

Recent Advances in Photodynamic Therapy in the Treatment of Dental Diseases

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Abstract: Photodynamic Therapy (PDT) is a new technology that utilizes the photodynamic effect for disease diagnosis and treatment. Its action is based on the photodynamic effect. It is a kind of photosensitization reaction accompanied by biological effects with the participation of oxygen molecules. The process is that specific wavelength laser irradiation causes the photosensitizer absorbed by the tissue to be excited, and the photosensitizer in the excited state passes the energy to the surrounding oxygen, generating highly reactive singlet oxygen, which undergoes oxidative reaction with neighboring biological macromolecules to produce cytotoxicity, which leads to cellular damage and even death. Current research shows that photodynamic therapy shows great advantages in the treatment of caries, periodontal disease and oral squamous carcinoma. This paper mainly provides a further overview of the current status of research at home and abroad on the application of photodynamic therapy in the treatment of dental diseases in recent years.

Keywords: Photodynamic Therapy; Caries; Periodontal Disease; Endodontics; Oral Squamous Cell Carcinoma.

1. Introduction

Photodynamic therapy (PDT) is a non-surgical treatment modality, the main mechanism of PCT is activation by photosensitizer molecules receiving laser light. These reactive dye molecules form cytotoxic and highly lethal monoclinic oxygen in the presence of endogenous oxygen, which helps in the destruction and elimination of bacteria [1]. It is a non-invasive treatment widely used in skin oncology for the treatment of many skin cancers, but over the past few years its use has gradually expanded to an increasing number of infectious and inflammatory skin diseases. Existing studies have shown that PDT is widely used in dentistry and has a positive effect in the treatment of caries, periodontal disease, and squamous carcinoma of the oral cavity.

2. Application of Photodynamic Therapy

2.1. Dental Caries

Antimicrobial Photodynamic Therapy (aPDT) is a technique that utilizes a low-power laser of a specific wavelength in combination with a photosensitizing agent called a photosensitizer to kill microorganisms. By inducing damage through reactive oxygen species (ROS), aPDT offers a new approach to addressing plaque and associated microbial biofilms designed to improve oral health outcomes. Photosensitizers have been incorporated into dental materials to create photosensitive dental materials. The use of photosensitized dental materials in aPDT has been used as an innovative antimicrobial option in dentistry, which in turn enhances oral health [2]. Molar incisor hypomineralization (MIH) is a defect in enamel development that occurs during the mineralization phase. patients with MIH are at increased risk of caries, hypersensitivity, and restorative failures. A minimal intervention protocol combining antimicrobial photodynamic therapy and selective chemomechanical removal of carious tissue using Papacárie Duo® products was

developed. This protocol is promising for decontamination and allergy control in MIH teeth[3]. Curcumin photosensitizer improves the adhesive strength of bleached enamel to composite while reducing marginal microleakage [4]. aPDT is very effective in killing bacteria, but the problems of deep tissue hypoxia and limited light penetration have not been properly addressed. In addition, few aPDT efforts take into account the modulation of inflammation, which is an important regulatory process after antimicrobial therapy and the ultimate goal of treatment. It was investigated that by incorporating simple nanocomposites not only could aPDT be enhanced to provide substantial auto-oxidative replenishment, but also to promote effective inflammatory modulation of a wide range of deep infections via CO. This approach utilizes the unique properties of these materials to combat bacterial infections by simultaneously killing bacteria, modulating inflammation and increasing oxygen levels in the affected microenvironment. This aPDT therapeutic system based on O₂ and CO gases offers a promising approach for comprehensively addressing infectious diseases caused by microorganisms, especially deep infections, with potential clinical applications[5].

2.2. Teeth Whitening

Conventional teeth whitening techniques often result in enamel damage and soft tissue toxicity due to the use of biologically incompatible whitening reagents and continuous bright light exposure. Carbon dot-based nanostructures can extend the half-life of reactive oxygen species (ROS) and increase the degradation rate of dyes by aPDT. It can completely whiten teeth by eliminating stains deep within the enamel without damaging the enamel structure and causing any tissue toxicity. This study further confirms the superiority of aPDT in tooth whitening as well as exploring carbon dot based nanostructures for the treatment of oral diseases [6].

2.3. Endodontic and Periapical Diseases

Root canal therapy is the mainstay of treatment for

endodontic and periapical diseases. Photodynamic therapy (PDT) is a suitable adjunct to improve the disinfection of conventional root canal therapy [7]. As an emerging adjunct to disinfection, photodynamic therapy utilizes photosensitizers and light to eliminate microorganisms through an oxidative reaction. PDT has shown promise in improving apical healing and reducing microorganisms. In this case, curcumin diluted with 2% chlorhexidine gel can be used as an effective photosensitizer with antimicrobial properties. In addition, photobiomodulation was performed to aid in cellular recovery and reduce postoperative discomfort. The results showed that the combination of curcumin PDT in endodontic microsurgery (EMS) protocols produced positive results [8]. However, further randomized clinical trials are needed to evaluate the efficacy of this approach in EMS. The combination of Er: YAG laser and PDT significantly enhanced the bactericidal effect of PDT on *Enterococcus faecalis* in root canals. It had a similar effect on the elimination of *Enterococcus faecalis* compared to the effect of using Er:YAG laser and NaOCl[9]. Antimicrobial photodynamic therapy aPDT mediated by rutin-Ga(III) complex effectively reduces *E. faecalis* biofilm growth by disrupting biofilm structure and down-regulating virulence genes. These findings highlight the potential of aPDT with the rutin-Ga(III) complex as an adjunctive therapeutic approach targeting *E. faecalis* biofilms[10]. In addition, traditional methods such as mechanical instruments, chemical rinses and intracanal medications pose a huge limitation to root canal disinfection because they kill both bacteria and tooth stem cells. Researchers have combined antimicrobial drugs with antimicrobial photodynamic therapy (aPDT) and methylene blue (MB) as a photosensitizer, which has been shown to be effective in reducing the death of dental pulp stem cells (DPSC). This study reveals the promise of combining aPDT, methylene blue MB and antibiotic drugs to reduce dental stem cell death[11]. Compared to indocyanine green (ICG) and methylene blue (MB), curcumin, with its superior mean depth of penetration, is a promising option for effective root canal disinfection in endodontic treatment. Consideration of these findings may enhance the selection of photosensitizers for clinical applications[12]. Future studies should focus on clinical outcomes associated with reduced microbial counts to determine the efficacy of aPDT in primary dentin disinfection [7]

2.4. Periodontal Disease

Periodontitis is a chronic multifactorial inflammatory disease caused by bacterial dysbiosis, leading to loss of tooth supporting structures and tooth loss. Among the non-surgical methods, scaling and root planing (SRP) are considered the basic methods to bring maximum improvement. However, complete elimination of subgingival tartar is difficult. Studies point to alternative treatments by ozonated water to achieve suppression of the subgingival microbiota. Recently, photodynamic therapy (PDT) has been proposed in periodontal therapy in an effort to improve the efficiency and effectiveness of bacterial elimination and root surface debridement[13]. PDT promotes soft tissue healing to a certain extent, but provides no additional help in the healing of extracted sockets of periodontally damaged teeth. PDT showed no benefit on postoperative pain, changes in bone density and bone height after tooth extraction [14]. The potential of PDT in periodontal therapy has been emphasized not only to effectively reduce periodontal pathogens and

improve periodontal health indicators. Notably, it positively affects periodontal immune response, tissue integrity and alveolar bone preservation. Clinical trials have shown that PDT improves periodontal health and alters the microbial composition of dental plaque when used with conventional therapy[15]. Dendrimers can effectively encapsulate curcumin and improve its low bioavailability and water solubility. Decreased *Porphyromonas gingivalis* survival after dendrimer curcumin and blue laser photodynamic therapy suggests that this technique may be an effective method for eradicating *Porphyromonas gingivalis* infections[16]. Photodynamic therapy using photosensitizer nanoparticles irradiated via gingival penetration better inhibits the growth of subgingival flora without causing pain and discomfort to the patient [17]. PDT offers a promising adjunctive treatment for periodontitis with bacterial reduction, tissue healing, and immunomodulatory benefits. However, further studies are needed to refine its clinical application and efficacy.

2.5. Oral Potential Malignant Disorders (OPMDs)

A total of 15 oral mucosal diseases are defined as OPMDs, including oral leukoplakia (OLK), oral erythema (OE), and oral submucous fibrosis. Evidence suggests that conventional treatment leads to suboptimal clinical outcomes. Even with complete excision, the recurrence rate remains high and impairs a number of oral functions such as chewing, articulation, swallowing and taste. Since PDT is a cold photochemical process, there is no tissue heating and the risk of damaging the integrity of underlying functional structures is much lower compared to thermal laser technology and other invasive methods[18]. Photodynamic therapy (PDT) is now a new treatment option that offers the possibility of a cure for opmd patients. It combines specific wavelengths of light, tissue oxygen, and tumor-targeted photosensitizers to produce cytotoxic single-linear oxygen and free radicals[19], which inhibit the proliferation and induce apoptosis of oral precancerous and squamous carcinoma (OSCC) cells. Lin Lin et al.[20] developed a new type of organic photosensitized titanium dioxide nanoparticles (ITICTh NPs) for OLK photodynamic/ photothermal therapy (PTT), which is more convenient and efficient than conventional photosensitizers. The researchers established a dynamic precancerous animal model similar to humans in terms of pathogenesis, pathological changes, host immune activity and molecular level, and in vivo studies have shown that phototherapy can effectively block malignant transformation. This study is the first time to apply multifunctional organic nanomedicine to photodynamic/ photothermal treatment of OLK, and the established treatment model is closer to the clinical reality, which has a broad application prospect in the treatment of oral precancerous lesions.

2.6. Oral Squamous Cell Carcinoma (OSCC)

Oral cancer is one of the most common malignant tumors worldwide and has become a major public health problem. Oral cancer has a high incidence, high mortality rate, and poor prognosis, with a 5-year survival rate usually less than 40%[21]. Traditional treatments, such as surgery, radiotherapy, and chemotherapy, are far from satisfactory for oral cancer, usually cause pain, inevitably impair oral function, and have a limited role in improving the 5-year survival rate of oral cancer patients [22]. PDT, as a primary or adjuvant therapeutic modality, offers a promising approach

to the treatment of early-stage oral cancer. It has superior advantages over traditional surgical, radiotherapy and chemotherapy modalities. However, most clinically applied photosensitizers have some shortcomings, including oxygen dependence, poor water solubility, and lack of tumor targeting ability. Moreover, the therapeutic process of PDT is accompanied by a continuous consumption of oxygen, which exacerbates the degree of hypoxia at the tumor site, leading to a decrease in the efficacy of PDT [23]. To address these limitations, Yuan Tao et al [24] designed and constructed dandelion-shaped size-contractable nanoparticles for tumor-targeted delivery of the hypoxia modulator resveratrol (RES) and the photodynamic agent chloro e6 (CE6). The synergistic effect of RES and CE6 promoted PDT-enhanced autophagic cell death and apoptosis, resulting in a stronger anti-tumor in situ OSCC model effects. Thus, hypoxia modulators enhance the efficacy of PDT by increasing the oxygen content in tumor cells and inducing cellular autophagic death and apoptosis, which provides a way to enhance the effect of PDT on OSCC.

3. Summary and Prospects

In terms of basic research, photosensitizers, as one of the key elements of PDT, how to further improve the selectivity and specificity of photosensitizers and synthesize functional photosensitizers with different organelle targeting is an important research topic in the future. Secondly, the research and development of new light sources with stable performance, low price and easy clinical manipulation, especially represented by light-emitting diodes (LEDs), is of great importance in the promotion of PDT applications. Moreover, there are few clinical trials of PDT for children, and parents and adults are generally reluctant to allow children to participate in trials, especially because of the fear of unpredictable side effects in the pediatric population. In addition, PDT has been used in adults to treat other dermatological conditions with satisfactory results, and these conditions may also be explored in pediatric patients.

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