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REVIEW ARTICLE

LOW LEVEL LASER THERAPY IN DENTISTRY.

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Abstract

These lasers are cost effective, easy to use and the power required is in milli watts ranging from, 1-500 mw. "Low level laser therapy" (LLLT) includes all the procedures performed with such lasers is also referred to as "Therapeutic lasers". All commercially available LLLT system are usually composed of Gallium, Aluminum, Arsenide (Ga, Al, As) which emit in the near infrared spectrum (700 – 940 nm). Therapeutic lasers or LLLT work in the visible and the infrared spectrum ranging from 600 – 900 nm wavelengths. The energy used is indicated in joules. Appropriate LLLT energy range from 1 – 10 joules per point. The scope for using low-level laser light (LLLT) varies and has many applications which may be either direct or indirect for tissue-related procedures, in the dental field. The applications of low-level laser light operate either under the specific wavelength/chromophore relationship, or the inherent accuracy of a collimated beam

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Introduction:-

Low level laser therapy (LLLT) works under the principle to directly supply biostimulative light energy to the cells of the body. This light energy is absorbed and stimulates the molecules and atoms of cells. Using low-intensity laser radiation on the tissues increases the tissue temperature which is slow and consistent [1]. Among the various lasers used for periodontal procedures, a semiconductor diode laser is usually used for subgingival curettage and periodontal pocket disinfection [2, 3]. Effort has also been made to use LLLT for root conditioning to improve the result of regenerative periodontal therapies by favoring the attachment of the regenerated periodontal structures.

History:-

Investigation and clinical usage of Low-level laser (or light) therapy (LLLT) has been carried out for over 40 years. However, only recently LLLT has become scientifically and clinically accepted in the medical community (Hamblin 2010) [2].

The lasers are cost effective, easy to use and the power required is in milli watts ranging from, 1-500 mw. The procedures performed with such lasers is referred to as as "low level laser therapy" (LLLT) or also known as "therapeutic lasers" [2].

The history of the use of clinical application of laser phototherapy in medicine dates from the late 1960s, which is eight years post- invention of the first laser (Ruby laser) by Theodore Maiman. In 1967, Endre Mester in

Semmelweis University, Budapest, Hungary was the first to test whether laser radiation might cause cancer in mice models [2, 3].

Dorsal hair of the mice was shaved and then they were divided into two groups. He irradiated the shaved areas with a low powered ruby laser (694-nm), in one of the group and the other group was left untreated. As a result the mice did not get cancer and surprisingly the hair on the treated group grew back more quickly than the untreated group. The first demonstration of "laser biostimulation" was by Hamblin, Waynant et al. 2006.

The first low level laser, Helium-Neon was developed by Professor Ali Javan in the early 1960's which emits visible, red light in the wavelength of 632.8nm. This laser was then tested and used extensively in experimental and therapeutic studies. Presently, the semiconductor laser which includes the InGaAlP lasers (633-700nm), GaAlAs lasers (780-890nm, invisible, near infrared area), GaAs laser (904nm, invisible, near infrared area) are being used by researchers for possible clinical applications [46].

LLLT was thought to have an unusual property of laser light (soft or cold lasers); however there has been changing concepts with the use of non-coherent light (light-emitting diodes, LEDs). Today, in the field of medical treatment with coherent-light sources (lasers) or noncoherent light (LEDs) is widely practiced (Hamblin, Waynant et al. 2006). Currently, low-level laser (or light) therapy (LLLT) is practiced as a part of physical therapy globally. According to Hashmi, Huang et al. 2010), although LLLT was primarily used only for wound healing and pain relief, the applications of LLLT have broadened which include diseases such as stroke, myocardial infarction, and degenerative or traumatic brain disorders [46].

Since there has been many studies carried out that have reported the positive effects of phototherapy like promoting wound healing, pain relief and anti-inflammatory effects, however some negative reports also have been published, (Demidova-Rice, Salomatina et al. 2007), regarding the application of laser phototherapy on wound healing (Posten, Wrone et al. 2005). This controversy is based on 2 main factors; first of all, the basic biochemical mechanisms for the biological effects are not clear and secondly, the complexity of a large number of laser irradiation parameters (such as wavelength, fluence, power density, pulse structure and treatment timing), inappropriate anatomical location and simultaneous patient medication (such as steroidal and non-steroidal anti-inflammatory drugs which can inhibit healing) has led to conflicting and biased results. A biphasic dose response has been frequently observed which shows that low levels of light have a much better effect than higher levels (Gigo-Benato, Geuna et al. 2005; Aimbire, Albertini et al. 2006; Hamblin, Waynant et al. 2006; Goncalves, Souza et al. 2007; Huang, Chen et al. 2009; Hamblin 2010) [46].

LLLT has various terminologies which includes "cold laser", "soft laser", "biostimulation", "photobiomodulation", "low intensity laser therapy", "low energy laser therapy", "laser phototherapy (LPT)", "laser therapy", and "non-ablative irradiation". Some investigators have reported that using terms, such as "low power laser therapy" is misleading because high power lasers also can be used for laser phototherapy (Tuner and Hode 2010) (as we will discuss in the next sections, CO₂ laser is applied as a low level (therapeutic laser) in NACL, too). Some of the researchers support the term "laser phototherapy (LPT)" which is a most commonly used terminology (Tuner and Hode 2010).

Therapeutic lasers generally operate in the visible and the infrared spectrum, 600 – 900 nm wavelengths. The energy used is indicated in joules. Suitable therapeutic energies range from 1 – 10 joules per point. All commercially available LLLT system are generally variants of Gallium, Aluminum, Arsenide (Ga, Al, As) which emit in the near infrared spectrum (700 – 940 nm) [46].

The use of laser light which has power levels below that capable of direct tissue change like protein denaturation, water vaporization and tissue ablation, has been performed in various branches of medicine and veterinary practice, yet it is less accepted in general dental practice. However, the scope for using low-level laser light (LLLT) is vast including either direct or indirect tissue-related changes, in the field of primary dental care. A number of applications of low-level laser light have emerged, which utilize either the specific wavelength/chromophore relationship, or the inherent accuracy of a collimated beam.

The most significant uses are as follows:

Photobiostimulation:-

The main objectives of a dental treatment are the control/eradication of disease, the control/relief of pain, and the restoration of form/function. The effectiveness of Low-level laser therapy (photobiostimulation) is based on the use of visible red and near-infrared light on the tissues in order to stimulate and improve healing, as well as reduce pain. The incident wavelength determines the effect of the laser - visible light is transmitted through the superficial cellular layers (e.g. the dermis, epidermis and the subcutaneous tissue). Light waves in the near-infrared ranges potentially penetrate several millimeters and these wavelengths stimulate deep cellular function. Light energy is absorbed within living tissue by cellular photoreceptors, eg. cytochromophores.

LLLT has stimulatory effect on the following:

1. Proliferation of macrophages
2. Proliferation of lymphocytes
3. Proliferation of fibroblasts
4. Proliferation of endothelial cells
5. Proliferation of keratinocytes
6. Increased cell respiration/ATP synthesis
7. Release of growth factors and other cytokines
8. Collagen synthesis [46].

The dosimetry of low-level laser light which is based on the Arndt Schultz law is crucial to the infra-surgical effects of the wavelengths used. It states that, as 'small doses stimulate living systems, medium doses impede, and large doses destroy'.

A brief review on biological effects of Low level laser (or light) therapy (LLLT) states that, the application of light (at a low power laser or LED in the range of 1mW – 500mW) on a diseases area, promotes wound healing and tissue repair, reduces inflammation and relieves pain. The light of typically narrow spectrum in the red or near infrared region (600nm – 1000nm); at power densities (between 1mw-5W/cm²) (Huang, Chen et al. 2009), is not associated with macroscopic thermal effects, in contrast to the thermally mediated surgical applications (Chow, David et al. 2007). When using high power surgical lasers, the collimation of laser light leads emits narrow, intense beam of light which is used for precise tissue destruction (photothermal effect). However, in LLLT, light radiation intensities are less and thus the resulting biological effects are due to physical or chemical changes associated with the interaction between the cells of the tissues and the laser radiation, and not simply as a result of heat (Snyder, Byrnes et al. 2002; Gigo-Benato, Geuna et al. 2005).

The main areas of medicine where laser phototherapy are predominantly use are as follows: promoting wound healing, tissue repair and prevention of tissue death, relief of inflammation in chronic diseases and reducing associated pain and edema, relief of neurogenic pain and some neurological problems (Hamblin, Waynant et al. 2006).

The first law of photobiology states that for visible light of low power to produce any effect on a living biological system, the photons must be absorbed by electronic absorption bands belonging to some molecular photo acceptors, or chromophores (Sutherland 2002; Huang, Chen et al. 2009). Red and near infrared light is absorbed by photoreceptors present in the protein components of the respiratory chain situated in mitochondria, particularly cytochrome-c oxidase and flavoproteins like NADH-dehydrogenase. This may result to activation of respiratory chain for a short time and oxidation of NADH pool leading to changes in the redox state of both mitochondria and cytoplasm, which increases ATP production, and biological responses at the cellular level through cascades of biochemical reactions (Karu 1989; Karu, Pyatibrat et al. 2004; Karu and Kolyakov 2005). These effects in turn increases cell proliferation and migration, modulation in levels of cytokines, growth factors, inflammatory mediators, and increases the tissue oxygenation. The outcome of these biochemical and cellular changes in animals and patients lead to important biological effects such as promoting wound healing and tissue repair, relief of inflammation, pain reduction, and amelioration of damage after heart attacks, stroke, nerve injury and even retinal toxicity (Hamblin, Waynant et al. 2006).

Pain relieving effects of low level therapeutic lasers Low-level laser therapy (LLLT) is being widely accepted as a treatment option. In fact, it is for this effect that biostimulative lasers have been approved for marketing by the U.S. Food and Drug Administration through the premarket notification/510(k) (Gigo-Benato, Geuna et al. 2005). Many studies have demonstrated the efficacy of phototherapy in various syndromes associated with pain (Tuner and Hode

2010). With the increasing levels of evidence, the World Health Organization's Committee of the Decay of the Bone and Joint has also recently introduced LLLT into guidelines for treatment of neck pain (Haldeman, Carroll et al. 2008; Chow, Armati et al. 2011).

Mechanisms Of Analgesic Effects Of Low Level Laser Therapy:-

The basic biological mechanisms behind the analgesic effects of conventional LLLT are still not clear. Some of the possible explanations for the pain relieving effects of lasers are as follows:

1. Reversible blockage of action potential generation of nociceptive signals in primary afferent neurons along with specific reversible inhibition and functional impairment of A δ and C fibers, thus inhibition of transmission of nociceptive stimuli (Wakabayashi, Hamba et al. 1993; Kasai, Kono et al. 1996; Orchardson, Peacock et al. 1997; Chow, Armati et al. 2011).
2. Increase in β -endorphin synthesis (Labajos 1988; Montesinos 1988; Hagiwara, Iwasaka et al. 2007).
3. Inhibition of cyclooxygenase, thus interrupting conversion of arachidonic acid into prostaglandins, especially prostaglandin E2 (PGE2) (Shimizu, Yamaguchi et al. 1995; Mizutani, Musya et al. 2004).
4. Suppression of Substance P, a neuropeptide responsible for nociception (Ohno 1997), along with suppression of bradykinin activity, a pro-inflammatory neuropeptide that stimulates nociceptors and is a major element in clinical pain and the associated inflammation (Maeda 1989; Jimbo, Noda et al. 1998)
5. Increased production of serotonin, which negatively affects neurotransmission (Tuner and Hode 2010)
6. Increased synaptic activity of acetylcholine esterase (Simunovic 2000)
7. Addition of nitric oxide in analgesic effects of therapeutic lasers (Mrowiec 1997)
8. Singlet oxygen production, which in small quantities, is essential in biochemical processes and may be important in biostimulation
9. Reduction of inflammation and subsequent decrease in inflammatory sensitization of small-diameter afferent nerve endings.
10. Increased local microcirculation, increased tissue oxygenation, shift of metabolism from anaerobic to aerobic pathways, thus reduced production of acidic metabolites which leads to stimulation of the pain receptors
11. Increased lymphatic flow and reduced edema, thus decreasing sensitization of pain receptors
12. Systemic effect, some studies report that laser phototherapy has both local effect in the treated area by laser light, and a systemic effect through the release of metabolites (Tuner and Hode 2010).

Low Level Laser Therapy In The Periodontal Inflammatory Process:-

Periodontitis is the chronic periodontal inflammatory process leads to the destruction of the periodontal ligament, and subsequently, to loss of alveolar bone [3]. Authors have reported that LPT leads to reduction of gingival inflammation and metalloproteinase-8 expression when used after scaling and root planning. [6, 7, 8] Ozawa et al. [9] showed that LLLT significantly reduces plasminogen activity induced in human periodontal ligament cells in response to mechanical force. Plasminogen activity is capable of activating latent collagenase, which results in cleaving collagen fibers. LLLT also inhibits PGE2 synthesis which modulates the periodontal inflammatory process [10] [11].

Low Level Laser Therapy In Wound Healing:-

Periodontal wound healing is necessary when periodontitis and gingivitis, or trauma from occlusion, affects the composition and integrity of the periodontal structures. LLLT (low level laser periodontal therapy) also causes vasodilation, increasing the local blood flow. This vasoactive effect is of importance in regard to the treatment of joint inflammation. LLLT also causes the relaxation of smooth muscle associated with endothelium. This vasodilation increases oxygenation and also allows for greater traffic of immune cells into tissue. These two effects contribute to faster healing.[12,13]

Several in-vitro studies have shown that LLLT at certain wavelengths with certain combinations of exposure parameters and power densities may stimulate fibroblast proliferation [14-23].The range of radiation doses is wide (0.45-60 J/cm²), at which stimulation of fibroblast proliferation has been noted. However high dose LPT suppresses both fibroblast proliferation and autocrine production of basic fibroblast growth factor.[24]

Effects of LLLT on macrophages include increased ability to phagocytose, and greater secretion of fibroblast growth factor. Macrophages resorb fibrin during phagocytosis and wound healing phase faster with LLLT, because of their

enhanced phagocytic activity during the initial phases of the repair response (for example, 6 hours after trauma). Faster wound healing establishes conditions necessary for the proliferative phase of the healing response to begin.

Wound healing consists of several distinct phases, all of which can be affected at the cellular level by LLLT. Pro-inflammatory and vaso-active are the initial phases of inflammation include clotting of injured vessel and deposition of a platelet plug, after which the site is infiltrated by neutrophils and macrophages.[25]

The second phase of wound healing involves proliferation, with the formation of granulation tissue as a result of growth of a new blood vessel. Studies have reported direct evidence for enhanced collagen gene expression both in skin fibroblast cultures in vitro, as well as in animal models of wound healing in vivo [26]. A final aspect of the effect of LLLT on cells relates to the effects of laser light on the cytoskeleton. Several studies have suggested that LLLT can modulate cell behavior by modifying the cytoskeleton [27, 28]. Faster wound closure is of great importance in medically compromised patients, such as diabetics, and patients undergoing treatment for malignancies. LLLT is able to improve wound healing in such compromised patients as it can enhance the release of growth factors from fibroblasts and can stimulate cell proliferation. Histological studies have demonstrated that laser irradiation improves wound epithelialization, cellular content, granulation tissue formation, and collagen deposition in laser-treated wounds is enhanced, compared to untreated sites [29, 30]. These findings have been confirmed enhanced oral mucosal wound healing in clinical studies in humans [31].

Effects Of Low Level Laser Therapy On Bone Cells:-

In the laboratory setting, LLLT using a HeNe laser shows pronounced effects on proliferation, differentiation and calcification of cultured osteoblastic cells, although there is a specific therapeutic window for these effects. Cell proliferation and DNA synthesis are increased by LLLT particularly when the cells are in a phase of active growth. LLLT can cause increased accumulation of calcium and accelerates calcification in vitro. If this report holds true then LLLT of healing sites within bone would be expected to increase bone deposition and promote bone regeneration. In a study of wound healing after tooth extraction in a rat model, LLLT was delivered per day for one week using a gallium-aluminum-arsenide (Ga Al As) laser, which showed increased fibroblast proliferation as well as accelerated formation of bone matrix were found[32].

However, studies of the influence of LLLT on bone and connective tissue regeneration in the palate in a canine animal model failed to report any effect. While at a glimpse this would suggest major species variations in the response of bone cells to LLLT, in the case in point irradiation levels were low and LLLT treatments were administered every second day rather than daily. Whether LLLT exerts positive results on bone regeneration following tooth extractions in humans remains doubtful, although there are reports that the formation of granulation tissue during post-extraction healing is accelerated by the therapy [33].

For the treatment of intrabony defects, the use of barrier membranes and different types of grafting materials are usually indicated. In the study of effect of LLLT on the healing of bone defects associated with autologous bone grafts, bone remodeling was both quantitatively and qualitatively more evident in irradiated animals than in non-irradiated animals [34]. The association of matrix protein derivative with the LLLT irradiation has shown a reduction in post-operative pain, which suggests that LLLT may improve the effects of matrix protein derivative by reducing post-operative complications [35]. LLLT biostimulation for bone tissue approximation to implant surfaces has also been reported. It has been reported that LLLT influences the expression of osteoprotegerin, receptor activator of nuclear factor κ B ligand and receptor activator of nuclear factor κ B, which leads to increase in bone cells metabolic activity [36, 37].

Low Level Laser Therapy And Analgesia:-

Historically, clinical applications of LLLT and its ability to exert analgesic effects have been of major importance. In vivo studies of the analgesic effect of LLLT on neural network of the oral cavity have demonstrated that LLLT reduces the firing frequency of nociceptors, with a threshold effect long-standing post-surgical IDN injury were assessed[38,39]. LLLT involved effect was studied along the distribution of the nerve for a total of 20 treatment procedures. Control subjects received placebo Laser therapy. The degree of impairment of mechanoreceptor and thermal sensitivity disability was similar in test and control groups before treatment. Following LLLT, the test group showed a significant improvement in mechanoreceptor sensory testing, as well as a subjective improvement in sensory function, indicating that LLLT can improve mechanoreceptor perception in long-standing sensory aberrations in the IDN. However, there was no significant improvement in thermal responses in both the groups.

Antimicrobial Photodynamic Therapy:-

Unlike high-power lasers, low-power lasers do not increase tissue temperature [40]. Thus, when used alone, the same antimicrobial effect as that of high-power lasers in active disease sites cannot be expected [41]. The antimicrobial effect of low-power lasers is achieved by its association with extrinsic photosensitizers, which results in the production of highly reactive oxygen species [42] that cause damage to membranes, mitochondria and DNA, resulting in the death of the microorganisms. [43-45] This is the mechanism of a PDT, and it is being increasingly studied with the aim of complementing the microbial reduction achieved by conventional mechanical periodontal therapy.

Low Level Laser Therapy Equipment:-

Semiconductor diode lasers are compact and have high conversion efficiency from electrical energy to heat energy. In contrast to He-Ne lasers, semiconductor laser diodes do not require a high voltage supply, and thus can be used in portable, battery-operated devices. It is also possible to use it in pulse mode at various frequencies using simple external circuitry. Laser diodes have a life-expectancy ranging from 1,00,000 and 6,00,000 hours [48]. Semiconductor diode lasers are usually variants of either Aluminium: Gallium: Arsenide (AlGaAs) which have wavelength in the near infrared spectrum (wavelength 700-940nm), or Indium: Gallium: Arsenide: Phosphorous (InGaAs) devices which emit in the red portion of the visible spectrum range (wavelength 600-680nm). The beam emitted from a typical diode laser is rectangular in shape, with a high divergence along the long axis and low divergence on short axis. Laser units used for LLLT are generally classified as Class 3 and 3b based on the optical hazards which the staff and patients are under. A monochromator distinguishes easily between a true laser diode and a LED.

Composite Resin Curing:-

Most commonly argon lasers emit the 488 nm 'blue' wavelength. This wavelength coincides with the absorption peak of camphoroquinone, which is an accelerator used during composite resin restorations [46].

Caries Detection:-

More than a century ago the use of fluorescence had been suggested for caries detection. The present optical caries detection techniques started with the introduction of laser technology into the dental field. In the 1980s, a clinically applicable visual detection method focusing on the natural green fluorescence of tooth tissue was invented. The technique used an argon-ion laser with a 488 nm excitation wavelength to differentiate bright green fluorescing healthy tooth tissue from poorly fluorescing caries lesions. The technique was modified further in the early 1990s, which is now known as quantitative light-induced fluorescence (QLF), which uses the digitization of fluorescence images to quantify the observed green fluorescence lost, giving an indirect measure of mineral loss [47].

Quantitative Light - Induced Fluorescence:-

This is a very sensitive method for determination of short-term effects in lesions in the mouth. The control unit consists of an illumination device and imaging electronics. In 1995 the argon ion laser was replaced by a xenon based arc-lamp where the light from this lamp is filtered by a blue-transmitting filter. A liquid light-guide transfers the blue light to the teeth in the oral cavity and a dental mirror provides uniform illumination of the area of interest. The system produces an excitation wavelength of around 405 nm which allows visualization and quantification of both the intrinsic green fluorescence of the dental tissues as well as the red fluorescence from bacterial origin as observed in calculus, plaque and advanced caries [46].



Fig15:-Quantitative light induced fluorescence. QLF unit and computer hardware

Photo-Activated Disinfection (PAD):-

This is a development which proves to be better than the conventional use of chemicals to achieve bacterial decontamination in restorative dentistry. In contrast to chemicals that spontaneously interact with cellular structures, PAD therapy uses a photo-activated liquid, i.e. a solution of toluidine blue O (a pharmaceutical grade of the vital stain toluidine blue O). Exposure of this chemical to low-level visible red light (635 nm) releases singlet oxygen that ruptures bacterial cell walls resulting in bactericidal action [46].

During the early 1990s at the Eastman Dental Institute, London, Professors M. Wilson and G. Pearson first reported that PAD killed significant populations of *Streptococcus mutans*, and said that PAD could kill all etiological bacteria associated with oral infections, caries, root canal procedure, and periodontitis, thereby eliminating or preventing oral infections. Trials were carried out to determine the effectiveness of photo-activated disinfection (PAD) of *Streptococcus mutans* when the organism was present in a collagen matrix – an environment similar to that within a carious tooth. This research has led to the development of a commercial unit for use in dental surgery [46].

Recent in vitro and in vivo studies into the use of PAD in endodontics have demonstrated that it is effective against a number of anaerobic bacterial strains associated with endodontic infections (*Fusobacterium nucleatum*, *Peptostreptococcus micros*, *Prevotella intermedia* and *Streptococcus intermedius*). In addition this therapy was also effective against *Enterococcus faecalis* [46].

LASER SCANNING (ORTHODONTICS, RESTORATIVE DENTISTRY):-

With the development of laser-based measuring devices (eg. the confocal micrometer), has enabled accurate replication of the morphology of dental and oral structures and materials used in restorative dentistry, which utilizes beam-splitting of a low-energy laser and an optical detector [46].

Conclusion:-

Based on the various studies the results have shown that low intensity laser therapy can accelerate bone healing in extraction sites, in cases of bone fracture and distraction osteogenesis, carried out in animal models. The mechanism of action might be through stimulation of cellular proliferation and differentiation thus accelerating the healing process. Further clinical trials with LLLT applications in dentistry are required which should make use of standardized, validated outcomes, and should explore how the effectiveness of the LLLT protocol may be influenced by wavelength, treatment duration, dosage, and the site of application.

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