

Efficacy of LLLT in swelling and pain control after the extraction of lower impacted third molars

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Introduction and aim: Low Level Laser Therapy (LLLT) can facilitate wound healing stimulating a more rapid resolution and an earlier start for the proliferation phase. The purpose of this study is to evaluate the effects of LLLT on postoperative pain and oedema following the removal of impacted lower third molars.

Materials and methods: Fifty-nine patients, who were to undergo surgical removal of their lower third molars, were studied. Patients were randomly allocated to one of three groups:

1. 17 patients LLLT + traditional drug treatment
2. 17 patients traditional drug treatment as control group
3. 25 patients treated with LLLT only on one side+traditional drug treatment.

The laser we have used for this study is a diode laser, GaAs, which delivers both in the infrared band at the wavelength of 910 nanometers (pulsed and superpulsed source), and in the visible (continuous source) at the wavelength of 650 nanometers (red). LLLT was performed just after the intervention and approximately 12 hours after surgery delivering 240 J in 15 minutes with theoretical fluence values of 480 J/cm² and 31 J/cm² for every minute of irradiation.

We considered and signed with a label constant landmarks on both sides of the face of each patient; measurements were taken: before the surgery, after the surgery right after the 1st laser treatment, after approximately 24 hours after the 2nd laser treatment.

Results: We collected all the values of the oedema measurements and the VAS reports and performed a statistical analysis by means One-way Analysis of Variance (ANOVA) test: for the evaluated values (X, Y, Z) an extremely significant difference was found with p values of 0.003 for Y at the first evaluation (pre-12 hours) and less than 0.001 for the other evaluations. A significant result was obtained for VAS recorded at hospital discharge (p<0.0001).

Conclusions: This study demonstrates that LLLT is effective on postoperative pain and oedema accelerating healing time and reducing patients distress.

Key words: Lower third molars · extraction · Low Level Laser Therapy · LLLT; Pain · Quality of life

Introduction and aim

The Low Level Laser Therapy was born historically in Hungary in 1967 at Semmelweis clinic thanks to doctor Mester: during an experiment on mice to value the

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carcinogenic power of the laser light ^{1,2)}, he noticed how the group of mice irradiated by the laser beam did not show any neoplasia but he observed, with a great surprise, that the growth of their fur, shaved previously for the experiment, was faster than the non-treated ones. He called this effect “Biostimulation” and, since that moment forward the laser light biostimulation effect has been deeply studied.

The importance of laser light in Redox processes was demonstrated by Tina Karu in 1993 ^{3,4)} describing the very important role of secondary effects which had

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been studied and measured in different situations: increased cell metabolism and collagen synthesis in fibroblasts ⁵⁾, increased action potential of nerve cells ⁶⁾, stimulation of the formation of DNA and RNA in the cell nucleus ⁷⁾, local effects on the immune system ⁸⁾, increased new formation of capillaries by the release of growth factors ⁹⁾, increased activity of leukocytes ¹⁰⁾, transformation of fibroblasts to myofibroblasts ¹¹⁾, and a great number of other measured effects. These results and the interest created by LLLT led to use this technique clinically in different branches of medicine with good results, particularly in East Europe and South America, even if the problem of the “dose” seems quite impossible to solve.

The extraction of mandibular third molars impacted appears to be the most frequently performed in Oral Surgery ¹²⁾.

The extractive surgery can be very difficult for the operator and expose the patient to temporary or permanent damage to these structures.

One of the main requirements for a clinician who performs oral surgery is to prevent and to manage complications that may arise.

For this purpose, the extraction of a mandibular third molar must be preceded by a proper planning intervention including patient history, examination of the oral cavity (evaluation of mucosal lesions, caries, periodontal pockets, presence of inflammation / infection signs; ability to open the mouth; compliance of the patient), X-rays (intraoral, panoramic radiograph and computed tomography), any use of oral medications (antibiotics, analgesics, oral antiseptic), correct diagnosis, therapeutic indications for extraction, assessment of the degree of operating difficulty and the risk of complications, planning surgery (flap, osteotomy, odontotomia) and informed consent.

In order to standardize the evaluation of third molars inclusion, several classifications systems have been proposed based on the radiological picture and allowing to define in an approximate way the difficulty of the extraction during planning. The first classifications proposed, which are still the most widely used, are the Winter (1926) and that of Pell and Gregory (1933) ^{13, 14)}.

Materials and methods

The purpose of this study is to compare the effects of low-level laser therapy (LLLT) on post-operative pain and oedema following the removal of impacted lower third molars. We choose only patients needing the bilateral extraction of the lower impacted third molar.

59 patients, who were to undergo surgical removal of their lower third molars, were studied and this double blind study has been divided in two parts:

- 1st part of the study regarded the swelling quantification of 17 patients treated with extra and intra-oral laser irradiation and other untreated patients as control.
- 2nd part of the study regarded 25 patients intra and extra-oral laser irradiated only on one side to evaluate the “bystander effect” of the LLLT.

Treatments were realized in blind mode for the patient using a placebo fake laser treatment on the non treated side or patients.

The choice of intra- and extra-oral irradiation was made on the base of the literature: a great number of studies demonstrates that extra-oral irradiation gives better results in swelling reducing than intra oral ¹⁵⁾: the reason to use both irradiations was the gain of the strongest effect.

Patients were randomly allocated to one of three groups:

1. 17 patients: LLLT + traditional drug treatment
2. 17 patients: traditional drug treatment as control group
3. 25 patients: treatment only on one side for the 2nd part of the study +traditional drug treatment.

All the extractions were performed with the same protocol by the same surgeon belonging to the Department of Oral and Maxillofacial Surgery of Maria Cecilia Hospital: realization of narcosis, local anesthesia, mucoperiosteal flap, osteotomia and odontotomia, dental extraction and resorbable suture.

During the hospitalization patients got 400 mg cp of cefazoline (1 cpr pro die) (Cefixoral®) and 30 mg fl Ketorolac (3fl) in Elastomeric pump during the 24 hours (Toradol®).

We considered and signed with a label constant landmarks on both sides of the face of each patient to identify. (**Figure 1**):

- ▣ Line from the angle of the eye to the angle of the mandible (Z)
- ▣ Line from the angle of the lip to the angle of the mandible (X)
- ▣ Line from the angle of the lips to the ear (Y)

Measurements, expressed in centimeters, were taken every time with the same tool by the same two persons deferred:

- ▣ before the surgery
- ▣ after the surgery right after the 1st laser treatment
- ▣ after approximately 24 hours after the 2nd laser treatment

Before giving any treatment each patient was informed

on the LLL Therapy and asked to sign for the informed consent.

The laser used in this study (Lumix II Dental - Fisioline) was a diode laser, emitting both in the infrared band at the wavelength of 910 nanometers (pulsed and superpulsed mode), and in the visible band (continuous wave) at the wavelength of 650 nanometers (red). A handpiece producing a spot of 8 millimeters diameter was used at a working distance of 10 millimeters and in scanning mode for extra (Figure 2) and intraoral (Figure 3) irradiation.

The chopped emission is obtained by a train of 200 nanoseconds duration pulses at a frequency variable from 1000 Hz to 80000 Hz and cyclically interrupt-

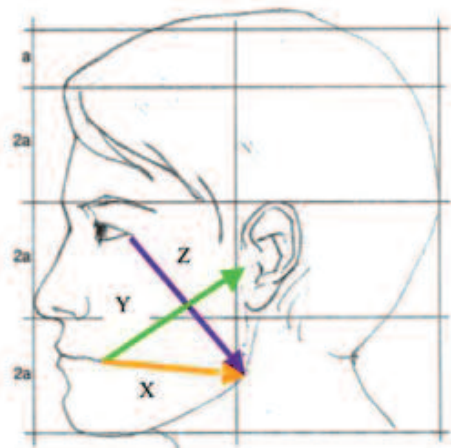


Figure 1: Landmarks realized on both sides of the face of each patient: Line Z from the angle of the eye to the angle of the mandible, Line X from the angle of the lip to the angle of the mandible and Line Y from the angle of the lips to the ear.

ed every 5 seconds, this corresponding to the period of the fixed modulating at 0,2 Hz. By varying the on/off ratio of the irradiation it is possible to change the Duty Cycle and so the Fluence to the tissues.

LLLT was performed just after the intervention and approximately 12 hours after surgery using the laser equipment on the LLLT program named “necrosis” delivering 240 J in 15 minutes with theoretical total fluence values of 480 J/cm² and 31 J/cm² for every minute of irradiation.

We collected all the values of the oedema measurements and the Visual Analogue Scale (VAS) reports in three tables:

1. Bilateral irradiated group
2. Control group (non irradiated)
3. Monolateral irradiated group (the left side was the treated one)

An interview of the patients was realized in order to understand their behaviour in relation to discomfort and pain.

Statistical analysis was performed by means One-way Analysis of Variance (ANOVA) test with results considered significant for $p < 0.05$ and extremely significant for $p < 0.001$.

Results

After collecting all the values, we compared the average of X, Y, Z of both sides of each group:

- LLLT bilateral,
- Control Group,
- Non LLLT monolateral,
- LLLT monolateral



Figure 2: Extraoral application of LLLT.



Figure 3: Intraoral application of LLLT.

Twelve hours after surgery, having performed one session of LLLT in the laser groups, we observed the most important increase of X values in subjects bilaterally irradiated; in the same group of patient 24 hours after surgery this value was the lowest (Table 1- Figure 4). At this time, patients not receiving LLLT at all showed the greatest values in X measures.

Twelve hours after surgery, after performing one LLLT session in the laser groups, we observed the most important increase of Y values in subjects bilaterally irradiated; in the same group of patient 24 hours after surgery the value was the lowest (Table 2 - Figure 5). At this time, patients not receiving LLLT at all showed the greatest values in Y measures.

Table 1: Mean X values variations (with SD) in the different groups between preoperative and 12 hours after surgery measures and between preoperative and 24 hours after surgery measures.

X VALUES	LLLT bilateral	Control Group	Non LLLT monolateral	LLLT monolateral
DIFFERENCE PRE - 12 H	0.26 ± 0.17	0.19 ± 0.11	0.17 ± 0.09	0.17 ± 0.09
DIFFERENCE PRE - 24 H	0.06 ± 0.09	0.33 ± 0.07	0.2 ± 0.1	0.06 ± 0.08

Table 2: Mean Y values variations (with SD) in the different groups between preoperative and 12 hours after surgery measures and between preoperative and 24 hours after surgery measures.

Y VALUES	LLLT bilateral	Control Group	Non LLLT monolateral	LLLT monolateral
DIFFERENCE PRE - 12 H	0.23 ± 0.17	0.19 ± 0.10	0.12 ± 0.09	0.11 ± 0.08
DIFFERENCE PRE - 24 H	0.05 ± 0.13	0.31 ± 0.08	0.15 ± 0.08	0.07 ± 0.09

Table 3: Mean Z values variations (with SD) in the different groups between preoperative and 12 hours after surgery measures and between preoperative and 24 hours after surgery measures.

Z VALUES	LLLT bilateral	Control Group	Non LLLT monolateral	LLLT monolateral
DIFFERENCE PRE - 12 H	0.31 ± 0.22	0.17 ± 0.11	0.20 ± 0.11	0.12 ± 0.07
DIFFERENCE PRE - 24 H	0.11 ± 0.16	0.31 ± 0.07	0.18 ± 0.11	0.05 ± 0.07

Twelve hours after surgery, having performed one session of LLLT in the laser groups, we observed the most important increase of X values in subjects bilaterally irradiated (followed by patients not receiving mono or bilaterally LLLT); in the same group of patient 24 hours after surgery this value was the lowest (Table 3 - Figure 6). At this time, patients not receiving LLLT at all (control groups) showed the greatest values in X measures.

Statistical analysis performed for the evaluated values (X, Y, Z) showed an extremely significant difference with p values of 0.003 for Y at the first evaluation (pre-12 hours) and less than 0.001 for the other evaluations.

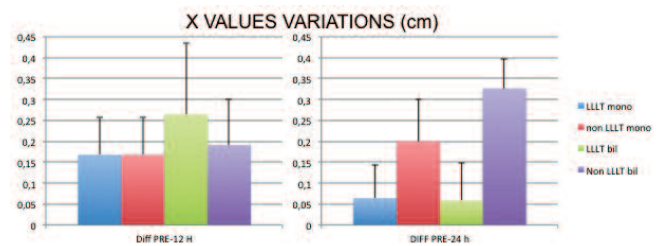


Figure 4: Values comparison of the difference X at 12 hours and preoperative, and X at 24 hours and preoperative of the three groups of patients.

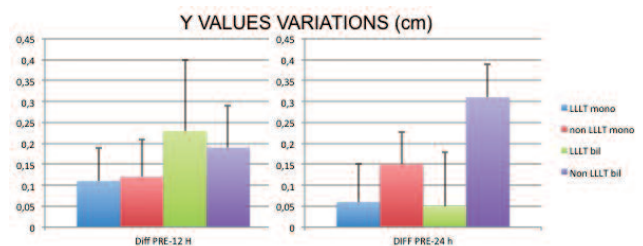


Figure 5: Values comparison of the difference Y at 12 hours and preoperative, and Y at 24 hours and preoperative of the three groups of patients.

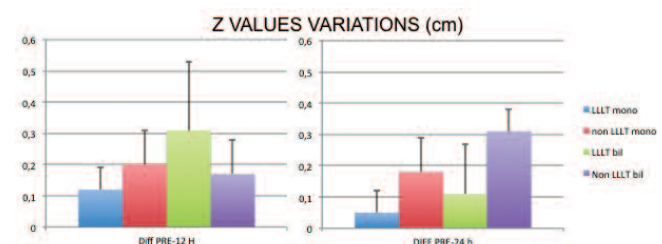


Figure 6: Values comparison of the difference Z at 12 hours and preoperative, and Z at 24 hours and preoperative of the three groups of patients.

Mean value of VAS at 12 hours was greater in Control group than in monolateral or bilateral LLLT groups with the smallest values for patients receiving LLLT bilaterally. The same difference was found for VAS values at 24 hours and at hospital discharge (**Table 4 – Figures 7-8**).

Statistical analysis did not retrieve significant results for VAS recorded after 12 hours ($p=0.6452$) and after 24 hours ($p=0.0730$); a significant result was found for VAS recorded at hospital discharge ($p<0.0001$): multiple comparison found extremely significant difference between bilateral LLLT group and monolateral LLLT group and between bilateral LLLT group and no LLLT group.

Discussion and conclusions

After 12 hours from the intervention and after the first laser irradiation, we noticed an increase of all the values (an augmentation of swelling) in the patients treated with bilateral LLLT compared to the swelling all the other groups.

After 24 hours the bilateral LLLT treated group showed a severe decrease of swelling as the values of X, Y, Z and the charts confirmed; compared to the other groups the reduction of oedema was the highest. In the monolateral LLLT treated group we observed a linear behavior of the swelling during the 12 and 24 hours.

Edema was measured also in this group after 12 hours, but it didn't increase as much as the bilateral LLLT treated group at the same time. At 24 hours the values showed a reduction of the oedema wider on the treated side than on the non treated one; we also observed a reduction of swelling on the non treated side in comparison with the control group: there was a

reduction on both sides of the monolateral LLLT treated group.

As we can see in the charts, the higher amount of swelling after 12 hours is in the bilateral treated group, which decreases to the lowest value after 24 hours/hospital discharge of the patient.

Based on previous studies and literature, we expressed two different hypotheses:

1. Acceleration of healing

LLLT has been shown to be effective in treating various acute and chronic conditions in different animals by accelerating wound healing through neovascularization, angiogenesis, and collagen synthesis by preventing cell apoptosis and increasing cell proliferation, migration, and adhesion.

The enhancement of ATP production promotes metabolic processes, synthesizes DNA, RNA, proteins, enzymes, and other biological materials needed to repair or regenerate cells and tissue components, rapid mitosis or cell proliferation and restore homeostasis ¹⁶⁾.

Petrova et al. ¹⁷⁾, demonstrated by using LLLT, a high phagocytic activity of macrophages as early as 6 hours. LLLT enhances the job of mononuclear cells through production of leukotrien-B4 which is derived from arachnoid acid and production of interleukin-8, so promoting fibroblasts. In general, fibroblasts are known to be essential in the healing of tissue injuries including surgical wounds, creating the epithelialization and granulation tissue for the repair stage; fibroblasts begin to synthesize collagen and ground substances ^{18, 19)}.

A previous study of Baxter and Hopkins ²⁰⁾ indicated the possibility of laser-induced fibroblast proliferation during healing mechanism. The effect of laser

Table 4: Mean VAS values (with SD) 12 hours after surgery, 24 hours after surgery and at the hospital discharge in the different groups.

VAS ± SD	LLLT monolateral	LLLT bilateral	Control Group
12 HOURS	7.12 ± 0.91	7.03 ± 0.82	7.26 ± 0.81
24 HOURS	6.42 ± 0.91	6.14 ± 1.12	6.88 ± 0.74
HOSPITAL DISCHARGE	5.98 ± 0.79	4.85 ± 0.74	6.59 ± 0.71

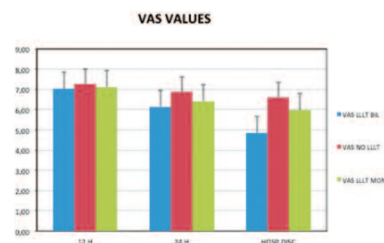


Figure 7: VAS values comparison of all the three groups of patients at 12 hours, at 24 hours and at the hospital discharge.

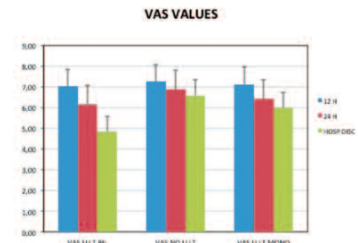


Figure 8: VAS values comparison of the three times of evaluations for patients receiving monolateral or bilateral LLLT and for control group.

stimulation of fibroblasts on wound regeneration is by the maintenance of a high mitotic activity of the fibroblast in the later healing period ²¹⁾, in which it was demonstrated that LLLT preferentially stimulates resting cells rather than proliferating ones.

LLLT can facilitate wound healing, due to acute inflammation, so resolving it more rapidly and may accelerate the proliferation phase of healing ²²⁾, therefore, the LLLT decreased the inflammatory reaction of wound healing.

2. Time-dependent effects of LLLT

The results of previous studies have shown that in the normal healing process, although ROS production increases: LLLT also enhances antioxidant enzyme activity, minimizing the occurrence of oxidative damage to the healing tissues ²³⁾. Therefore, the balance between ROS production and the effect of the antioxidant system is believed to be directly related to the healing time and the quality of the wound tissue ²⁴⁾; however, this is a question that has still to be fully clarified. It has been suggested that LLLT, depending on the dose, duration of irradiation applied to the wound, and the energy density used, may alter ROS production and antioxidant defense mechanisms. Nevertheless, the data available up to the present time are inconclusive. The dose-dependent effects of LLLT are frequently explained using the Arndt-Schulz law ²⁵⁾ that states that while smaller amounts result in biostimulation, as the amount increases, the effect is reversed, and bioinhibition occurs ²⁶⁾.

The VAS evaluation showed us a higher improvement in the bilateral treated group compared to the others. The monolateral treated group showed a different trend: there is a slight cutback of the pain, more similar to the bilateral treated group than the non treated one, but not as strong as it.

During the treatments patients felt immediately a sensation of less strain and discomfort. The patients of the monolateral group didn't know which side was treated (because of the use of a fake laser treatment), but they expressed a better sensation on the irradiated side.

We preferred to analyze more accurately the X,Y,Z values than the VAS because of many variables that influence patients evaluation of pain: subjective (physical and psychological), type of inclusion of the tooth and difficulty of extraction.

Critical points

Wavelength. This is probably the parameter where there is most agreement in the LLLT community.

Wavelengths in the 600-700 nm range are chosen for treating superficial tissue, and wavelengths between 780 and 950 nm are chosen for deeper-seated tissues, due to longer optical penetration distances through tissue. Wavelengths between 700 and 770 nm are not considered to have much activity. Some devices combine a red wavelength with a NIR wavelength on the basis that the combination of two wavelengths can have additive effects, and this can also allow the device to be more broadly utilized to treat more diseases. Of course, other studies will be necessary to define what is the optimum wavelength for the different indications where LLLT is indicated.

Laser vs non-coherent light. One of the most topical and widely discussed issues in the LLLT clinical community is whether the coherence and monochromatic nature of laser radiation have additional benefits, as compared with more broad-band light from a conventional light source or LED with the same center wavelength and intensity. Two aspects of this problem must be distinguished: the coherence of light itself and the coherence of the light-matter interaction (biomolecules, tissues). The latter interaction produces the phenomenon known as laser speckle, postulated to play a role in the photobiomodulation interaction with cells and subcellular organelles but, for the following reason, it is very difficult to design an experiment to directly compare coherent laser light with non-laser light. In fact, due to laser light is almost always monochromatic with a bandwidth of 1 nm or less, it is very difficult to generate light from any other source (even LED) having a bandwidth narrower than 10-20 nm, so it is not easy to understand if observed differences are due to coherent versus non-coherent light, or due to monochromatic versus narrow bandwidth light.

Dose. Because of the possible existence of a biphasic dose response curve referred to above, choosing the correct dosage of light (in terms of energy density) for any specific medical condition is difficult. In addition there has been some confusion in the literature about the delivered fluence when the light spot is small. If 5J of light is given to a spot of 5 mm², the fluence is 100 J/cm², which is nominally the same fluence as 100 J/cm² delivered to 10 cm², but the total energy delivered in the latter case is 200 times greater. The dose of light used depends on the pathology being treated, and in particular upon how deep the light is thought to need to penetrate into the tissue. Doses frequently used in the red wavelengths for fairly superficial diseases tend to be in the region of 4 J/cm² with a range of 1-10 J/cm². Doses of the NIR wavelengths employed for deeper-seated disorders can be higher than these

values, i.e., in the 10-50 J/cm² range. The light treatment is usually repeated either every day or every other day, and a course of treatment can last for periods around two weeks.

Pulsed or CW. Some reports affirmed that pulse structure is an important factor in LLLT: for instance Ueda et al.^{27, 28)} found better effects using 1 or 2 Hz pulses than 8 Hz or CW 830 nm laser on rat bone cells, but the underlying mechanism for this effect is unclear.

Polarization status. Some studies demonstrated that polarized light has better effects in LLLT applications than otherwise identical non-polarized light (or even 90-degree rotated polarized light)²⁹⁾. However, it is known that polarized light is rapidly scrambled in highly scattering media such as tissue (probably in the first few hundred μ m), and it therefore seems highly

unlikely that polarization could play a role, except for superficial applications to the upper layers of the skin.

Systemic effects. Although LLLT is mostly applied to localized diseases and its effect is often considered to be restricted to the irradiated area, there are reports of systemic effects of LLLT acting at a site distant from the illumination^{30, 31)}. It is well known that UV light can have systemic effects³²⁾, and it has been proposed that red and NIR light can also have systemic effects. These have been proposed to be mediated by soluble mediators such as endorphins and serotonin. There is a whole field known as laser acupuncture³³⁾ in which the stimulation of specific acupuncture points by a focused laser beam is proposed to have similar effects at distant locations to the more well known needle acupuncture techniques.

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