripheral neutrophils affects neutrophil function. E.g. generation of reactive oxygen species and phagocytosis. Laser irradiation affects cytokine production and causes inhibition of IL-1β.

Possible applications and advantages (Nilu Jain *et al*., 2008)

- As an adjunct to mechanical therapy in difficult access areas. E.g. furcation, deep concavities and invaginations.
- It may reduce treatment time, patient discomfort and need for flaps.
- It also reduces risk for bacteremia in patient with systemic involvement.E.g. cardiovascular and diabetic patients.
- For maintenance therapy because it may act on biofilm and eliminate the need for the removal of additional root substance by mechanical treatment, hence less dentin hypersensitivity.
- Lesser gingival recession with photodynamic therapy use may be because of atraumatic use of optic fibres.
- As photosensitizer is applied topically no systemic side effects reported as with systemic antibiotics.
- No reports showing resistant strains of bacteria to photodynamic therapy
- No localized adverse reactions. E.g ulceration or abcess formation.
- No need to anaesthetize
- Non invasive, less time consuming procedure
- In management of periimplantitis, as cleaning rough implant surface is difficult since bacteria are protected in microirregularities or undercut of surfaces.
- Photodynamic has been shown to be effective in decontaminating smooth machine polished plasma sprayed and hydroxyapatite coated titanium surface of A.actinomycetemcomitans, P.gingivalis and P.intermedia. Major advantage of this method is lack of any surface alterations and proved to be very effective.
- Photodynamic therapy in association with autogenous bone grafts and membranes show significant reduction in periimplant bone defects.
- Management of oesophageal candidiasis in HIV patients. Photodynamic therapy causes proliferation of cell wall or membrane which oxygen radicals, thereby allowing photosensitivity dye to translocate into cell which can photodamage inner organelles, e.g mitochondria and induce cell death.
- Photodynamic therapy has been shown to be effective in gingivitis, chronic and aggressive peirodontitis.

Limitations (Konopka1, 2007; Nilu Jain *et al*., 2008)

As a rule, biofilms are more resistant to photodynamic therapy. Some dyes e.g toluidine blue O causes blue staining of teeth Spectrum of activity of various photosentizers and laser not clear. Antibacterial action needs further investigation Full mouth photodynamic therapy for decontamination is cumbersome as each site has to be irradiated for effect after delivery of photosensitizer Can't be used for treatment of periodontal abscesses.

REFERENCES

Katie O'Riordan, Oleg E. Akilov, Tayyaba Hasan. The potential for photodynamic therapy in the treatment of localized infections

Killoy, W.J. 2002. The clinical significance of local chemotherapies. *J ClinPeriodontol* 29 (Suppl 2): 22–29.

Konopka1, K. and Goslinski, T. 2007. Photodynamic Therapy in Dentistry. J Dent Res 86(8):694-707.

Muller P, Guggenheim B. *et al*. 2007. Efficacy of gasiform ozone and photodynamic therapy on a multispecies oral biofilm in vitro. *Eur J Oral Sci.,* 115: 77–80.

Natalie J. Medlicott, Michael J. Rathbone A. *et al*. 1994. Delivery systems for the administration of drugs to the periodontal pocket. *Advanced Drug Delivery Reviews*, 13 181-203.

Nilu Jain, Gaurav K. Jain, *et al*. 2008. Recent approaches for the treatment of periodontitis. *Drug Discovery today*, Vol 13, Nov.

Osterberg S. K.A. *et al*. 1979. Long-term effects of tetracylineMinocycline on the subgingival microflora. *Journal of Clinical Periodontology*, 6: 133-140.

Phillippe Bidault, Fathia Chandad, Daniel Grenier. 2007. Systemic antibiotic therapy in the treatment of periodontitis. JCDA, VOL 73, No 6.77-82.

Shackley, D. C. Whitehurst. C 1999. Photodynamic therapy Journal of the royal society of medicine Volume 92 November

Thomaes. Rams & Jbrgen Slots. 1996. Local delivery of antimicrobial agents in the periodontal pocket. *Periodontology,* Vol. 10, 139-159.

****