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The visible ray of hope - photo biomodulation in periodontics - A review

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Abstract

Periodontal disease is a chronic inflammatory disease characterized by breakdown of supporting and investing structures of teeth. Periodontal bone loss (PBL), is a direct consequence of any periodontal disease that results in the loosening and eventual loss of teeth. Hence, early detection and accurate diagnosis of periodontally compromised teeth (PCT) is of paramount importance in the management of oral health. Periodontal treatment of periodontitis and periimplantitis includes either nonsurgical or surgical periodontal therapy. With time, techniques have evolved and led way to various newer techniques which can be used as adjuncts to the conventional treatment methods to enhance health and function of oral tissues. One among them is Low Level Laser Therapy, which is a type of non-invasive, non-thermal therapy based on non-ionizing light sources like lasers, light-emitting diodes (LEDs) and broadband light, in the visible and infrared spectrum hence this review focuses on the importance of Photo biomodulation (PBM) as adjunct to periodontal therapy.

Keywords: Low level laser therapy, Photo bio modulation, periodontics, periodontal therapy, laser.

Introduction

Periodontal disease is defined as chronic inflammatory disease of supporting tissues of the teeth as a result of polymicrobial infection, which leads to progressive destruction of the periodontal membrane and alveolar bone, with formation of periodontal pockets and alveolar bone loss. Treatment of periodontal disease includes nonsurgical and surgical methods; however, many adjunct therapies have evolved for the same.

Photo biomodulation is known as a form of light therapy that utilizes non-ionizing forms of light origin, ranging in the visible and infrared spectrums. The use of PBM has been researched extensively as it has numerous advantages such as anti-inflammatory action, acceleration of wound healing process, enhancing bone repair and remodelling, restoring normal neural function following nerve injury, pain reduction, stimulation of endorphin release, increasing collagen production, reducing the inflammatory exudation and enhancing revascularization, epithelization and modulation of the immune system. Thus, PBM can be considered as a beneficial adjunct in management of periodontal and peri-implant disease.

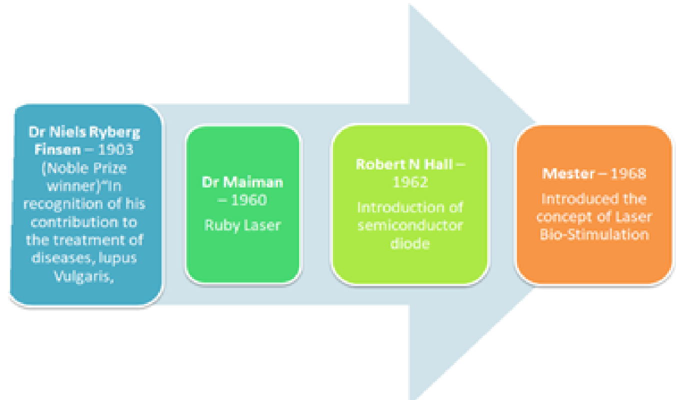
Definition and terminologies

Photo biomodulation is a non-invasive form of light therapy for wound healing, whereby several biological, chemical, and cellular processes are stimulated to speed up healing. A diode laser is considered a semi-conductor laser and it is also called "soft" or "cold" laser. Diode lasers are most commonly applied in procedures termed as "low-level-laser therapy (LLLT)." These procedures are according to the concept of bio-stimulation.

History

The era of LLLT began with Dr. Nils Finsen who treated diseases such as lupus vulgaris using concentrated light energy and was awarded Nobel Prize in 1903, for his achievement. The first working ruby laser was developed by Professor Maiman TH in 1960. Ruby laser was used for healing wounds, activation of the immune system, and proliferation of endothelial cells. In 1960, Helium-Neon (He-Ne) laser was introduced in different wavelengths; 633 nm as a basic wavelength for erythropoiesis (red blood cells production). Semi-conductor (diode) laser was put to use in 1962 for its anti-inflammatory effect and its ability to induce proliferation and activate micro-circulation. In 1968 Mester E et al. came up with the phenomenon of "laser bio-stimulation.

Figure 1:



The mechanism of photo biomodulation

Photo biomodulation works on the principle that the cytochromes absorb low-level light which interacts with mitochondria, which produces the cell's fuel, adenosine triphosphate (ATP), reactive oxygen species (ROS), and nitric oxide (NO). ATP has a role in increasing the cell's ability to fight infection and accelerates the healing process. ROS has been identified to have an impact on cell repair and healing, and the release of NO increase circulation, decreases inflammation, and enhances the transport of oxygen and immune cells through the tissues.

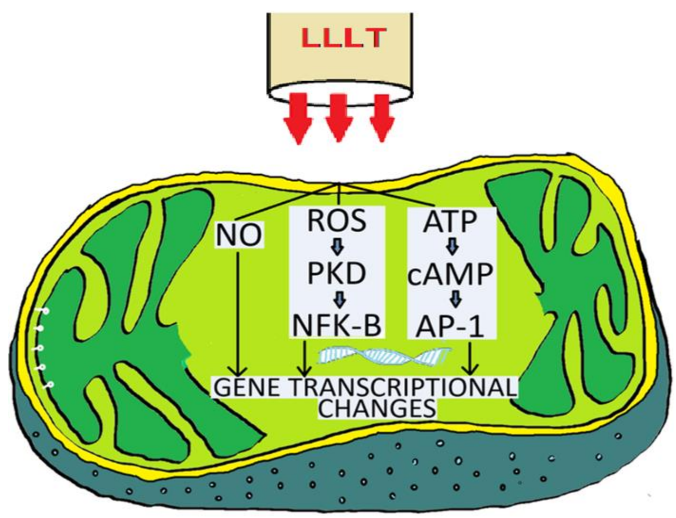


Figure 2: The cellular effect of low-level light therapy (LLLT)on cellular metabolism.

LLLT is proposed to act via mitochondria by displacing nitric oxide (NO) from the respiratory chain and increasing levels of adenosine triphosphate (ATP) and reactive oxygen species (ROS).These changes act via intermediaries cyclic adenosine monophosphate (cAMP) and protein kinase D (PKD) to activate transcription factors AP-1 and NF-kB resulting in changes in gene expression and subsequent downstream production of chemical messengers implicated in the cellular changes seen following LLLT exposure

Effects of photo biomodulation therapy

There are various effects of LLLT on biologic tissue and are as follows

Primary Effect

Absorption by cytochrome c oxidase (cco) absorbs red and near-infrared light, the transfer of light energy by this enzyme triggers a series of downstream effects

Secondary effect

Modulation of ATP, nitric oxide and reactive oxygen species Changes in ATP, reactive oxygen species and nitric oxide occur due to light absorption by CcO, which are redox state and dose dependent. In hypoxic or otherwise stressed cells it has been shown that following LLLT, nitric oxide is released from CcO, ATP synthesis is increased and oxidative stress is reduced.

Tertiary effect

Downstream intracellular responses (gene transcription, and cellular signalling) There are many downstream effects of LLLT including nitric oxide release, increased ATP synthesis and reduced oxidative stress. These effects are context and cell type dependent. Either directly or indirectly these biochemical intermediates affect components in the cytosol, the cell membrane, and nuclear functions that control gene transcription and subsequently regulate cellular responses such as proliferation, migration, necrosis and inflammation

Quaternary effect

Extracellular, indirect, distant effects Tissues that have not absorbed photons can also be affected indirectly via bioactive molecules released from cells that have been stimulated by absorbed light. Cells in the blood and lymph can also be activated and subsequently promote systemic effects such as autocrine, paracrine, and endocrine and termed as "bystander" effects

Equipment, parameters and dosage calculations for photo biomodulation

Dental therapeutic lasers are available in the size of an electric toothbrush and comes with an attachable intraoral probe-shaped device akin to handheld wand used in dental composite curing light systems

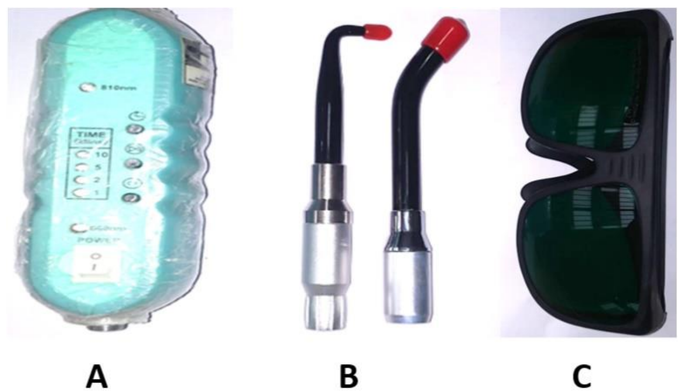


Figure 3: Armamentarium used in LLLT: A - LLLT unit, B - Intra and extraoral operating tip, C- Safety goggles

Low power laser light or LED is used with a radiation power range between 10 mW-500 mW. Energy is calculated as mW X seconds and dose is calculated by dividing the energy with the irradiated area (Bjorndal JM et al., 2001). The mode of laser operation is continuous, modulated, and pulsed. The spectrum of light used is between red to infrared region with a wavelength of 630-940 nm. Power density (irradiance) of 5 W/cm^2 and beam power of 1 W is used. Light and surface density of 5 mW/cm^2 at 5 cm deep is applied on the tissues with an application time of around 30-60 s (Huang et al., 2011).

Clinical applications

Application of lllt in systemic condition

LLLT is used for three main purposes: to promote wound healing, tissue repair, and the prevention of tissue death; to relieve inflammation and edema because of injuries or chronic diseases; and as an analgesic and a treatment for other neurological problems. These applications appear in a wide range of clinical settings, ranging from dentistry, to dermatology, to rheumatology and physiotherapy. Various preclinical and clinical studies has been in table no 1, 2 & table no 3 and pictorial representation of the use of LLLT is shown in Figure 4.

Table 1: Pre-clinical studies on animals with low level light therapy for different conditions used in Systemic disease

Author and year	**Disease**	**Parameters**	**Effect**
Oron 2007	Myocardial infarction Rats	804 nm; 38 mW; 4.5 ± 0.1 mW/cm2; 0.27 J/cm2; CW, 1.5 9 3.5 mm	Reduces the loss of myocardial tissue
Lapchak 2007	Stroke Rabbits	808-nm; .5 mW/cm2; 0.9 J/cm2 at cortical surface; CW; 300 ls pulse at 1 kHz; 2.2 ms at 100 Hz	The results showed that laser administered 6 h following embolic strokes in rabbits in P mode can result in significant clinical improvement and should be considered for clinical development
Rubio 2010	Arthritis Rats	632.8-nm; 3.1 mW/cm2 CW, 1 cm diameter; 15 min; 3 times a week for 8 week	He–Ne laser treatment enhanced the biosynthesis of arthritic cartilage

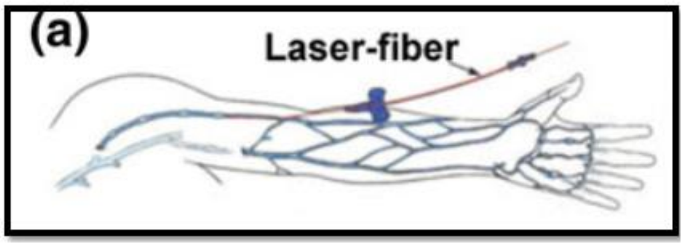
Table 2: Clinical studies on patients with low level light therapy for different conditions used in Systemic condition

Author and year	**Disease**	**Parameters**	**Effect**
Zycinski 2007	Myocardial infarction	632.8-nm, 5 mW; CW; 15 min; 6 days a week for 4 weeks on chest skin - 39 patients	An improvement of functional capacity and less frequent angina symptoms during exercise tests
sLampl 2007	Stroke (NEST-1)	808-nm; 700 mW/cm2 on shaved scalp with cooling; 1 J/cm2 at cortical surface; 20 predetermined locations 2 min each - 120 patients	The NEST-1 study indicated that infrared laser therapy has shown initial safety and effectiveness for the treatment of ischemic stroke in humans when initiated within24 h of stroke onset
Schiffer 2009	Major depression and anxiety	810-nm, 250 mW/cm2; 60 J/cm2 on scalp; 2.1 J/cm2 at cortical surface; CW; 4 cm2; 240 s at each of 2 sites on forehead - 10 patients	Significant improvement in Hamilton depression and anxiety scales at 2 weeks

Schiffer 2008	Carpal tunnel syndrome (CTS)	830-nm; 60 mW; 9.7 J/cm2; 10 Hz, 50% duty cycle, 10-min per day for 5 days a week - 75 patients	Alleviate pain and symptoms, improve functional ability and finger and hand strength for mild and moderate CTS patients
Hegedus	Arthritis	830 nm, 50 mW; 10 W/cm2; 6 J/point; 48 J/cm2; CW, 0.5-mm2; 2 times/week for 4 weeks - 27 patients	Reduces pain in knee osteoarthritis and improves microcirculation

Pictorial representation of clinical application of lllt

Intravascular laser therapy



Laser Acupuncture and Trigger Points:

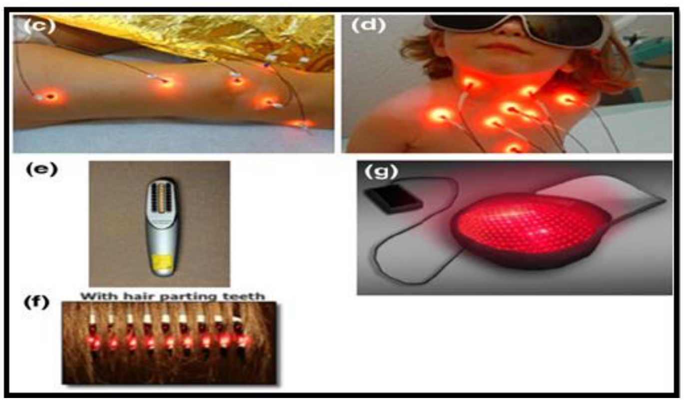


Figure 4: Some examples of LLLT devices and applications. (a and b) Intravascular laser therapy (Institute of Biological Lase) Intravascular Laser Therapy: Intravenous or intravascular blood irradiation involves the in vivo illumination of the blood by feeding low level laser light generated by a 1–3 mW low power laser at a variety of wavelengths through a fiber optic inserted in a vascular channel, usually a vein in the forearm therapy, Gottingen, Germany). (c and d) Laser needle acupuncture system (Laser needle GmbH, Glienicke-Nordbahn, Germany). (e and f) Laser comb (Lexington Int LLC, Boca Raton, FL) for hair regrowth. (g) Laser cap (Transdermal Cap Inc, Gates Mills, OH) for hair regrowth.

Application of lllt in dentistry

The application of LLLT in dentistry can be used to treat various oral conditions. LLLT can be used both, intraorally and extra-orally.

Figure 5:

Intraoral application of LLLT.

Extraoral application of LLLT.

Table 3: studies with low level light therapy for different conditions used in dentistry.

Author and year	Disease	Parameters	Effect
Gerschman JA 1996, Orhan K 2011, Flecha OD 2013S	Endodontics	Dentinal hypersensitivity pulp	Reduced tactile and thermal sensitivity Pulp Improved dentin formation in the dental pulp Promotion of HDP cell mineralization
Scoletta M, 2010 Vescovi P 2012	Maxillofacial	Bisphosphonate related osteonecrosis of the jaw Mandibular distraction Mandibular advancement Temporo-mandibular joint disorder Trauma to the mandibular	Reduced pain, reduced edema, pus and fistulas, improved healing. Improved bone trabeculation and ossification Improved bone formation in condylar region Improved osteogenesis Reduced pain Improved range of mandibular movement Improved bone healing
Yang HW 2011 Kato IT 2010 dos Santos Lde F 2010	Oral pathology	Burning mouth syndrome HSV Lichen planus Xerostomia/dryness	Reduced symptoms, reduced pain Improved healing and reduced reoccurrence Reduced lesion size, less pain As effective as corticosteroids Regeneration of salivary duct epithelial cells Improved salivary flow, improved antimicrobial characteristics
Igic M, Pejcic A, Amorim JC 2006	Oral surgery	Paraesthesia/alveolar nerve Third molar extraction	Improved mechanical sensory perception Third molar extraction Reduced pain, reduced swelling, improved trismus
Artes-Ribas M 2006, Genc G 2013, Vidovi´c Juras D 2010	Orthodontics	Orthodontic pain Titanium implants Tooth movement	Reduced pain Faster remodelling Improved healing Improved attachment Improved osseointegration Accelerated tooth movement Improved osteoblast/osteoclast activity Improved collagen deposition
Igic M, Mihailovic D, 2012 Miloro M, Miller JJ 2007 Tanboga I, Eren F 2011	Pediatric	Pediatric Cavity preparation Mandibular distraction Gingivitis	Reduced pain Faster healing

Boldrini C 2013 Omasa S, Motoyoshi M 2012 Naka T, 2012	Prosthodontics	Denture stomatitis Implants	Reduced yeast colonies Reduced palatal inflammation Faster bone formation Improved bone–implant interface strength Improved osseointegration

Application in periodontology

Lasers have been used in non-surgical periodontal therapy with the aim of improving disinfection / debridement and promoting wound healing after mechanical debridement (e. g, scaling and root planning) of deep periodontal pockets (≥ 5 mm). Lasers are increasingly used in the non-surgical treatment of chronic and aggressive periodontitis. Additionally, lasers are increasingly used as part of surgical periodontal therapy (e.g., pocket reduction and regenerative procedures)

The advantages of lasers over conventional periodontal surgeries include

1. Tissue ablation
2. Vaporization, hemostasis
3. Pocket disinfection.

Table 4:

Author & year	**Aim/research focus**	**Result**
Igic M et al 2011	PBM in reducing inflammation	Reduction of gingival inflammation is observed after effective nonsurgical and surgical periodontal treatments; however, it is proposed that adjunctive application of low levels of light can also be beneficial in this process
Wang et al 2015	PBM as an adjunct to soft tissue wound healing	daily 10 J/cm2 LED irradiation observed better wound closure, re-epithelialization, and collagen, and the amount of sequestrum formation, infiltration of inflammatory cell, and TNF-a decrease significantly
Francesca Angiero 2019	PBM used as an adjunct to SRP on clinical parameters and on levels of bradykinin, vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF) in the gingival crevicular fluid (GCF) of subjects with chronic periodontitis	application of PBM as an adjunct to non-surgical periodontal treatment may help to reduce inflammation, with significant improvement of bradykinin, VEGF, and EGF levels and of the clinical parameters promoting the healing of periodontal tissues in patients with CP
Makhlouf M et al 2012 & Annaji S, et al 2016	Non-surgical treatment	SRP + laser therapies, compared to SRP alone, promoted more significant reductions in the levels and proportions of periodontal pathogens of the red and orange complexes (e.g., Porphyromonas gingival is, Prevotella intermedia, Tannerralla forsythia and Treponema denticola and Aggregatibacter action my cetecomitans three at six months

Gaspirc B et al 2007	As a adjunct to Nonsurgical treatment of chronic periodontitis	Er: YAG, and Nd: YAG lasers, respectively, were superior to SRP at 3 to 6 months, 9 to 12 months, and 24 months, evaluations; however, the excellent outcomes seemed more evident at deep periodontal pockets (≥ 7 mm)
Eltas A et al 2012	As a adjunct to open flap debridement modalities	significant improvements in PD and CAL after flap access and Er: YAG laser debridement, compared to conventional open flap debridement, at 6-, 12-, 24- and 36-months re-evaluation
Dong et al 2016	PBM and bone regeneration as an adjunct to periodontal regenerative surgeries	guided tissue regeneration (GTR) surgery alone with GTR plus low-level laser therapy to treat Grade II furcation defects and reported more improvement in the horizontal probing depth of the defect's alkaline phosphatase levels of GCF with adjunctive LLLT compared with GTR alone
Pereira et al 2009	PBM as adjunct in bone formation around implants - Titanium implants inserted in rabbits	irradiated Titanium implants inserted in rabbits' tibia with low-intensity laser with a 48-h interval for 14 days. they reported that there is increase in BIC T 3- 6 weeks with laser therapy. However, it doesn't show any effect on the area of bone formed within the threads
Marleny Elizabeth Marquez de et al 2018	evaluate the efficacy of Photo biomodulation for bone repair of critical surgical wounds with implants of bone morphogenetic proteins (BMPs) and bovine biological membranes, using histological and histomorphometric analysis	Histological analysis confirmed the histomorphometric results, with the experimental groups showing bone neoformation of significantly higher quality and quantity at the end of 30 days compared with the control group
Suleyman et al 2020	to address implant stability and influence of microbiota around dental implants in the early stage of osseointegration	PBMT did not have a clinically significant effect on implant stabilization, especially in terms of ISQ values at early alveolar bone healing term

Indications of photo biomodulation

- Temporomandibular disorders
- Hypersensitive dentin
- Post extraction and bone-healing therapy
- Herpes labialis
- Orthodontics
- Aphthous ulcers
- Paresthesia
- Trigeminal neuralgia
- As an adjunct to non-surgical and surgical periodontal therapy

Advantages

- Anti-inflammatory action
- Acceleration of wound healing process
- Enhancing bone repair and remodelling
- Restoring normal neural function after nerve injury
- Pain reduction
- Stimulation of endorphin release
- Increasing collagen production
- Reduces the inflammatory exudation and enhances revascularization, epithelization and modulation of the immune system

Relative contraindications and precaution employed in lllt

- Damage to eyes – Both operator and patient should wear appropriate safety spectacles
- Cancer – Do not treat over the site of any known primary carcinoma or secondary metastasis unless the patient is undergoing chemotherapy
- Pregnancy – Do not treat directly over a developing foetus
- Epileptic patients – Low frequency pulsed visible light with less than 30Hz may trigger the seizures in patients sensitive to light (photosensitive epileptic patients)

Discussion

In 2006, Rocha Jr. et al. studied the effect of LLLT (Twin laser) on cutaneous wounds created on

rats. They were divided into a laser group and a control group. In the laser group, the wounds were exposed for 15 s to a 3.8 J/cm2 laser dose, 15 mW of potency. The laser applied three times immediately after operation, 2 days, and 7 days later. Ten days following surgery, histopathology and histomorphology were performed. In the laser group, there was increased vascularization, fibroblast proliferation, and decreased inflammatory infiltrate

A study was carried out by Nussbaum *et al.* 1999 Conducted a study on human patients to test the efficacy of LLLT in bur Nineteen patients were included, and in each patient, one burn was considered as control and another burn was treated with a soft laser device (Helb or, Gallspach, Austria) with a circular application of a continuous diode laser using a 400-mw potency emitting a red laser light with a 670 nm wavelength. A dose of 4 J/cm2 was applied two times a week. All burns treated with laser showed visible improvement except two lesions. As a conclusion, LLLT could be beneficial for burn patients.

Iijima et al., conducted a trial examining 36 patients suffering from PHN (Post herpetic neuralgia) after exposure to low-power He-Ne laser. The laser was applied 2 to 3 times weekly. The study resulted in 88.9% efficacy and 55.3% pain relief

Emshoff et al., in 2008, utilized a randomized double-blinded design to carry out a trial examining

the effectiveness of LLLT in the treatment of TMDs. Fifty-two patients were evenly randomly assigned into two groups. The test group received LLLT using He-Ne laser (632.8 nm, 30 mW), 2 to 3 times per week for 8 weeks. The control groups were subjected to placebo laser. Comparing the two groups, the improvement in the functions was not shown to be significant. They concluded that LLLT is not better than the placebo in managing pain.

Nonsurgical CP treatment has identified additional clinical gains in moderate-deep pockets with SRP + lasers or Laser alone compared with manual and ultrasonic or sonic debridement (SRP). concerning the use of lasers plus SRP, Crespi et al [22] and Eltas and Orbak [23] showed that Er: YAG, and Nd: YAG lasers, respectively, were superior to SRP at 3 to 6 months, 9 to 12 months, and 24 months, evaluations; however, the excellent outcomes seemed more evident at deep periodontal pockets (≥ 7 mm)

Pamuk et al 2017 The effect of low-level laser therapy as an adjunct to non-surgical periodontal treatment on gingival crevicular fluid levels of transforming growth factor-beta 1, tissue plasminogen activator and plasminogen activator inhibitor 1 in smoking and non-smoking chronic periodontitis patients: a split-mouth, randomized control study did not observe any significant differences between the clinical parameters in LLLT and sham groups of either the smokers or non-smokers. Overall, they recommended LLLT as an adjunctive treatment of periodontitis in smokers.

Aykol et al 2011 In vivo 808 Diode 4 250 mW 10 s to the gingiva of incisors and premolar as a adjunct to scaling root planning for 20 s to the gingival of molars and concluded that Gingiva Improvement in bleeding index (SBI), clinical attachment level, and probing depth (PD) levels

Sema et al in 2012 investigated the effects of a diode laser (940 nm) with different settings i, e.

1. Infected pocket setting (power 2 W, pulse interval 1 Ms, pulse length 1 Ms, 20 s/cm2, 20 J/cm2) is used in the periodontal abscess.
2. Perio pocket setting (power 1.5 W, pulse interval 20 Ms, pulse length 20 Ms, 20 s/cm2, 15 J/cm2) is used for decontamination of the periodontal pocket.
3. Bio stimulation setting (power 0.3 Win continuous wave, 20 s/ cm2, 6 J/ cm2) is used to stimulate wound healing.

In this study, they applied laser irradiation only one time, and they checked cell proliferation for 80 h and mRNA expression of the gingival fibroblasts at 48 h. They observed no significant difference in fibroblast proliferation during 80 h; significant changes in mRNA expressions were noted in gingival fibroblasts irradiated with different settings. The results of this study showed that PBM therapy increased the proliferation of HGF cells and release of Bf GF, IGF-1, and IGFBP3 from these cells. PBM therapy may play an important role in periodontal wound healing and regeneration by enhancing the production of the growth factors. The difference between the results could be attributable to cell origin, methodology, and types of laser, or a different application time/mode of lasers.

Ozcelik et al 2008 conducted clinical trail and showed that adjunctive application of 4 J/cm2 of diode laser used together with enamel matrix derivatives (EMD) in the treatment of intrabony defects can improve the effect of EMD

Bhardwaj et al 2016 also had concluded addressing the successful results with 4 mm of CAL gain and 37% bone fill and minimal amount of recession after adjunctive low-level laser in treatment of a periodontal intrabony defect

Decreasing the duration of osseointegration has been a topic of interest in laser implant research for many years. Since it is proposed that low-level light therapy may influence osteoblastic cells and the process of osseointegration, it seems possible that it may also be effective in increasing the stability of Ti implants

Pereira et al 2009 use the irradiated Titanium implants inserted in rabbits' tibia with low-intensity laser with a 48-h interval for 14 days. they reported that there is increase in BIC T 3- 6 weeks with laser therapy. However, it doesn't show any effect on the area of bone formed within the threads

Another animal study by Kim et al.,2007 showed that the expression of osteoprotegerin (OPG), activator of the kappa-B nuclear factor ligand receptor (RANK L), and RANK were shown to be influenced by low-level laser irradiation, increased bone metabolic activity and bone tissue cellular activity have been observed

Torkzaban et al. reported that no significant effect of low 940 nm adjuvant laser therapy on implant stability. Garcia-Moral et., 2012 reported that LLL could not significantly increase implant stability when assessed by resonance frequency analysis (RFA). Implant stability values (IQS measurements) were shown to be increased in low-level laser therapy (LLLT) groups.

Recommendations for future research

Use of photo biomodulation as an adjunct to non-surgical and surgical periodontal therapy has proven effective in numerous clinical trials. Early stimulation of osteoblastic cells by LLLT in the implant osseo integration may prove to be effective in increasing the stability of titanium implants. Hence, more clinical trials with longer follow up period has to be focused to prove the beneficial application of PBM in implant osseointegration.

Conclusion

PBMT reduces the inflammation and could facilitate hard and soft tissue regeneration, promote osseointegration, and improve implant stability. The field of laser dentistry is endlessly expanding and LLLT continues to be a promising modality through its several extra-oral applications in different dental specialties. LLLT is a safe effective treatment to enable enhanced healing, better tissue remodelling, reduced inflammation and analgesia for use in treatment of oral conditions. Studies with LLLT in managing periodontal and peri-implant diseases have shown favourable results. However, LLLT is still considered a recent alternative that demands high-quality trials with longer follow up durations and larger sample sizes for it to be considered in routine clinical practice

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