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PHOTOBIOMODULATION IN DENTAL IMPLANT THERAPY: A REVIEW

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ABSTRACT Photobiomodulation (PBM) or formerly known as low-level laser therapy (LLLT) is nothing but low-dosage biophotonics for therapy which presents an advancing new era of regenerative modalities in dental implantology. It utilizes light emitting diodes (LEDs), broad light sources and lasers for this purpose. Photobiomodulation is intended for relieving pain and inflammation, regulating immune responses as well as stimulating wound healing and tissue regeneration. This helps in combatting the main pathological causes of implant failures that are, peri-implant mucositis and peri-implantitis as well as helps promote osseointegration and improve stability of implants. While the scope of photobiomodulation has been thoroughly investigated in in-vitro and animal studies, human clinical trials are still scarce which makes appropriate protocol formation with respect to dosage and mode of delivery among other parameters difficult. A recently introduced and potential application of photobiomodulation in the field of implantology aims to deliver the positive effects of biophotonics through in-situ ambulatory PBM therapy called the smart dental implant (SDI) system. This comprehensive review presents the current and future trends in the application of photobiomodulation in the field of dental implantology.

KEYWORDS : Photobiomodulation, dental implant, lasers, periimplantitis

INTRODUCTION

PBMT or photobiomodulation therapy, also known as low level laser therapy (LLLT), is defined as 'a type of non-invasive and nonthermal therapy based on non-ionizing light sources, including lasers, light-emitting diodes (LEDs), and broadband light, in the visible and infrared spectrum'.[1] LLLT was discovered in 1967 by Endre Mester at the Semmelweis Medical University in Hungary. It has become a routine treatment modality in many dental clinical settings and has been demonstrated to be a useful aid in wound healing and tissue regeneration.

In the 1990s, the Food and Drug Administration (FDA) approved laser therapy for oral treatment, therefore its application in surgery and endodontic treatment has been among the most popular topical treatments, e.g. treatment of mucosal leukoplakia, pediatric dental diseases, and alveolar osteitis.[2] In the field of oral implantology, research has been directed toward the potential of photobiomodulation to reduce the healing time following implant placement, to improve the potential of bone regeneration and to act as an adjunct in the management of peri-implant mucositis and peri-implantitis.[3]

Lasers have a fascinating range of applications for implants, from their initial stages of fabrication (e.g., laser sintering) to generating surface modifications to promote ideal implant-bone interfaces. Further, lasers are used in the clinical setting where they are rapidly becoming a popular surgical tool to prepare soft and hard tissues for implant placement, to decontaminate surgical sites, and finally, to reduce pain and inflammation and promote healing.[4-7] The latter procedures are within the scope of PBM and can be performed either at the time of implant placement or during follow-up visits.[6] This article presents a comprehensive review on the scope of photobiomodulation in dental implant therapy.

MECHANISM OF ACTION (Flow chart 1)

LLLT is a non-thermal modality which are those physical agents that do not raise the subcutaneous tissue temperature greater than 36.5ºC. Therefore the therapeutic effects of LLLT are not associated with a heating response, but rather a photochemical response. When light (photons) enters the cell, certain molecules called chromophores react to it, and trigger a photochemical reaction that leads to desirable physiologic effects. LLLT is simply another form of energy that can be used to create physiological changes in tissue.[8]

Photobiomodulation acts on the mitochondria and is mainly mediated by cytochrome C oxidase (CCO), the terminal enzyme of the 3 respiratory chain. As CCO absorbs light in the near infrared range, photons excite wavelength specific chromophores to initiate signaling pathways.

The activation of CCO directly increases adenosine triphosphate (ATP) production. Cytochrome C oxidase is known to dissociate from inhibitory nitric oxide, a free radical and an important signaling molecule to further increase ATP bio availability. When released, nitric oxide participates in biologic processes such as vasodilatation and angiogenesis to provide analgesic effects. Photobiomodulation has been shown to promote bone and connective tissue remodeling probably due to involvement of reactive oxygen species produced by mitochondria and found to be functioning through an increased vascular activity which would also contribute to rapid turnover of the bone and is amenable to light.[9]

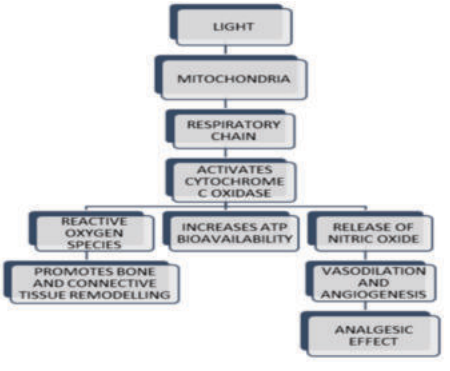
The biphasic response follows the Arndt-Schulz law which states that weak stimuli slightly accelerate vital activity, higher stimuli raise it more until a peak is reached, while stimuli even stronger suppress it until a negative response is obtained.[10]

CONTRAINDICATIONS

- Cancer (tumors or cancerous areas)[8,11-17]
- Direct irradiation of the eyes[8,11,13,15,16]
- Photophobia or abnormally high sensitivity to light[8,11,13,16]
- When using photosensitizing medication[8,13,16]
- Direct irradiation over the fetus or the uterus during pregnancy[8,11-14,16,17]
- Direct irradiation over the thyroid gland[14-17]
- Symptoms of unknown cause[14]
- Over hemorrhaging lesions[8,11,12,15,16]

Principles of Dosing

Photobiomodulation is associated with a dose-related response which is best described as a multiphasic outcome, as at relatively low doses of radiant exposure there can be photobiostimulation and at higher levels photobioinhibition. The former is associated with enhanced healing, whereas the latter has been found to be optimal for pain relief.[18-23] The dosage is the energy delivered in J/cm^2. However, the challenge is to deliver the essential cellular level of photonic input to depth and volume in Joules/cm^3. To cover large areas of sub-surface tissues, either a scanning technique or multiple overlapping spots may be used. As an alternative, a large surface optical spot can also be used. This latter approach saves time as a larger area can be treated more quickly. Moreover, with a larger optical spot size, the overall energy delivered to the target is greater, whilst still keeping the therapeutic dose to the recommended range of 2–8 joules/cm^2 for enhanced healing and 10–30 joules/cm^2 for analgesia.[24]



Flow Chart 1: Mechanism of Action

Photobiomodulation In Dental Implant Therapy

The mechanisms through which PBM works are multifaceted and are involved in versatile biological actions such as gene expression, energy metabolism, cell proliferation, differentiation, survival, and cell death.[25]

1. Effect On Post-Extraction Socket Bone

The socket healing process might be conceptualized as a sequence of biological steps occurring after tooth extraction, to fill the dental alveolus with bone tissue.[26] Socket preservation consists of conservative procedures designed to maintain the volume of bone after the extraction. It helps counteract bone resorption and reduces the need for later bone augmentation, in anticipation of a fixed partial denture-pontic or implant placement. PBM therapy stimulates bone regeneration when organic or inorganic materials are synergically added to the bone defect.[27]

Amaroli A et al[27] conducted a review to analyse the available evidence on the effect of photobiomodulation socket bone preservation and came to the conclusion that PBM delivered by LED or diode, Nd:YAG, and CO2 lasers, can positively affect alveolar ridge retention, independent of the laser used. When irradiated using the appropriate parameters, PBM could improve osteoproliferation and osteoinduction for socket preservation in healthy and sick animal models and human subjects, as well as in the presence or not of an allograft or biomaterial. Wavelengths higher than 800 nm and irradiation longer than three applications, resulted in a better bone healing effect.

2. Effect On Implant Stability

Bone tissues have a high regeneration capacity and an ability to regain their mechanical properties and architecture.[28] However, impaired vascularization around the implant because of osteotomy leads to an increased osteoclastic activity and loss of stability.

To ascertain the effect of PBMT on improving implant stability, previous studies have focused on animals, including rodents, rabbits, beagles, and primates. A number of studies and systematic reviews have been conducted, and suggested that PBMT provided a positive effect in animal models. However, due to the lack of clinical data, these studies could not provide powerful evidence for a positive effect of PBMT in humans. Fortunately, a number of clinical trials have recently been published, thereby increasing the cohort of treated patients.[1]

The effect of PBMT on implant stability is related to the treatment protocol, including wavelength, mode, output, energy density, exposure time, and frequency of treatment.[29] Studies have shown an increase in implant stability 3 to 10 weeks after implant placement while some did not show any improvement.[1]

3. Effect On Osseointegration

Dental implant stability depends on the implant's capacity to successfully osseointegrate, that is, successful bone-to-implant union while preserving the structural and functional integrity of the host site.[30] Experimental studies have evaluated the use of PBM to stimulate osteoblast activity in vitro and concluded that PBM enhances the stability of dental implants. Furthermore, it was found to be capable of boosting the healing process around the surgical site by increasing adenosine triphosphate synthesis and angiogenesis, in addition to increasing the proliferation of osteoblast and reducing inflammation.[31-33]

4. Effect On Post Surgical Healing (Fig. 1)

In implant surgery, postoperative pain usually originates from the surface region (soft tissue incision) and deep region (bone preparation). Photobiomodulation with the aid of red and infrared laser radiation has been shown to reduce post surgical healing and consequently, post surgical pain. Laser beams stabilize cellular membranes involved in regulating nerve impulse transmission. Such a regulation inhibits depolarization by increasing ATP synthesis, thereby causing a significant increase in the slow nerve function. As soon as the sensory nerve conductivity speed declines, pain reduction can be observed.[34,35] Another pathway that has been postulated to lead to reduced pain is the vascular effects of laser therapy. By delivering low-intensity laser beams, especially the red wavelength, increased blood circulation occurs, which in turn enhances the oxygenation in the lymphatic drainage, the activity of neutrophils, macrophages, and fibroblasts, and metabolism of damaged cells, eventually diminishing pain at the very early minutes following irradiation.[36-40]

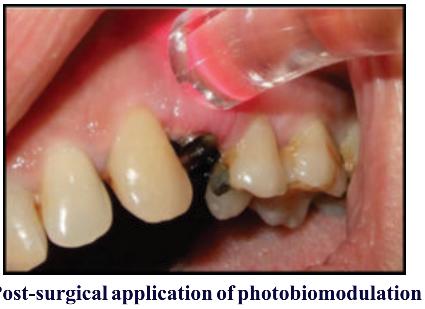


Figure 1. Post-surgical application of photobiomodulation

In a split-mouth study conducted by **Reza B et al**[41]**,** concurrent irradiation of 660 nm and 810 nm low-intensity lasers with a dose of 6 J/cm2 in the primary stages of acute inflammation resulted in pain relief and improved wound healing in the implant placement area in the posterior mandible of patients.

In addition, in the study by **Lopez-Ramirez**[42], although the level of the determined dose seems appropriate, and according to Arant-Schulz law[43], it lies within the range of 1□10 J/cm^2, the irradiation time or its frequency of application might have been inadequate since the inflammation resulting from a surgical wound, which is often associated with pain, is not a phenomenon that happens immediately after surgery. Instead, it occurs gradually and peaks 24–48 hours after the surgery. Therefore, laser irradiation should be repeated within the first two or three days after the surgery to relieve the pain resulting from inflammation.

5. Effect On Peri-implantitis

The application of low lever laser therapeutic (LLLT) in cases of peri-implantitis presents effects on biostimulation and assists in the inflammation and repair of the surgical wound. According to **Friggi et al** [44]**,** the low intensity laser most used for this purpose is the gallium aluminum arsenide laser (AsGaAl), with wavelength ranging between 660 and 980 nm, power variation between 40 and 100 mW and energy density or creep recommended to biostimulate peri-implant bone tissue is 16J, distributed in four application points. It was recommended that the time between these applications is 48 hours, starting in the immediate post-surgical and lasting up to 30 days.

Future Trends

Park M et al [45] have developed a smart dental implant (called SDI) system for in situ ambulatory PBM therapy which augments the immunity of gingival cells against potential peri-implant diseases without patient dependency. Their SDI system is essentially a counterpart of the existing conventional dental implant but enables energy harvesting and light delivery using a piezoelectric dental crown and embedded light emitting diodes (LEDs). **(Fig. 2)** Oral mechanical motions, such as chewing or brushing, strike SDI to cause the electrical energy generation, which is accumulated in temporary energy storage (a capacitor) for irradiating embedded LEDs. Such active and localized light delivery significantly enhances PBM therapy due to consistent light delivery at extreme proximity to the peri-implant tissues.

CONCLUSION

The scope of photobiomodulation since its advent and introduction in the field of dentistry has grown in the recent decades. As we approach an era that aims at rehabilitating oral tissues as conservatively as possible, dental implants have

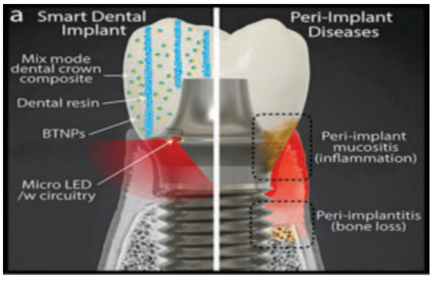


Figure 2. Smart Dental Implant versus normal dental implant without therapeutic function can cause severe oral diseases[45]

taken center stage. However, a certain percentage of cases result in complications as a consequence of infections, inadequate blood supply or tissue damage. Altered blood supply and reduced oxygen supply to the tissues can lead to further problems such as delayed wound healing, impaired implant stability as a result of failure to osseointegrate as well as peri-implantitis. Photobiomodulation using red and infrared laser increases the proliferation of epithelial cells and fibroblasts, consequently increasing collagen deposition, which is an important prerequisite for wound healing. While current evidence is mostly in-vitro and animal studies, human studies on photobiomodulation are lacking. The most significant challenge to using PBM in the clinic today is defining effective clinical dose parameters, specifically, the wavelength, irradiance, fluence, and delivery protocols for its use in a specific biological scenario to manage pain and inflammation or modulate the immune response to promote wound healing and tissue regeneration. These parameters are mandatory to promote PBM as a clinical therapy and not only as promising experimental evidence.

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