Photodynamic Therapy – A Review

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Introduction:
The use of light as a therapy in human diseases has a very long history, stretching back into antiquity. The first uses of light as a therapeutic agent go back many centuries. It was used by the Egyptians, Chinese and Indians in the treatment of many diseases including vitiligo, rickets, psoriasis, skin cancer and even one of the earliest known reports of the sun as a therapeutic agent was heliotherapy, introduced by the Greeks 3000 years ago.

Over the past decade, extensive investigation has been carried out on photodynamic therapy and the antimicrobial action of photosensitizing agents and light. Photochemotherapy, or use of an exogenous sensitizer to absorb photons and then react for a therapeutic effect, has a long history. Psoralens were used in India as early as 1400BC. Detailed descriptions in India's sacred book AtharvaVeda (1400BC) indicate that Hindus practised the ancient Ayurvedic system of medicine using psoralens obtained from the seeds of Psoralea corylifolii for repigmentation of vitiligenous skin.

There was a long period in which uses of light were not appreciated, however, and only this century, through photodynamic therapy and psoralen molecules and ultraviolet A radiation (PUVA) therapy of some dermatological conditions, has light undergone a renaissance as a useful therapeutic tool in medicine and in the past decade into the field of dentistry. The term 'photodynamic therapy' was coined by Von Tappeiner in the year 1907 to describe the phenomenon of oxygen-dependent photosensitization. He is probably the most important early pioneer of photodynamic therapy, and also the first to attempt phototherapy of tumors. Wilson first proposed the use of lethal photosensitization as a tool for the treatment of periodontal disease.

Mechanism Of Action Of PDT

Photodynamic therapy is based on the dye-sensitized photooxidation of biological matter in the target tissue. This requires the presence of a dye (sensitizer) in the tissue to be treated. Although such sensitizers can be naturally occurring constituents of cells and tissues, in the case of PDT they are introduced into the organism as the first step of treatment. In the second step, the tissue-localized sensitizer is exposed to light of wavelength appropriate for absorption by the sensitizer. Through various photophysical pathways, also involving molecular oxygen, oxygenated

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<td>Chlorine e6-2.5 N methyl-d-glucamine</td>
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| Monoterpenes        | Azuleze                                    |

Light sources
The light source for PDT can be an ordinary light bulb, a diode array emitting a broad band incoherent spectrum, or a laser. Initially, PDT was performed with broad spectrum light sources such as xenon arc lamps or slide projectors.
equipped with red filters to eliminate short wavelengths. However, the light intensities are low with these devices.

Lasers have become the standard light sources for PDT applications, due to their monochromatic character, high power output, and ease of coupling to fiber optics for endoscopic light delivery within a body cavity or for interstitial implants. One of the more practical recent advances in PDT is the availability of diode lasers at wavelengths compatible with currently used photosensitizers. These systems have minimum electrical power requirement and are cooled thermoelectrically to provide a compact laser system. The potential advantages of the diode lasers for PDT are the low capital cost, negligible running costs, high reliability, small size and portability.

Applications Of PDT In Dentistry

Phototargeting Oral Biofilms – Dental Caries

Management of early carious lesions includes preventive approaches, such as dental plaque removal, through dental home care (toothbrushing, antimicrobials), professional placement of sealants and topical fluoride applications.

- Treatment of cavitated lesions involves the surgical removal of the infected tooth structure followed by tooth restoration. Photodynamic therapy could be used as dental caries preventive by targeting dental fermentative plaque microorganisms and as a minimally invasive technique to eliminate bacteria within carious lesions. This technique could offer the following benefits:
  - Rapid noninvasive topical in vivo application of the drug to the carious lesion.
  - Rapid bacterial killing after a short exposure to light.
  - Unlikely development of resistance considering the widespread generic toxicity of reactive oxygen species.
  - Confined killing by restricting the field of irradiation and the inherently short diffusion radius of reactive oxygen species.

Several laboratory studies have demonstrated (using toluidine blue O) the susceptibility of cariogenic bacteria, either in the planktonic phase or in the biofilm phase to photodynamic therapy.

Pdt In Endodontics

The ultimate goal of endodontic treatment is the elimination of infection from the root canal system. Endodontic treatment failures, however, are frequently associated with gram-positive aerobic and facultative microorganisms. The complexity, however, of the root canal system with its isthmuses, ramifications, as well as the presence of dentinal tubules, make complete debridement and removal of bacteria with instrumentation, irrigation and the standard medicaments almost impossible. Recent studies suggested the potential of photodynamic therapy as an adjunctive technique to eliminate residual root canal bacteria after standard endodontic chemo-mechanical debridement.

The synergism of red light and methylene blue reduced the viability of E. faecalis in the root canals of experimentally infected teeth by 40%. Recently, two studies described the application of root canal photodynamic therapy in vivo using toluidine blue O and light. It was suggested that photodynamic therapy offered a means of destroying microorganisms remaining after using sodium hypochlorite alone or citric acid and sodium hypochlorite as co-irrigants.

Oral Candidiasis

Candida albicans becomes a serious opportunistic infectious agent in immuno compromised patients. C. albicans can grow as biofilms on oral mucosal surfaces and prosthetic devices. Antifungal treatment with agents such as nistatin and miconazole often induce resistance, severely limiting their ability to eradicate fungal biofilms, so that recurrent infection occurs. Numerous in vitro studies have shown that photodynamic therapy is effective in killing Candida in planktonic and biofilm phases using methylene blue, toluidine blue O, photofrin, tiron, porphyrins, phthalocyanine and malachite green.

Topical treatment of oral candidiasis by photodynamic therapy may be an alternative to traditional antifungal drug therapy, especially in patients with human immunodeficiency virus (HIV) for whom persistent infection is a major problem.

Photodynamic Therapy In Periodontics

The main objective of periodontal therapy is to eliminate deposits of bacteria and bacterial niches by removing the supragingival and subgingival biofilm. Plaque removal with eradication of niches of causative pathogens is currently performed using mechanical methods, such as nonsurgical therapy, which results in significant clinical improvements and varying success rates. However, it has been demonstrated that conventional mechanical therapy cannot completely remove all periodontal pathogens; this is because of the anatomical complexity of the tooth roots, which may contain furcation areas and concavities, especially in deep periodontal pockets, and the bacteria invading the surrounding soft tissues.

- Local or systemic chemotherapy in conjunction with mechanical debridement (mechano-chemotherapy) are currently accepted approaches in the treatment of periodontal disease. However, the use of antimicrobial agents suffers from two major drawbacks.
• The first is the difficulty experienced in maintaining stable therapeutic concentrations of the agent in the periodontal pocket for a sufficient length of time to ensure eradication of the organisms present, because the mixture of gram-positive and gram-negative bacteria grow as complex aggregates within a polymeric matrix (biofilms) on the surfaces of the teeth, leading to inhibition of the action of antimicrobial agents and antiseptics.

• The second drawback is the strong possibility of the development of resistance to antibiotics by the target organisms.

For the elimination of bacteria in supragingival and subgingival plaque, antimicrobial photodynamic therapy has been applied with various combinations of lasers and photosensitizing agents. With respect to antimicrobial photodynamic therapy, it has been demonstrated that methylene blue and toluidine blue O are very effective photosensitizing agents for the inactivation of both gram-positive and gram-negative periodontopathic bacteria. The light sources of a specific wavelength mostly applied in photodynamic therapy are those of helium–neon lasers (633 nm), gallium–aluminum–arsenide diode lasers (630–690, 830 or 906 nm) and argon lasers (488–514 nm), the wavelengths of which range from visible light to the blue of argon lasers, or from the red of helium–neon and gallium–aluminum–arsenide lasers to the infrared area of some diode lasers. High-level-energy laser irradiation is not used to activate the photosensitive dye because relatively low-level exposure produces a high bactericidal effect.

Recently clinical photodynamic therapy kits that include methylene blue are already commercially available (Periowave™; Ondine Biopharma Corporation, Vancouver, Canada) (Helbo®; Photodynamic Systems GmbH & Co. KG, Grieskirchen, Austria).

Pdt In The Treatment Of Peri-Implant Disease

In the treatment of peri-implantitis, it has been proven that complete eradication of the causative bacteria, which are similar to the pathogens responsible for the development of periodontal disease, and disinfection and detoxification of the diseased implant surface, as well as of the peri-implant pockets, are essential to achieve effective healing with regeneration of the lost bone around the affected implants. Conventional mechanical methods are apparently ineffective for complete debridement of the bone defect as well as of the contaminated microstructured implant surface. However, because of the potential problems related to antibiotics (such as resistance) and antiseptics, as mentioned previously and the generally insufficient effect of the antimicrobial agents for bacterial eradication as well as poor results of re-osseointegration following their adjunctive application during nonsurgical and surgical therapy of peri-implantitis, novel approaches are still necessary in the treatment of peri-implant diseases.

High-level lasers have been used successfully in the surgical management of peri-implantitis. However, in nonsurgical therapy, high-level lasers have shown limited clinical efficacy. Moreover, following the application of some lasers, surface alterations (such as melting and carbonization) have been observed on the treated titanium surface. Thus Antimicrobial photodynamic therapy was recently proposed as an adjunctive for bacterial elimination in the treatment of peri-implantitis, based on its successful application in the treatment of periodontitis.

Summary And Conclusion

The main favorable features of antimicrobial PDT can be summarized as follows:

• Broad spectrum of action, since one photosensitizer can act on bacteria, fungi, yeasts, and parasitic protozoa.

• Efficacy independent of the antibiotic resistance pattern of the given microbial strain.

• Possibility to develop PDT protocols which lead to an extensive reduction in pathogen population with very limited damage to the host tissue.

• Lack of selection of photoresistant strains after multiple treatments.

• Small probability to promote the onset of mutagenicity.

• Availability of formulations allowing a ready and specific delivery of the photosensitizer to the infected area.

• Use of low cost light sources for activation of the photosensitizing agent.

If the resistance against antibiotics may become worse, PDT may be a valuable alternative for most indications in which hitherto antibiotic drugs were administered. If the number of immunosuppressed patients bring new challenges for treatment strategies. The concept of PDT is plausible and could foster new therapy concepts for plaque associated diseases. The available knowledge should enable and encourage steps forward into more clinical oriented research and development.

References


2. Wilson M. Bactericidal effect of laser light and its potential use...


