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A COMPREHENSIVE REVIEW ON LOW LEVEL LASER THERAPY (LLLT) BIOSTIMULATION & INTRABONY DEFECTS IN PERIODONTAL REGENERATION

Periodontology

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ABSTRACT

Intrabony defect regeneration is achieved by various regenerative techniques one of which is Low Level Laser Therapy (LLLT) biostimulation along with open flap debridement (OFD). Conversely, LLLT through its biostimulatory effects it promotes faster wound healing through fibroblast proliferation and release of various growth factors and improves vascularity. It also induces advanced new bone formation and matrix production from osteoblastic cells. Additionally, it causes less post-operative pain, hematoma and good patient compliance compared to conventional therapy.

KEYWORDS

Low Level Laser Therapy, Open Flap Debridement, Scaling And Root Planing, Intrabony Defects, Regeneration

INTRODUCTION

Periodontal disease constitutes a complex biological process related to interaction between group of microorganisms and host immune/inflammatory response that alters the morphology of bone leading to bony defects[1]. Defects in bone are not infrequent sequelae when compared to other pathological conditions. Changes that occur in bony defects are crucial because the height and density of the alveolar bone are normally maintained by an equilibrium, regulated by local and systemic influences between bone formation and bone resorption[2,3].

The primary etiologic factors that directly initiate periodontal disease are microorganisms and their by-products followed by endogenous proteases, such as MMPs (matrix-metalloproteinases) and inflammatory mediators like prostaglandin E_2 (PGE_2) and tumor necrosis factor-α (TNF- α), resulting in activation of the bone resorption mechanism. Considering these factors and the slow regenerative potential of bone in such defects can pose therapeutic problems. Thus the ultimate goal of periodontal treatment involves regeneration of defects with new cementum, periodontal ligament and bone formation on the periodontally diseased root surfaces[2-4].

Periodontal therapy include reduction or elimination of tissue inflammation induced by bacterial plaque its byproducts and correction of defects or anatomic problems caused by the disease process. It comprises of non-surgical debridement of the diseased root surface which is usually performed by scaling and root planing. However, conventional mechanical debridement using curettes is still technically demanding and time consuming, complete removal of bacterial deposits and their toxins from the root surface and within the periodontal pockets is not necessarily achieved with conventional mechanical therapy[5]. In addition, access to areas such as furcation's, concavities, grooves, and distal sites of molars is limited. In this context, systemic and local antimicrobials have emerged as an adjunct in administrating into deeper periodontal pockets for the purpose of disinfection. Potential risks associated with these antimicrobials are resistance to microorganisms. Therefore, development of novel systems for non-surgical therapy and accessing deeper pockets are required for the successful management of periodontal pockets associated with infrabony defects. In order to achieve this predictably, several regenerative surgical- techniques have been put forth. Since the highest goal of periodontal therapy is the regeneration of the periodontium including new cementum apposition with inserting periodontal ligament fibers and defect fill with alveolar bone[6-8].

Various regenerative treatment strategies where used for treating intrabony defects which includes autografts, alloplasts, growth factors and membranes. Although above methods are now established modes of treatment, still failures occur due to many disadvantages such as donor site morbidity, expensiveness, time consuming and more post-operative pain and discomfort[10-13]. In this context, the use of lasers in the form of low level laser (LLLT) biostimulation is attracting considerable attention. Two principal mechanisms are proposed for the beneficial role of LLLT in early bone formation; namely stimulation of osteoblast precursor cell proliferation and later stimulation of cell differentiation, increasing the number of osteoblastic cells, with a subsequent increase in bone formation. LLLT may also increase local blood flow, enhancing the supply of circulating cells, nutrition, oxygen and organic salts to the defect site[14,15]. It has also shown the production of growth factors such as bFGF, IGF, BMPs and TGF super family. Thus LLLT biostimulation in intrabony defect regeneration has shown favourable results in terms of reduction in clinical parameters, bone fill and the evidence comes from several studies done on animal models and human subjects as well[16-30]. However, the bone regeneration achieved using LLLT alone was comparable to other regenerative techniques. This suggests that LLLT by itself is equally effective in stimulating bone regeneration.

GENERAL REVIEW

DEFINITIONS:

BONE FILL[31]:

It is the clinical restoration of bone tissue in a previously treated periodontal defect. The term bone fill does not address the presence or absence of histological evidence of new connective tissue attachment or the formation of a new periodontal ligament.

INTRABONY DEFECT[31]:

The base of the defect is located apical to the surrounding bone. It is also called as infrabony defect.

According to the glossary of terms of the American Academy of Periodontology (AAP-1999), an intrabony defect is defined as a periodontal defect within the bone surrounded by one, two or three bony walls or a combination[9]. The three-wall intrabony defect is classically considered ideal for regeneration as this defect having three osseous walls, with the tooth forming the fourth wall considered to be a contained defect.

EXTENSIVE CLASSIFICATION OF INTRABONY DEFECTS:

A) According to Glickman (1964)

- Osseous craters
- Vertical/angular defects
- Bulbous bony contours
- Inconsistent margins and ledges
- Reversed architecture
- Furcation involvement

B) According to Karn et al (1983):

- Horizontal bone loss
- Crater
- Trench
- Moat

- Ramp
- Cratered ramp
- Ramp into a crater or trench

C) According to Prichard's classification (1985)[32]:
- Interproximal craters
- Inconsistent margins
- Hemisepta
- Furcation involvement
- Intrabony defects
- Combination of these defects

D) Grants classification:
1) Vestibular, lingual or palatal defects associated with
a) Normal anatomic structures :
- External oblique ridge
- Retromolar triangle
- Mylohyoid ridge
- Zygomatic process

b) Exostoses or tori :
- Mandibular lingual tori
- Buccal and posterior palatal exostoses

c) Dehiscence
d) Fenestration
e) Reverse osseous architecture

2) Vertical defects:
- Three wall
- Two wall
- One wall
- Combination

3) Furcation involvement

E) Papapanou and Tonetti (2000) classification:
1) Suprabony defects
2) Infrabony defects:
a) Craters
b) Infrabony defects:
- One wall
- Two wall
- Three wall
- Combination

3) Inter radicular defects:
a) Horizontal defects (Glickman's)
- Class I
- Class II
- Class III

b) Vertical defects (Tarnow & Fletcher)
- Sub-class A
- Sub-class B
- Sub-class C

F) According to Goldman and Cohen (1958) classification:
- Suprabony pocket: It is defined as the base of the pocket is located coronal to the alveolar crest
- Infrabony pocket: It is defined as the base of the pocket is located apical to the alveolar crest

HORIZONTAL BONE LOSS:
- Most common pattern of bone loss.
- Bone is reduced in such a way that the bone margin is perpen dicular to the tooth surface.
- Interdental septa and facial and lingual plates of bones are affected, but necessarily to an equal degree around the same tooth.

VERTICAL OR ANGULAR DEFECTS:
- They occur in oblique direction.
- This creates a hollowed-out-trough in the bone alongside the root.
- The base of the defect is located apical to the surrounding bone.
- In most instances angular defects has an accompanying infrabony periodontal pockets.

TYPES OF ANGULAR/VERTICAL DEFECTS:
Classification based on number of osseous walls. (Goldman& Cohen, 1958)[33]

1. One wall defects
2. Two wall defects
3. Three wall defects
4. Combined osseous defects

ONE WALL DEFECT (HEMI SEPTUM): (FIG 1)
- Proximal wall
- Buccal wall
- Lingual wall

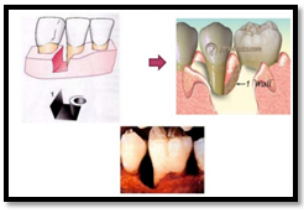

Fig 1 One wall defect

TWO WALL DEFECTS: (FIG 2)
- Buccal and lingual wall
- Buccal and proximal wall
- Lingual and proximal wall

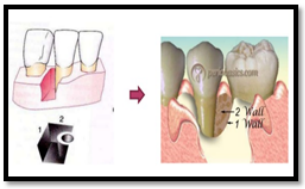

Fig 2 Two wall defect

THREE WALL DEFECTS: (FIG 3)
- Proximal, buccal and lingual walls
- Mesial, distal and buccal wall
- Lingual, mesial and distal wall

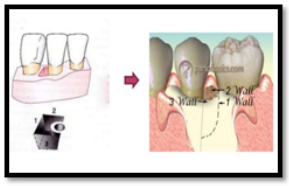

Fig 3 Three wall defect

COMBINED OSSEOUS DEFECTS: (FIG 4)
- Three walls plus two walls
- Three walls plus two walls plus one wall

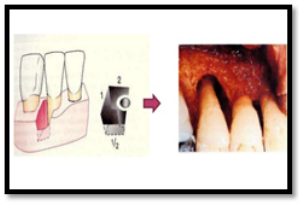

Fig 4 Combined osseous defects

OSSEOUS CRATERS:
- They are concavities in the crest of interdental bone confined within the facial and lingual walls.
- Craters have found to make up about one third of all defects and about two thirds of all mandibular defects.
- They occur twice as often in posterior segments as in anterior segments.

Ochsenbein divided bony craters into three basic types:

Crater type	Dimension
Shallow crater	1-2 mm
Medium crater	3-4 mm
Deep crater	5mm or more

BULBOUS BONE CONTOURS:
- They are bony enlargements caused by exostoses, adaptation to function or buttressing bone formation.
- More frequently found in maxilla than mandible.

REVERSED ARCHITECTURE:
- They are produced by loss of interdental bone, including facial plates, without concomitant loss of radicular bone.
- The normal architecture of the bone is thus reversed.
- More commonly seen in maxillary teeth.

LEDGES:
They are plateau like bone margins caused by resorption of thickened bony plates.

MECHANISMS OF BONE DESTRUCTION:
There are several possible pathways by which products in plaque absorbed by periodontal tissues could cause alveolar bone loss as described by Hausman E (1974)[31]:
1. Absorbable products from plaque could stimulate bone progenitor cells in the periodontium to differentiate into osteoclasts, which resorb alveolar bone.
2. Absorbable products from plaque as, for example, complexing agents and hydrolytic enzymes could destroy alveolar bone through non-cellular mechanisms by dissolving bone mineral and hydrolyzing the organic matrix.
3. Absorbable products from plaque could stimulate cells within the gingival to release mediators, which in turn could trigger bone progenitor cells to differentiate into bone resorbing osteoclasts.
4. Gingival cells in response to plaque products could release agents which by themselves have no effect on bone, but could potentiate as co-factors for other bone resorptive agents.
5. Gingival cells could release agents, which destroy bone by direct chemical action without osteoclasts.

PERIODS OF DESTRUCTION[31]:
Periodontal destruction occurs in an episodic, intermittent fashion, with periods of inactivity or quiescence. The destructive periods result in loss of collagen and alveolar bone with deepening of the periodontal pocket. The reasons for the onset of destructive periods have not been totally elucidated, although the following theories have been offered.

1) Bursts of destructive activity are associated with subgingival ulceration and an acute inflammatory reaction, resulting in rapid loss of alveolar bone.
2) Bursts of destructive activity coincide with the conversion of a predominantly T-lymphocyte lesion to one with predominance of B lymphocyte – plasma cell infiltrate.
3) Periods of exacerbation are associated with an increase of the loose, unattached, motile, gram negative, anaerobic pocket flora, and periods of remission coincide with the formation of a dense, unattached, non-motile, gram positive flora with a tendency to mineralize.
4) Tissue invasion by one or several bacterial species is followed by an advanced local host defense that controls the attack.

Different types of lasers have been proposed as an adjunct to conventional surgical periodontal therapy like Nd: YAG, Er: YAG, Er, Cr: YSGG and diode lasers which have shown to be effective in non-surgical and surgical periodontal therapy. Each of them have different mechanisms of action. Among the various physiological effects like improved wound healing, tissue repair and hemostasis; the most significant is the bio stimulatory effect. This might be beneficial by allowing faster wound healing in the process of periodontal tissue repair, which may not occur during conventional mechanical therapy[34-37].

LASER is defined as an acronym for Light Amplification by Stimulated Emission of Radiation[38]. The physical principle of laser was developed from Einstein's theories in the early 1900s, and the first device was introduced in 1960 by Maiman[39]. Laser light is a man-made single photon wavelength. The process of lasing occurs when an excited atom is stimulated to emit a photon before the process occurs spontaneously. This stimulated emission generates a very coherent (synchronous waves), monochromatic (a single wavelength), and collimated form (parallel rays) of light. They exert a strong effect on tissues at an energy level that is much lower than that of natural light. The characteristics of a laser depend on its wavelength. The term 'waveform' describes the manner in which laser power is delivered over time, either as a continuous or as a pulsed beam emission (fig 5)[34].

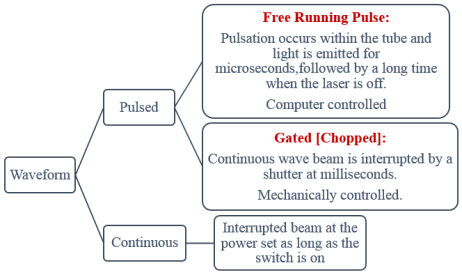

Fig 5: Various waveforms of laser

PENETRATION DEPTH OF LASERS[34]:
When laser light reaches a tissue, it can reflect, scatter or either be transmitted or absorbed to the surrounding tissues (fig 6).

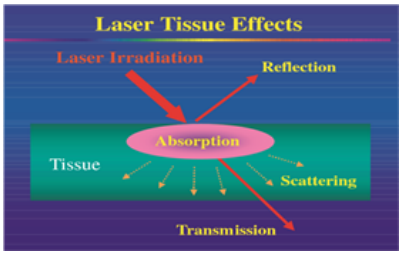

Fig 6: Laser tissue interactions

Lasers are generally classified into two types, depending on their wavelength[34-38]:
1. A deeply penetrating type, in which the laser light penetrates and scatters deeply into tissue, such as neodymium-doped yttrium-aluminium garnet (Nd: YAG) and diode lasers.
2. A superficially absorbing type, in which the laser light is absorbed in the superficial layer and does not penetrate or scatter deeply, such as carbon dioxide (Co2), Erbium : Yttrium Aluminium Garnet (Er: YAG) and Erbium Chromium: Yttrium Scandium Gallium Garnet (Er,Cr:YSGG) lasers.

Table 1: Classification of Lasers according to penetration depth in tissue.

Er:YAG, Er,Cr:YSGG CO_2	Diode Nd:YAG
Superficially-absorbing type	Deeply-penetrating type

As shown in tab 1, a lower absorption coefficient into water indicates deeper penetration into biological soft tissues, whereas a higher absorption coefficient exhibits superficial absorption. In biological tissue, absorption is mainly due to the presence of free water molecules, proteins, pigments, and other macromolecules[34]. Generally, the degree of absorption (i.e. the depth of penetration of a laser in biological tissue) of a laser is dependent on its wavelength (Fig 8).

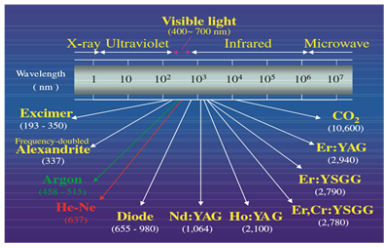

Fig. 8. Depicting various wavelengths of laser under electroma gnetic spectrum

LOW-LEVEL LASER THERAPY: (PHOTOBIOMODULATION)
Photobiomodulation, also conventionally termed as low-level laser therapy, that delivers light energy to targeted tissue and produces specific, non-thermal and biostimulative effects at the cellular level.

However, the real underlying cell mechanisms following laser therapy are still not completely understood[40]. The first commercialized biostimulative laser was a helium neon (HeNe) laser with output power of <1 mW. The use of HeNe laser for biostimulation is limited by the need for an optic fiber. An advantage of the diode lasers is the small size and option for battery operation, making them rather handy and portable. These lasers work in continuous mode, but can be mechanically or electronically pulsed. The most frequently used laser for LLLT in dentistry is the gallium-aluminium arsenide laser. It often operates in the spectrum between 780 and 830 nm with output powers ranging from 10 and 500 mW with pulsed or continuous-wave emission[38-40].

MECHANISM OF ACTION OF LOW-LEVEL LASERS:

The bio stimulatory and inhibitory effects of LLLT are governed by the Arndt-Schulz law[38]. According to this law, low-dose will increase physiologic processes, and strong stimuli will inhibit physiological activity. Low-level lasers do not cut or ablate the tissues and they do not cause temperature elevation within the tissues, but rather produce their photo biostimulation effects within the tissues. The therapy performed with low-level lasers is called as LLLT and this therapy has been referred as 'bio stimulation' and 'bio modulation'[38].

Bio stimulatory effect of laser irradiation acts directly on stimulating components of the so-called antenna pigments of the respiratory chain and manifest increase in adenosine triphosphate (ATP) mitochondrial production. Laser enhanced biostimulation has been reported to induce intracellular metabolic changes, resulting in faster cell division, proliferation rate, migration of fibroblasts and rapid matrix production. The mechanisms of LLLT are complex, the alterations in photo acceptor are the primary reactions and alterations in cellular signaling, cellular functions are secondary reactions [38,40].

PRIMARY REACTIONS AFTER LIGHT ABSORPTION:

The first mechanism, proposed in 1981 for the action of LLLT was the singlet oxygen hypothesis. Certain photo absorbing molecules like porphyrins after absorption of laser light lead to the generation of singlet oxygen, which are needed for stimulation of RNA and DNA synthesis rate[40]. The next mechanism proposed in 1988 was redox properties alteration hypothesis. According to this hypothesis, photo excitation of certain chromatophores in the cytochrome c oxidase molecule influences the redox state. The latest NO hypothesis states that laser irradiation and activation of electron flow in the molecule of cytochrome C oxidase could reverse the partial inhibition by NO[41,42]. Transient local heating hypothesis states that local transient rise in temperature of absorbing biomolecules may cause structural changes and trigger biochemical activity.

SECONDARY REACTIONS AFTER LIGHT ABSORPTION (CELLULAR SIGNALLING):

The secondary reactions that occur after light absorption are cellular signalling pathways and mitochondrial retrograde signalling. The mitochondrial retrograde signalling is the communication in cells from mitochondria to the nucleus that influences many cellular activities, under both normal and pathophysiological conditions. Absorption of light by cytochrome C oxidase can increase the mitochondrial membrane potential, thereby releasing ATP and reactive oxygen species, which leads to increased energy availability and signal transduction. The overall redox state of a cell represents the net balance between stable and unstable reducing and oxidizing equivalents[42,43]. In phagocytic cells, irradiation initiates a non-mitochondrial respiratory burst (production of reactive oxygen species, especially superoxide anion) through activation of nicotinamide adenine dinucleotide phosphate-oxidase located in the plasma membrane of these cells[42-44].

BIOLOGICAL EFFECTS OF LLLT:

ABSORPTION OF LASER ENERGY IN LLLT:

The major absorbing structures for the red visible and near infra-red laser wavelengths used in LLLT are most likely proteins. Several studies have suggested that either elements in the mitochondrial cytochrome system or endogenous porphyrins in the cell are the energy-absorbing chromophores in LLLT[38,40]. Since the tissue penetration of the laser energy used in LLLT can be in the order of 5-10 mm, both superficial and deeper structures can be affected (FIG 9 a,b).

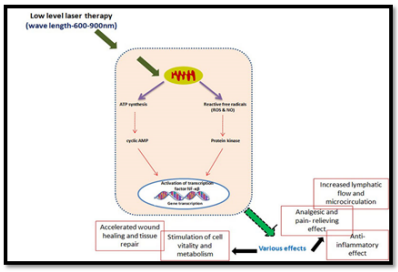

FIG 9 A: Biological effects of laser

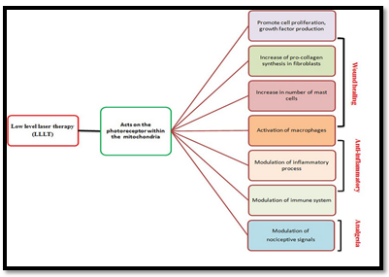

Fig 9 B: LLLT effects on mitochondria

EFFECTS OF LLLT ON FIBROBLASTS:

The stimulatory effects of LLLT on fibroblast proliferation *in vitro* are well established. At low doses (e.g., 2 J/cm2), LLLT stimulates proliferation, while at high doses (e.g., 16 J/cm2) it is suppressive. There are several mechanisms by which LLLT may stimulate the proliferation of fibroblasts by stimulating the production of basic fibroblast growth factor (bFGF), which supports fibroblast proliferation and differentiation. Other effects of LLLT on fibroblasts are transformation of fibroblasts into myofibroblasts, which are responsible for wound contraction. Various *in vitro* and *in vivo* studies have shown increase in growth factor release mainly the bFGF, IGF-1, VEGF and BMPs from the osteoblasts and fibroblast proliferation[45-49].

EFFECTS OF LLLT ON IMMUNE CELLS:

In both *in vitro* and *in vivo* systems, LLLT influences macrophage function by promoting the secretion of factors which enhance fibroblast proliferation. An additional effect of LLLT which has been observed *in vivo* is an enhancement of the phagocytic activity of macrophages during initial phases of the repair response. LLLT may affect immune cells which secrete cytokines and other growth-regulatory factors for fibroblasts[50,51].

EFFECTS OF LLLT ON EPITHELIAL CELLS:

Other possible mechanism by which LLLT may enhance wound healing *in vivo* is via stimulation of epithelial cells. It increases the motility of human epidermal keratinocytes *in vitro* at wound sites treated with LLLT. Thus, clinical use of LLLT under conditions which enhance keratinocyte migration should not alter the ultimate integrity or differentiated function of the epidermis that migrates to cover the wounded area[52,53].

EFFECTS OF LLLT ON BONE CELLS:

LLLT exerts pronounced effects on proliferation, differentiation, and calcification of cultured osteoblastic cells. Cell proliferation and DNA synthesis are increased by LLLT only when the cells are in a phase of active growth. It causes increased accumulation of calcium and accelerates calcification *in vitro*. Various *in vitro* and *in vivo* studies demonstrated increase in proliferation of osteoblasts, advanced new bone formation and matrix production with LLLT biostimulation[55,56,38].

CLINICAL APPLICATIONS OF LOW-LEVEL LASER THERAPY:

The application of LLLT has become popular in a variety of clinical applications, including promotion of wound healing and reduction of pain. Low-level laser therapy could significantly improve the outcome of periodontal therapy, either when used alone or as an adjunct to conventional nonsurgical therapy, in the treatment of mild and moderate periodontitis[34,38]. In addition, LLLT should be used in the surgical site during the initial healing period when the proliferative activity is high. Repeated irradiation for 2-weeks produces pronounced effect. LLLT can also be used in combination with guided

tissue regeneration and different bone substitutes also for better therapeutic outcome. Various studies has done using bone grafts and membranes adjunct to LLLT and they have achieved better regenerative outcomes[34,57].

DISCUSSION

Regeneration of the lost periodontal tissues has always been the ultimate goal of periodontal therapy. When considering the technical aspects of reconstructive surgical procedures for the periodontal regeneration the major factors seemed to be important for successful outcome are lacked in conventional surgical techniques comparatively to that of LLLT biostimulation which are:

1. First is to eliminate or, to a great extent, reduce the chances of post-surgical infection and contamination of the blood clot which would unavoidably lead to impaired healing outcome.
2. The second is to minimize the postoperative pain and hematoma with the result of compromising the preexisting esthetic appearance of the patient.

Laser-enhanced biostimulation has been reported to induce intracellular metabolic changes, resulting in faster cell division, proliferation rate, migration of fibroblasts, and also increases the blood flow, activity of osteoblasts, and decreases the activity of osteoclasts, stimulates production of the bone matrix and also accelerates the dynamics of bone matrix by modifying the expression of the extracellular matrix components and increasing the area of new bone formation[34-40].

Literature evidence obtained from several *in vitro* and *in vivo* animal studies on the effects of LLLT in intrabony defects regeneration suggests that LLLT has a beneficial role in periodontal regeneration. Khadra et al. 2004 in a histological rat study model used LLLT for surgically created infrabony defects regeneration and demonstrated that LLLT had a beneficial effect in promoting advanced new bone formation and exhibit a more pronounced effect at day 14, suggesting that LLLT has a more favourable effect at early stages of bone healing[19]. Similarly, Adel et al.2011 in his histomorphometry study in rats observed that LLLT was efficient in promoting bone healing and increasing new bone formation[22]. Hayes et al.2016 also in his experimental study in rabbit model observed that LLLT could induce bone formation at a faster rate compared with PRF in infrabony defects[63].

LLLT has also shown to induce periodontal regeneration in intrabony defects when used alone or in combination with various bone grafts materials such as autografts, allografts and membranes[60-69].To provide periodontal regeneration, repopulation of the PDL cells to the wound area adjacent to the root surface is necessary. In recent studies by, Kreisler and Choi et al. demonstrated that LLLT had a stimulatory effect on the proliferation of cultured PDLFs, but the effects of LLLT on PDL cells have been not fully elucidated[70].

LLLT application exhibits extreme variations such as dose, wavelength, amount of energy density and time intervals. The dose applied during laser application is one of the important treatment parameters to benefit from LLLT. However, no precisely determined dose has been determined for each indication. According to "Arndt–Schulz law," weak stimuli slightly accelerate vital activity, stronger stimuli raise it further, but a peak is reached, and even stronger stimuli suppress it, until a negative response is finally achieved[34]. Another important factor is the time period of LLLT. A single application on a wound site may not be effective in the stimulation of the cells and to reach the borders of the surgical bed. Multiple irradiations are more effective than a single dose. This is an important factor in bone formation and fibroblast growth. This has been investigated by Beresescu et al.2015 in a human histologic study were they have shown bone regeneration at 6 months duration with LLLT at an intensity of 20 Mw/cm^2,for 20 minutes per day, for 21 consecutive days[66]. A possible reason for the shortening of the time for the regeneration process has been proposed by Karu et al, who demonstrated an increment in ATP level by stimulation of mitochondrial membranes in cell culture. The increase of intracellular energy results in an increment of protein synthesis, greater production of organic matrix and intense cellular mitosis. Another possible explanation is the effect of microcirculation activation, which elevates the levels of oxygenation and tissue nutrition, thus improving considerably the metabolism and tissue regeneration[41,42].

However, previous studies have shown limitations, such as the different laser wavelengths, laser irradiation parameter settings and small number of patients. Few studies in the literature have addressed the use of LLLT, before placement of grafts or biomaterials in bone defects. Future studies are necessary to evaluate the effects of LLLT in combination with different bone graft materials and/or biomaterials. Nevertheless, it has been clearly demonstrated that the effects of laser therapy are dose-dependent that is, wavelength, power, frequency, fluency or dose and energy parameters are of paramount importance for reaching good results.

CONCLUSION

The goal of periodontal surgery has always been to alleviate or eliminate the degeneration associated with progressive periodontal disease and to regenerate lost tissues. Introduction of low level laser therapy (LLLT) highlights various advantages such as less invasive surgery, shorter duration, favoured healing due to better clot stabilization, and benefiting the patient with reduced intra-operative and postoperative morbidity. In addition, future research designs should include standardized outcome measures, using different irradiation conditions, to allow better evaluation of the results and to define the most suitable set of laser-irradiation parameters for low-level laser therapy. Despite of all these positive factors, still there are some limitations noticed in previous studies such as less number of studies and inconsistencies in the protocols and methodology. Thus the role of LLLT in periodontal regeneration and its effects on human intrabony defects needs to be further validated.

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