The Application of Photobiomodulation Therapy in Endodontics

Subjects: Cell & Tissue Engineering

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Photobiomodulation therapy (PBMT) applied with a low-level laser (LLLT) provides endodontists with a non-invasive and non-thermal method that can be utilized as an adjunct to traditional root canal treatment (RCT) or as a therapeutic tool in regenerative endodontic procedures (REPs) due to its anti-inflammatory effects, apical cicatrization, and acceleration benefits.

photobiomodulation therapy | low-level laser therapy | regenerative endodontic procedures

1. Introduction

The typical method applied in endodontics is root canal treatment (RCT) to treat irreversibly inflamed or necrotic pulp tissue that has been damaged by infectious diseases or trauma [1]. However, this approach has several impairments, such as the possibility of reinfection due to microleakage [2], hypoesthesia, and increased susceptibility to root fracture due to brittleness [3]. To overcome these drawbacks, the purpose of regenerative pulp treatment is to maintain the vitality of dental pulp [4]. Regenerative pulp treatment is an alternative treatment modality during continuous tooth root development and root apical closure in the case of immature permanent teeth [5]. Traditionally, apexification has been performed to induce apical closure when the pulp of immature permanent teeth is infected [6], but it cannot maintain pulp vitality [7]. Since the 1960s, regenerative endodontic procedures (REPs) have been proposed to be used in uninfected, especially traumatic pulp tissue to replace the infected/inflamed pulp tissue with viable tissue. Nevertheless, REPs have also been successfully used to treat necrotic pulps and immature apices, with or without apical periodontitis [8][9].

The dental pulp is a neural-crest-derived, highly specialized mesenchymal tissue that comprises odontoblasts and cells that produce extracellular matrix (ECM). The two updated strategies for REPs to regenerate dental pulp-like tissues are cell transplantation (cell-based) and cell homing (cell-free) [1]. The first strategy requires exogenously transplanted stem cells (SCs) to form the dentin/pulp-like complex in the subcutaneous connective tissue after transplant of stem cells, including postnatal human dental pulp stem cells (hDPSCs) [10], stem cells from human exfoliated deciduous teeth, periodontal ligament stem cells, dental follicle progenitor stem cells, and stem cells from apical papilla (SCAPs) [11]. The second strategy uses the host's endogenous cells originated from the apical papilla to regenerate tissue, which may be more clinically translatable [1]. hDPSCs have the capacity to differentiate into multiple cell types, including odontoblasts, osteoblasts, and chondrocytes, by expressing specific markers, promoting alkaline phosphatase (ALP) enzyme activity, and producing precipitated mineralized nodules [12]. Basic research is aiming to establish more effective regenerative methods for hPDSC transplantation into root canals.

Therefore, to circumvent root canal decontamination problems, maintain the vitality of pulp, and regenerate pulp-like tissue, researchers are seeking strategies to regenerate pulp-like tissue through either cell therapy or tissue-engineering methods.

Laser-induced photobiomodulation therapy (PBMT) has been proposed as an adjunctive therapy with the potential to improve dental pulp tissue regeneration [13]. Notably, Marques et al. (2016) [14] identified PBMT as "the fourth element of tissue engineering along with stem cells, scaffolds, and growth factors" because of its benefits properties, which are able to overcome some drawbacks of tissue engineering. When applied with adequate parameters, PBMT stimulates cell proliferation and differentiation [15], ATP production [16], mitochondrial respiration [17], protein synthesis, and bone formation in human periodontal ligament stem cells, fibroblasts, and odontoblasts [18], which are directly involved in tissue repair [18][19]. It has also been demonstrated that DPSCs respond positively to laser phototherapy, indicating that PBMT may be a crucial therapy for tissue engineering associated with stem cells [20]. As a matter of fact, the possible cell sources for pulp regeneration through cell homing include DPSCs, SCAPs, and bone marrow stem cells (BMSCs) [21].

The term "PBMT" is used to characterize the various laser/LED light applications with low-energy densities and is based on photochemical mechanisms where the photo energy is absorbed by the mitochondrial chromophores and transmitted to respiratory-chain components [22]. PBMT is activated through an electromagnetic radiation source and has been demonstrated in many clinical applications to exert anti-inflammatory, analgesic, and trophic-regenerative effects [22][23]. Previous studies have illustrated that in endodontics, PBMT has been widely accepted for its beneficial effects, such as analgesia, sterilization/disinfection, reduction of dentin sensitivity, and transpiration of infected dentin and dentin formation in root canals [24]. The red and near-infrared light emitted by PBMT is absorbed by the mitochondrial respiratory chain, which is one of the main sources of reactive oxygen species (ROS), thereby causing the production of ROS, nitric oxide, adenosine triphosphate (ATP), and cyclic adenosine monophosphate (cAMP) to initiate stem cell proliferation and induce the signal cascade effect [25]. Lasers, such as diode lasers, are usually used for PBMT of DPSCs, and the light is absorbed by mitochondria, causing metabolic changes in the host cells through a cascade of photochemical and photoelectric reactions, inducing both primary and secondary effects on the irradiated tissue [23].

2. The Application of PBMT in Endodontics

2.1. PBMT-Induced Anesthesia

Being a non-invasive method, PBMT is able to produce anesthesia with an estimated significance of 60–95% [26]. In this regard, PBMT using an 810 nm diode laser (250 mW, 53.3 J/cm^2 per side, 120 s, and continuous mode) achieves good-quality anesthesia during conventional tooth excavation [27]. In another study, PBMT based on the 2940 nm Er:YAG laser (60 mJ/point in non-contact mode) was used to achieve an appropriate anesthetic effect during Er:YAG-assisted cavity preparation of primary teeth [26]. Previous systematic reviews have shown that the current clinical parameters in this field are inadequate, so it does not seem feasible to propose a precise treatment protocol.

2.2. Laser-Assisted Diagnostics of Initial Caries Lesions and Pulp Status

Approaches based on light-induced fluorescence or light scattering properties related to demineralization are laser fluorescence (LF) [28], quantitative light-induced fluorescence (QLF) [29], and optical coherence tomography (OCT) [29], each of which is regarded as a useful supplement to the conventional diagnostic tools for caries and has helped improve the accuracy of caries detection in recent decades.

The LF technique, which is applied using a diode laser at a wavelength of 655 nm, quantifies the fluorescence intensity of a tooth's surface and displays it. QLF detects the auto-fluorescence by irradiating teeth at 405 nm. OCT uses a 1300 nm wavelength to detect the light backscattered from tooth structures for dental caries detection applications. LF and QLF methods can quantify the severity of demineralization by measuring the fluorescence loss; however, the disadvantage of these methods is that they cannot measure the internal extension of carious lesions.

The patient will experience severe pain when the laser is used on a tooth with hyperemic pulp because laser irradiation increases the local blood flow in the pulp [30].

2.3. Laser-Based Prevention and Preparation of Enamel Caries

Diode lasers containing 810, 830, and 890 nm were used for caries prevention [31]. PBMT (810 nm, 30 mM, and 90 s) has been shown to increase calcium and phosphate levels [32][33]. PBMT applied at a wavelength of 830 nm suppressed the process of demineralization around orthodontic brackets on bovine teeth [34] and increased the hardness of the enamel surface [35].

The erbium laser is now also one of the options for cavity preparation, and it causes minimal invasive damage [36].

2.4. PBMT-Assisted Direct Pulp Capping

PBMT has been proposed to contribute to the outcomes of DCP procedures [37] and effectively improve the prognosis of DPC for permanent teeth [38], due to its considerable effects in shortening the inflammatory phase, reducing pain, promoting the process of wound healing, and stimulating the formation of hard dentin tissue [39][40]. The photo energy that penetrates into the pulp tissue coagulates the exposed pulp, thereby creating the biological basis for forming reparative dentin [12]. However, the findings of these in vitro and animal studies have shown that proper technique and materials (calcium hydroxide –$Ca(OH)_2$ and MTA [41]) in DPC are prioritized over optimization of PBMT [42], and so far, laboratory results have not been generalized to clinical studies [39][43][44]. Therefore, it is still unclear how to identify the contribution of a laser's application to the clinical-outcome improvement in the irradiated group, and further studies are needed to obtain more accurate results.

2.5. Decontamination of a Root Canal System

Due to infections by multiple and numerous aerobic and anaerobic bacteria, the key procedure of REPs comprises effective root canal decontamination (disinfection/sterilization). Decontamination of the root canal system is critical to the success of REPs and is accomplished through effective chemical-mechanical preparation, such as ultrasonically activated NaOCl [45]/EDTA [46] and the use of antibiotics in combination [47]. Aside from the ultrasonically activated NaOCl in endodontics, laser-assisted elimination of intra-canal microorganisms can be divided into two mechanisms: debris and smear-layer removal and disinfection of the root canal [48].

Maximum debris and smear-layer removal effects are achieved when laser light is used in root canals in conjunction with an appropriate concentration of a NaClO irrigating solution [48]. Many lasers, such as CO_2 [49], Nd:YAG [50][51], and erbium family (Er:YAG [52] and Er,Cr:YSGG [53]) ones have been reported to be used in removing debris and smear layers from infected canal walls. Er:YAG is the most appropriate laser for this purpose [52][54].

Nd:YAG, Ho:YAG, and Er:YAG lasers eliminated more than 99% of *Enterococcus faecalis* (*E. faecalis*) and *Escherichia coli* (*E. coli*) for root-canal disinfection [55]. Schoop et al. (2004) demonstrated the antibacterial effects of diode, Er:YAG, Er,Cr:YSGG, and Nd:YAG lasers as being efficacious for dentinal disinfection from *E. facaelis* and *E. coli* at varying thicknesses. Therefore, laser treatment is a convenient adjunct to regular canal disinfection, especially in combination with chemical-mechanical preparations [56].

The anti-bacterial effects of photodynamic therapy (PDT) [57] on the pulp of human teeth with periapical and necrotic lesions indicated that it was an appropriate solution for root-canal disinfections [58]. Photodynamic therapy using a diode laser at 60 J/cm^2 and 50 mW plus methylene blue eliminated *E. faecalis* from root canals to the degrees of 77% [59] and 99% [60]. Photodynamic therapy using diode red light at 30 J/cm^2 energy plus methylene blue reduced 80% of the colonies of *Actinomyces israelii*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, and *Prevotella intermedia*. Based on available studies [61], PDT provides endodontists with an antibacterial adjunctive device for RCT [62].

2.6. Postoperative Pain after Endodontic Treatment

Pain results from chemical-mechanical preparations or microbial damage to the pulp tissue or root apex, and its emergence is significantly higher after RCT [63][64][65]. This therapeutic technique, PBMT, makes endodontic treatment more comfortable by applying a preliminary phase to avoid the use of pharmacological agents for postoperative pain control [66].

PBMT using a 970 nm laser at 0.5 W reduced the postoperative pain after RCT in patients with symptomatic apical periodontitis [67]. However, another group showed that PBMT applied by an 808 nm laser with 100 mW of power at 70 J/cm^2 has limited effects on reducing the pain associated with root-canal retreatment [63]. Thus, research has indicated that PBMT can delay the onset of postoperative pain and decrease its severity and duration after an RCT.

The mechanisms of PBMT's actions in pain reduction are through facilitating the synthesis of anti-inflammatory prostaglandins (PGEs), immunoglobulins, β-endorphins, and lymphokines. Additionally, it decreases the production of pro-inflammatory factors and pain-related neurotransmitters. As a result, it has been suggested that PBMT could be useful in relieving pain after RCT or root-canal retreatment. However, due to a limited number of clinical studies, it is not yet time to formulate an exact clinical protocol; thus, further studies should be performed to achieve more conclusive results [68].

2.7. PBMT Used in Endodontic Surgery

Investigations have addressed the importance of PBMT in endodontic surgery with regard to pain relief, swelling reduction, and soft and hard tissue healing. The diode laser applied at 3–7.5 J/cm^2 showed desirable results of PBMT on pain relief and tissue healing; however, more clinical studies are needed to obtain further insights. [69][70].

2.8. Tooth/Dentinal Hypersensitivity (DH)

Matsumoto et al. (2018) used a laser to treat DH for the first time, and laser technology is gradually being recognized as an important method for DH [71].

Up till now, lasers studied for DH treatment address three different mechanisms: dentin tubal obliteration by high-power density output laser therapy, alteration in the pain threshold of the pulp's neural system, and stimulation of reactive dentine formation as a result of the PBMT effect [72][73]. Clinical studies have shown that PBMT using GaAlAs (795 or 830 nm) or InGaAlP (660 nm) at 1.8–10 J/cm^2 significantly reduced DH.

2.9. Tooth Bleaching

PBMT mainly reduces the mild to severe postoperative sensitivity that appears in most patients after tooth bleaching [74], particularly with the in-office technique [75][76][77]. Clinical studies suggested that PBMT applied with a diode laser at 12 J/cm^2 effectively reduced dental sensitivity after in-clinic bleaching. In vitro studies have investigated the effect of PBMT on odontoblastic cell responses or the neutralization of gel bleaching.

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