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Applications of Low Level Laser Therapy

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1. Introduction

1.1. Characteristics of the low level laser therapy (LLLT)

Laser is an acronym for 'Light Amplification by Stimulated Emission of Radiation'. The name of the low level laser is an abbreviation of its active medium such as GaAlAs (Gallium, Aluminum and Arsenide) or He-Ne laser (Helium and Neon).

1.2. Designation

LLLT are designated by several parameters. The first is laser power which ranges from 10^{-3} to 10^{-1} W followed by wavelength which ranges from 300 to 10.600 nm. Pulse rate can range from 0 (continuous) to 5000 Hz, the duration of pulse can range from 1-500 milliseconds with an interpulse interval of 1-500 milliseconds with a total irradiation time of 10-3000 seconds and with intensity (power x irradiation time/irradiated area) ranging from 10^{-2} to 10^2 J/cm² [1]. Therapeutic lasers are within visible red to near visible red electromagnetic spectrum ranging from 630 to 980 nm. The simplest way to categorize these lasers is according to their wavelength. The depth of laser penetration varies, and oral mucosa is quite transparent on the wavelengths (it does not absorb light well), bone and skin are quite transparent, whereas muscles absorb the most light [1].

1.3. Exposure

The greatest problem in the use of LLLT is finding the optimal dose of exposure. The tissue dose is expressed by energy density measured in joules per cm² (J/cm²). Produced energy is obtained by multiplying the laser output power in milliwatts by exposition time in seconds

(for example $50 \text{ mW} \times 40 \text{ seconds} = 2000 \text{ mJ}$ or 2 J). For example, the area which is irradiated is 2 cm^2 which is multiplied by 2 J and the fluence of $2/2$ is obtained (surface tissue dose is 1 J/cm^2). By decreasing the irradiated area, an increase in intensity is obtained. For example, the irradiated area is 0.5 cm^2 , 2 J are divided by 0.5 and the dose becomes 4 J/cm^2 since the energy is emitted through smaller area which increases local intensity. Since the dose is most affected by the size of the laser probe, a slim probe will result in high doses of joules per cm^2 . However, this does not imply that energy applied on the tissue is high, although the intensity of the light energy emitted at the end of the slim probe was high [1]. Joules per square centimeter (J/cm^2 , dose, fluence) denotes the irradiation intensity on the surface of the tissues, but not the dose in the depth. It is much easier to use the term 'energy on the spot' (only the number of joules is calculated at each spot) which is acceptable for clinical but not for scientific purposes. The spot denotes the size of the tip of the laser probe (spot size). A small tip of the laser probe produces a higher concentration of power per square millimeter, while a wider tip of the laser probe dissolves the same energy over a larger area [1]. The main absorption of wavelength occurs in the pigmented chromophores such as hemoglobin in the blood; therefore cardiovascular tissues absorb these wavelengths quite well. Another important factor is melanin quantity in the target tissues which absorbs large amounts of these wavelengths. More energy is absorbed on the surface in comparison to deeper tissues which can lead to local tissue overheating and pain [1].

1.4. Basic principles of LLLT effects

Principles of biostimulation via therapeutic lasers was introduced more than 20 years ago when they were used in dermatology for wound healing. According to Genovese, biological effects caused by low level lasers are due to low energy deposited into tissues where deposited energy results in primary, secondary and general therapeutic effects. This results in the analgesic and anti-inflammatory effects as well as in improvement in healing [2]. LLLT acts according to the Arndt-Schulz principle which states that if the stimulus is too weak, no effect is seen. Increased stimulation and optimal dose leads to the optimal effect; while, further dose increase leads to a decreased effect. Additional stimulation leads to the inhibition of stimulation [1]. It seems that LLLT act analgesically since they improve endorphin release and therefore inhibit nociceptive signals and control pain mediators [3]. They can also act analgesically by inhibiting pain signals which partially leads to the transient varicosities along the neurons which decrease impulse transmission. These lasers act on cellular reduction-oxidative potential. Cells are acidic in a lowered redox state, but after laser irradiation they become alkaline and afterwards they can act in an optimal way. In healthy cells, irradiation with this laser does not lead to the increase in redox potential; therefore, the laser does not affect healthy cells. It is well known that LLLT stimulate lymphocytes, activate mast cells, and increase production of adenosine-triphosphate in the mitochondria and proliferation of various cell types therefore acting as anti-inflammatory [3]. Furthermore, these lasers stimulate microcirculation which results in the change of capillary hydrostatic pressure which in turn results in edema absorption and elimination of intermediary metabolites [3]. Studies show that laser therapy leads to the increase in ascorbic acid in the fibroblasts, which increases hydroxyproline production and consequently, collagen production. Fur-

thermore, these lasers lead to the increase in mitotic activity of epithelial cells and fibroblasts [3]. On the vascular level, lasers improve proliferation of the epithelial cells, which results in the increased number of blood vessels as well as increased production of granulation tissue. LLLT lead to the relaxation of the smooth muscles which decreases pain [3]. Gallium-Aluminum-Arsenide laser (BTL-5000, www.btl.hr) was used at the Department of Oral Medicine, School of Dental Medicine, University of Zagreb. Results of some studies have already been reported while some studies are still in progress. The results of our studies have shown that this type of laser is quite useful in patients with hyposalivation. Also, it has been shown to be successful in treatment of patients with recurrent herpes infection since the lesions heal more rapidly. The best results are seen in patients who had lower alveolar nerve damage usually after the third molar surgery. The patients were suffering from paresthesia and neuropathic pain which subsided in a significant number of patients after therapy. It has also been noticed that 20 laser therapy sessions are needed instead of the usual ten. Chronic states (pain, paresthesia and wounds) are treated once or twice a week since there is a cumulative laser effect. Patients suffering from pain might experience even stronger pain after laser therapy. This condition is temporary and reflects actual improvement of the patient's condition. The pain level decreases within 24 hours. It is of utmost importance to inform the patient about this transient side effect before initiating therapy.

1.5. General contraindications for LLLT

Therapeutic lasers weaker than 500 mW are considered to be devices of low risk according to the USA Food and Drug Administration. Naturally, the use of protective glasses both for the patient and the clinician is a must. In patients with coagulation disorders the use of LLLT should be avoided since they interfere with blood circulation in a way still unknown. Presences of malignant disease as well as precancerous lesions are also contraindications since LLLT stimulates cell growth. Irradiation of all endocrine glands, especially the thyroid gland should be avoided. During pregnancy, menstrual cycle, febrile conditions, in epileptic patients and those who have cochlear implants the use of lasers is not indicated [1,2].

1.6. Laser hygiene

If the laser probe is inseparable from the device, it can be disinfected with disinfectants for surfaces and then it can be covered with sterile transparent materials or other disposable barrier protections. If the probe can be separated from the device, it can be sterilized [1].

2. Applications of lllt

2.1. Recurrent aphthous ulcers (RAU)

Tezel et al. [4] investigated the use of NdYAG laser on 20 patients with recurrent aphthous ulcerations. The patients reported significantly less pain as well as functional complications after laser therapy. Also, they stated that they experienced faster healing compared to the usual medication therapy.

Zand et al. [5] have investigated the use of CO₂ laser (1W of defocused continuous mode) in 15 patients with recurrent aphthous ulcerations in comparison to the placebo (recurrent aphthous ulcerations which were not treated). Both ulcerations were covered with transparent gel without the use of anesthetics. The power of CO₂ laser was 2-5mW after passing through gel which did not significantly increase the temperature. The results of the same study [5] show that one treatment with use of CO₂ laser of low intensity instantly reduces pain in patients with recurrent aphthous ulcerations without any adverse effects.

2.2. Oral lichen planus (OLP)

Jajarm et al. [6] investigated the use of 630 nm laser in 15 patients with erosive-atrophic lichen planus twice a week. The same authors (6) concluded that the laser was equally effective in the treatment of oral lichen planus as was topically applied corticosteroids and without any side effects.

Cafaro et al. [7] treated 13 patients with OLP using the pulsed diode laser (GaAs). The patients were exposed to the pulsed infrared laser (4J/cm² for one minute); the irradiated area was 0.8 cm. The same authors [7] concluded that there was a significant decrease in the lesions and decreased pain without any side effects.

Trehan and Taylor [8] used a 308 nm laser on nine patients with OLP with the first dose of 100 mJ/cm² once a week. The same authors [8] reported that treatments were pain-free and well tolerated. Five patients experienced improvement after seven therapy sessions with this laser and the authors concluded that the therapy was successful. In our opinion, the use of LLLT should be avoided in patients with oral lichen planus because OLP is a precancerous lesion and therefore additional stimulation of cell growth may be dangerous.

2.3. Herpes simplex infections

Schindl and Neumann [9] evaluated the effect of low level laser therapy (wavelength 690 nm, intensity 80 mW/cm², dose 48J/cm²) in 50 patients with recurrent perioral herpes (at least once a month during six months). Patients were given therapy every day for two weeks; the control group was given placebo therapy with laser as well. The average interval without herpes lesions was 37.5 weeks in patients who received laser therapy and 3 weeks in patients who received placebo and the difference was significant. The same authors [9] concluded that ten treatments with laser significantly decreased incidence of local recurrent herpes infection. De Carvalho et al. [10] used a laser of 780 nm wavelength, 60mW; 3 J/cm² or 4.5J/cm² once a week during ten weeks. In patients treated with laser (in comparison to the patients who were given medications), a significant decrease in herpes lesions and inflammatory edema was seen; however there was no significant decrease in pain or monthly recurrences.

Munoz Sanchez et al. [11] used a 670 nm wavelength laser, power output of 40 mW; 1.6J; 2.04J/cm², 51 mW/cm² applied to the each vesicle in the prodromal stage and 4.8J on the crust together with 1.2J on the cervical vertebra C2-C3. The same authors [11] concluded

that laser therapy improves healing in the beginning and prolongs the intervals between recurrences, that is, those patients have fewer recurrences.

Marrotti et al. [12] used a 660 nm wavelength laser, energy density of 120 J/cm², output power of 40 mW, during two minutes on spot and 4.8J of energy per spot on four spots. After 24 hours, the patients returned and then 3.8J/cm² and 15mW were applied to their lesions (the total dose was 0.6J). The same procedure was repeated after 72 hours and one week after. There were no significant side effects and herpetic lesions healed faster. Carvalho-Ferreira et al. [13] described two patients with herpetic infection who were treated five times with laser (660 nm wavelength, 30J/cm² of continuous mode and power density of 100mW which was applied for 8 seconds). Remission occurred after five days without reoccurrences during the next 17 months in both patients.

2.4. Xerostomia

Vidović-Juras et al. [14] treated 17 patients with xerostomia and reported a significant increase in salivary flow rate. The same authors [14] used the BTL-5000 laser with use of infrared laser with a density of 1.8 J/cm², frequency 5.2Hz, output power 30 mV during ten treatments. Salivary flow rate was initially 0.6±0.3 ml/5 min which increased to 1.1±0.8 ml/5 min. Lončar et al. [15] concluded that pulsed GaAlAs laser, wavelength 904 nm applied to the both parotid and submandibular glands was efficient in reducing xerostomia. The distance of laser probe was 0.5 cm whereas the irradiation was 246 mW/cm². Exposition time was 120 seconds a day during ten days. Average density of energy was 29.5 J/cm². Salivary flow rate increased to 0.13 mL/min from initial 0.05 mL/min and the result was significant. Simoes et al. [16] treated a 60-year-old person suffering from Sjogren's syndrome by use of laser with a wavelength of 780 nm and average density of energy 3.8 J/cm² and output power of 15 mW at the area of parotid, submandibular and sublingual glands, three times a week for 8 months. The same authors [16] concluded that this therapy was effective for xerostomia. Simoes et al. [17] also reported that diode laser was beneficial in patients after therapeutic head and neck irradiation (660 nm, 6J/cm², 0.24 J, 40 mW). One group of 12 patients was given laser therapy three times a week, while the other group received laser therapy once a week. The same authors concluded that laser therapy is beneficial to patients with xerostomia.

2.5. Burning mouth syndrome (BMS)

Yang and Huang [18] treated 17 patients with burning mouth syndrome by use of laser with the wavelength of 880 nm, output power 3W, 50 msec of intermittent pulse and frequency of 10 Hz which was equivalent to 1.5 W/cm² ($3W \times 0.05 \text{ msec} \times 10 \text{ Hz} = 1.5W/cm^2$). Depending on the involved area, laser was applied to the area 1cm² for 70 seconds. All the patients received therapy between one and seven times. The average pain score before treatment was 6.7 and the results showed average pain decrease of 47.6%. Kato et al. [19] treated 11 patients with BMS once a week during three weeks with wavelengths of 790 nm. Exposition time was calculated on the energy density of 6J/cm², output power of 120 mW. Burning

symptoms were significantly decreased (80% less) when compared to symptoms before treatment.

Dos Santos et al. [20] reported that 10 BMS patients were treated once a week during ten weeks by use of continuous wavelength of 660 nm, power 40 mW, 20 J/cm², 0.8 J/spot. All the patients reported improvement which was seen on visual analogue scale up to 58% after the tenth session. Vukoja et al. [21] applied the diode laser (800 nm, 3W, 50 msec, 50 Hz which is equivalent to average power of 1.5 W/cm²) to patients with BMS which was beneficial even when the laser was switched off which correlates with a placebo effect.

2.6. Mucositis

Cowen et al. [22] treated 30 patients who were exposed to chemotherapy and radiotherapy after transplantation of peripheral cells or bone marrow with LLLT in order to eliminate symptoms of mucositis. He-Ne laser (632.8 nm, 60 mW) was applied daily on five spots within the oral cavity. Cumulative findings of oral mucositis as well as daily mucositis index were significantly decreased in patients who were treated with laser. Furthermore, patients treated with laser had decreased pain scores and decreased xerostomia symptoms whereas their swallowing abilities were increased compared to the ones who did not receive laser therapy.

Campos et al. [23] directed continuous laser diode (660nm, 40 mW, 6 J/cm²) to the entire oral cavity while laser diode of greater power (1W, 10 seconds applied to 1 cm of mucositis, i.e 10 J/cm²) was used defocused only on ulcerative lesions. After the first application of laser therapy, patients reported decreased pain and xerostomia levels and significant improvement occurred after five laser therapy sessions. In the end, seventeen laser irradiations were needed in order to eliminate all lesions of oral mucositis. De Castro et al. [24] treated 75 patients by use of He-Ne laser after they had finished chemotherapy and radiotherapy due to head and neck carcinomas. They used laser of 2.5 J/cm² or placebo laser. The number of patients who had stage 3 and 4 mucositis and who were treated with laser was significantly lower compared to the ones treated with placebo laser. De Lima et al. [25] found out that low level laser therapy (GaAlAs; 2.5 J/cm², 600 nm, 10mW) was not efficient in reducing stage 3 or 4 of mucositis, although marginal benefits could not be excluded in terms of reducing unplanned pauses in radiotherapy.

2.7. Paresthesia

During the surgical procedures in oral surgery, various nerve disturbances may develop that usually affect the inferior alveolar nerve. During sagittal osteotomy in order to extract third molars, in 5.5% to 100% of cases the lower alveolar nerve may be damaged.

Miloro and Repasky [26] found that LLLT has significant influence on neurosensory recovery after sagittal osteotomy in the region of the mandibular ramus. The same authors applied a dose of 4-6 J during seven treatments. This was also confirmed by Khullar et al. [27] as well as by other authors. Khullar et al. [27] treated 13 patients with damaged lower alveolar nerves with the GaAlAs laser of 820 nm wavelength (4-6 J applied in every treatment

along the distribution of the nerve in 20 treatments). The same authors reported significant improvement in mechanoreceptive perception of the inferior alveolar nerve; however, there were no significant differences in thermal sensitivity of the nerve between the study and control groups. Ozen et al. [28] successfully treated four patients who had paresthesia one year after surgical procedures on the third molars. They used the GaAlAs diode laser of wavelength 820-830 nm, 6 J during every treatment for 90 seconds in 20 laser applications. In all patients, neurosensory improvement was seen which was shown in objective tests (visual analogue scale, two point discrimination test).

2.8. Implants

The efficacy of laser is highest immediately after implant placement and during the next two weeks. After implant placement in order to reduce postoperative pain and edema, one dose of infrared laser may be applied. If the patient is eager to attend laser therapy a few times, osseointegration will be enhanced [29].

2.9. Pain from orthodontic treatment

LLLT may be used during orthodontic treatment in order to reduce pain and also for the stimulation of tooth movement since it has been reported that a dose of 5.25 J/cm² leads to the increased orthodontic mobility. Higher doses of 35 J/cm² lead to the decreased orthodontic mobility [30]. Soussa et al. [31] retracted 13 teeth by use of force of 150 g on each side using coil spring for three days and after diode laser once a month. They reported significant increase in tooth movement in comparison with teeth which were not treated with laser. Also, there were no significant differences in bone resorption or canine roots whether the laser was used or not. Therefore, the same authors suggested that the use of lasers together with orthodontic treatment might shorten orthodontic treatment. Altan et al. [32] also reported that LLLT (diode laser, 780 nm, 20 mW, 10 sec., 5 J/cm²) enhances the process of bone remodeling by stimulating osteoblastic and osteoclastic cell proliferation. On the other hand, Marquezan et al. [33] could not confirm the efficacy of the GaAlAs laser of 830 nm and power output of 100 mW on orthodontic tooth movement in rats. However, the number of osteoclasts increased when the laser was used every day. Xiaoting et al. [34] reported that LLLT was efficient in patients who received orthodontic appliances. However, analgesics were more efficient regardless of the type used (ibuprofen, acetaminophen, and aspirin). Tortamano et al. [35] concluded that lasers (GaAlAs, 830 nm, output power 30 mW) were efficient during the arch insertion, because patients reported lower pain scores and pain intensity during the most painful day. Also, their pain subsided earlier in comparison to the ones who were not treated by laser. The patients were given a dose of 2.5 J/cm² on both sides of the tooth (buccal and lingual). Turhani et al. [36] used mini laser of 670 nm wavelength and output power of 75 mW during 30 seconds on each tooth. After bracket placement, the perception of pain was decreased after six and 30 hours. The same authors (36) concluded that LLLT may have positive effects on patients not only immediately after bracket placement but also during orthodontic treatment.

2.10. Periodontology

Obradović et al. [37] treated patients with diabetes mellitus and periodontal disease by use of LLLT (670 nm, 5 mW, 2 J/cm², 16 minutes for five days) together with conventional periodontal treatment and concluded that healing was improved as well as collagenization and homogenization in gingival lamina propria on the basis of histopathological findings. Igić et al. [38] treated 140 adolescents with chronic gingivitis by use of laser and conventional therapy and concluded that there was a significant difference in plaque and bleeding indices before and after therapy. The result was more pronounced in the group which was treated with laser. Theodoro et al. [39] used photodynamic therapy by use of LLLT in patients with chronic periodontal disease. The control group consisted of patients with periodontal disease who were subjected only to conventional periodontal therapy. After 180 days, there was a significant difference based on the finding of periodontal pathogens in patients treated with conventional periodontal therapy as well as with laser. However, there were no significant differences in the clinical outcome of both therapies. Aykol et al. [40] used the GaAlAs diode laser of 808 nm wavelength, power output 4J/cm² on the gingiva of the first, second and seventh day. On each evaluation, every day patients who were subjected to laser therapy had better scores in bleeding sulcus indices, depth of clinical attachment and probing depth in comparison to the control group. The same authors concluded that LLLT is a potent additional therapy to non-surgical periodontal treatments since it hastens periodontal healing. Lui et al. [41] found out that there were no differences in periodontal parameters after 3 months of therapy between persons who had laser therapy and those who had not. There was a significant difference after a week and month in those treated with laser; therefore the same authors concluded that laser therapy is effective only for a short period of time. However, Pejčić et al. [42] concluded that laser therapy was beneficial to patients with periodontal disease since there was a significant difference after six months in plaque index, gingival index and bleeding on probing. Rotundo et al. [43] reported that there were no differences in clinical attachment gain after 6 months of ErYAG laser therapy in comparison to the control group which was subjected only to supragingival scaling.

2.11. Dentin hypersensitivity

There are a few theories claiming that the use of LLLT decreases dentin hypersensitivity by decreasing the adhesion of dentin tubuli, by dissolution or dentin recrystallization, evaporation of dentin fluid, or analgesic effect which is connected with depressed nerve transmission or by obliteration of dentin tubuli with tertiary dentin [44]. Irradiation with the GaAlAs laser with maximal dose of 60 mW does not affect enamel or dentin surface morphologically. However, a small amount of laser energy of 830 nm wavelength passes through hard tissues in the pulp and therefore immediate analgesic effect is seen as a consequence of depressed transmission through nerves, probably by blocking afferent C fibers [44]. Yilmaz et al. [44] reported that one dose of irradiation with Cr YSGG (30 seconds, 0.25 W, 20 Hz, =% water and 10% air) or with GaAlAs laser (60 seconds, 8.5 J/cm²) was efficient in decreasing dentin hypersensitivity, which was confirmed in other studies (Kimura et al. [45], Corona et al. [46] as well as Sicilie et al. [47]. Sgolastra et al. [48] concluded that treatment of dentin

hypersensitivity by use of LLLT should be considered experimental since there are only three studies which might be considered as controlled randomized trials and all of them have serious drawbacks which lead to the conclusion that LLLT might be pure placebo effect in patients with dentin hypersensitivity. It seems that this treatment of dentin hypersensitivity would be too simple since dentists use multi-interventional measures to control dentin hypersensitivity (reduction of corrosive food and drinks, change in the brushing techniques, disuse of chewing gums, change of toothpaste, etc). Tanboga et al. [49] evaluated the efficacy of LLLT (Er:YAG) on pain before cavity preparation in children. They found out that the use of LLLT significantly decreased pain in comparison to the children who did not receive laser therapy before cavity preparation.

2.12. Temporomandibular disorders

Oz et al. [50] applied LLLT in twenty persons who suffered from myofascial pain dysfunction syndrome during ten treatments (820 nm, 3 J/cm², 300 mW) and concluded that LLLT was as efficient as the use of occlusal splint in pain management and improvement of mandibular movement in patients with myofascial pain. Marini et al. [51] reported that mandibular function was improved in patients treated by laser (superpulsed GaAs, 900 nm); ten treatments measured by use of visual analogue scale. Also, active and passive mouth opening as well as right and left lateral movements were improved after LLLT in comparison to the given parameters in patients treated by use of non-steroid anti-inflammatory medications. Fikackova et al. [52] treated patients with myofascial pain as well as patients with arthralgias of temporomandibular joint by use of LLLT. They used the GaAlAs laser of 10 J/cm² and 15 J/cm² and concluded that this is an effective therapy for patients with temporomandibular joint pain.

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