

Efficacy of low-level laser therapy on scar tissue

CARLA P. FREITAS, CRISTINA MELO, ANA M. ALEXANDRINO & ANDREIA NOITES

Department of Physiotherapy, School of Allied Health Sciences (ESTSP) Polytechnic Institute of Porto, Vila Nova de Gaia, Portugal

Abstract

Background: Physiotherapy has a very important role in the maintenance of the integumentary system integrity. There is very few evidence in humans. Nevertheless, there are some studies about tissue regeneration using low-level laser therapy (LLLT). *Aim:* To analyze the effectiveness of LILT on scar tissue. *Methods:* Seventeen volunteers were stratified by age of their scars, and then randomly assigned to an experimental group (EG) — $n=9$ — and a placebo group (PG) — $n=8$. Fifteen sessions were conducted to both the groups thrice a week. However, in the PG, the laser device was switched off. Scars' thickness, length, width, macroscopic aspect, pain threshold, pain perception, and itching were measured. *Results:* After 5 weeks, there were no statistically significant differences in any variable between both the groups. However, analyzing independently each group, EG showed a significant improvement in macroscopic aspect ($p=0.003$) using LILT. Taking into account the scars' age, LILT showed a tendency to decrease older scars' thickness in EG. *Conclusion:* The intervention with LILT appears to have a positive effect on the macroscopic scars' appearance, and on old scars' thickness, in the studied sample. However, it cannot be said for sure that LILT has influence on scar tissue.

Key Words: *low-level laser therapy, skin scars, physiotherapy, wound healing*

Introduction

Physiotherapy has a very important role in the maintenance of the integumentary system integrity, intending to improve or restore not only the skin's appearance but also its function (1, 2). There is very few evidence in humans. Nevertheless, there are some studies about tissue regeneration using low level laser therapy (LLLT) (3–13).

The wound-healing process can be roughly divided into three stages: inflammatory, proliferative, and remodeling phases. The inflammatory phase is dominated by hemostasis and acute inflammatory response that lasts about 24-48 h (14). The proliferative phase is responsible for the formation of a new functional barrier, and it lasts up to 4 weeks (14–16). In the final stage of wound healing, the remodeling phase, there are scar tissue formation and maturation of the wound that can be extended from 6 months to 2 years (14,17).

The result of the normal wound-healing process is the restoration of the architecture and function of damaged tissues with the formation of a thin scar and minimal fibrosis, but there are factors that can influence this process (16). The known factors that influence the normal wound healing are divided into general and local (18). The healing process also depends on the scar's anatomical location and its orientation (along Langer's lines), skin photo type, and incision type (19, 20).

The application of LLLT, as a therapeutic technology, has grown significantly in recent years, leading to developments in dermatological condition's treatment, which is being used as a promising method to improve the skin scars aesthetically and functionally (2).

Low-intensity laser radiation is characterized by its ability to induce a non-thermic process (bio stimulation), and it is monochromatic, coherent, and polarized. This can be transmitted, reflected, refracted, and absorbed. The differences between the various types of laser beams produced are determined using wave lengths, power, irradiance, energy density, pulse duration, pulse repetition rate, area, and beam mode (21).

LLLT is quite helpful in modulating different biological activities, such as trophic-regenerative (22-24), anti-inflammatory (24), and analgesic effects (25). In a specific form, changes can be observed in parameters such as *adenosine triphosphate* (ATP) viability, cytokine expression (*interleukin 6* – IL-6), cell proliferation (*alkaline phosphatase* enzyme activity), and *deoxyribonucleic acid* (DNA) damage, directly after LLLT. ATP production and cell membrane perturbation could lead to permeability changes and second messenger activity resulting in functional changes. The effect of laser irradiation on IL-6 is important because a direct association between IL-6, migration and proliferation may accelerate the inflammatory phase and reduce the time for complete wound healing (26,27). The results of LLLT on DNA damage (as oxidized bases and repair in prokaryotic and eukaryotic cells) may be influenced by fluencies, frequencies, and wavelength of laser along with tissue conditions and genetic characteristics of cells before treatment beginning (26,28).

The energy must be absorbed by the tissues in order to have effect. The depth of penetration is greater with the application of a perpendicular laser probe, due to reduced reflection and scattering, but it is always influenced by its wavelength. The range between 800 and 900 nm can penetrate beyond the epidermis, at a very superficial level (about 2-4 mm). However, it can influence the deeper tissues with the cascade reaction (29). LLLT's use in animals and humans almost exclusively involves red and near infrared light (600-1100nm) (24).

Considering that the scars have a functional and emotional impact on people, they should not be considered as an afterthought, but as a change that must be addressed. In this sense, LLLT physiotherapy should be applied, since there were observed effects and results in wound healing (3,4,6-10,13). The purpose of this study was to analyze the effectiveness of LLLT on scar tissue, evaluating its effects in thickness, length, width, macroscopic aspect (color, pigmentation, elasticity, and height), pain threshold, and pain perception and itching, in relation to the scar's age.

Materials and methods

The target population of this experimental and longitudinal study was all the students of an Allied Health School in Oporto, Portugal (ESTSP), who were invited to participate in the study by e-mail. Thirty-five students agreed to be part of the study. As inclusion criteria, the students had to be between 18 and 25 years, with scars older than three weeks prior to presentation (30). Laser contraindications, corticosteroids or anti-coagulants intake, overlapping scars, and performing another scar's intervention (18,31,32), and a total score of 0 on the Vancouver Scar Scale (VSS), or without any thickness confirmed by echography were defined as exclusion criteria.

Considering the previous criteria, 18 individuals were excluded. The final sample consisted of 17

participants who were stratified into four groups, taking into account the age of their scars: group 1 – < 6 months, group 2 – 6-12 months, group 3 – 12-24 months, and group 4 – > 24 months. Participants were randomized from each age scar group. At the end, the experimental group (EG) had 9 participants and the placebo group (PG) had 8 participants. Both the groups had sessions of LLLT thrice a week (Figure 1). Both the groups were prepared similarly for laser application. Nevertheless, in PG, the device was used in safe mode with a security key (it does not allow any radiation). Moreover, as all participants had security glasses, seeing the red light coming from the laser device was impossible for them.

Instruments

A social demographic questionnaire was handed to all individuals who volunteered to participate in the study for selection and characterization of the sample.

A pilot study took place before the study to analyze instruments' intra-rater reliability (ICC 3.1), standard error of measurement (SEM), and minimal detectable change (MDC) (33). ICC was classified according to the Fleiss's criteria (1986) (34). Measures were taken with 72 h of interval.

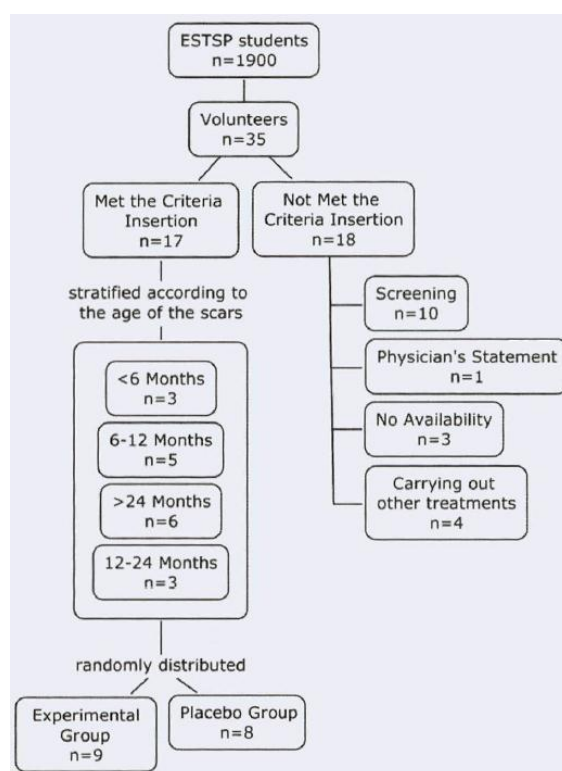


Figure 1 - Sample's Diagram

Scar's thickness was measured using TOSHIBA® Viano echo graph with a 7.5-MHz probe designed by a radiology expert. An excellent intra-observer reliability with an ICC (3.1) of 0.99, an SEM of 0.007 mm, and an MDC of 0.018 mm (33-36) was observed.

Scars' length and width were measured using a caliper, and intra-rater reliability found was an ICC (3, 1) of 1.0 (34).

The Vancouver Scar Scale was used to evaluate scars' pigmentation, color, elasticity and height, with a total score between 0 and 13, lower scores representing a better macroscopic aspect (37,38). This scale was adapted and validated to the Portuguese population with a content and construct validity of Cronbach's $\alpha=0.73$. VSS showed excellent intra-rater reliabilities with an ICC (3.1) of 1.0 for the height and color, 0.93 for elasticity, 0.91 for pigmentation, and 0.98 for the total score. Total score also presented an SEM of 0.33 and an MDC of 0.92 (33, 34).

Pain perception was assessed using a digital pressure algometer WAGNER® FPI, expressed in kilograms-force (kgf), placed perpendicularly on each edge of the scar. According to Fernández-de-las-Pefias and colleagues (2006), a pressure of 2.5 kgf maintained for 5 s is enough to measure pain perception

using a visual analogue scale (VAS) (39). This method showed an intra-rater reliability ICC (3.1) of 0.97, an SEM of 0.09, and an MDC of 0.24 (33,34).

Pain threshold was measured using the same digital pressure algometer placed perpendicularly on each edge of the scar and expressed in kgf, beginning in zero kgf and increasing the pressure until a participant presented a stop signal (39), showing an intra-rater reliability ICC (3.1) of 0.94, an SEM of 0.08 kgf, and an MDC of 0.21 kgf (33, 34). Itching was measured using VAS, showing an ICC of 1.0 (34, 40).

For LLLT application, an IDEA HP® terza series laser device with a probe of 808 nm was used.

Procedures

A pilot study took place to understand questionnaire and protocol feasibility.

Inclusion criteria were confirmed using echography taken by radiology expert, followed by the random distribution of individuals in the EG and PG.

The study had two moments of evaluation: an initial one (M1) and a final one (M2) after five weeks. The averages of three measurements of each variable (scar's thickness, length, width, pain threshold, pain perception, and itching and VSS) were used.

LLLT was administered to the volunteers according to security guidelines for low-level lasers (32). A diode laser light infrared 808 nm with continuous emission of 500 mW was used. It was performed throughout the scar, with a punctual application with a distance of 1 mm between each point (4 s per point). The applied energy density was 4 J/cm², and the irradiation was 1 W/cm². The probe had an angle of 90° and a distance of about 1 cm from the skin surface (4,21,24,32). The treatment began the day-after M1, and it was performed thrice a week (on Mondays, Wednesdays, and Fridays) over 5 weeks (4).

Ethics

This study was approved by the Ethics Committee of the ESTSP. Participants, after informed about the aims and procedures of the study and after agreeing with them, expressed their consent by signing the Declaration of Helsinki. All of them were able to refuse or discontinue the study at any time. The confidentiality of the data was maintained, and the opportunity to placebo subjects to carry out the intervention was given after the study's end.

Statistical analyses

For the statistical analysis of variables in this study, the software *PASW Statistics 18* for Windows 7® with a significance level of 0.05 (41) was used.

The sample characterization was performed using descriptive statistics. It was decided to use only non-parametric statistics due to a reduced number of participants. For the inter-group comparisons, the Mann-Whitney test for rational variables and the chi-square test for nominal variables were used. For intra-group comparisons, the Wilcoxon test for rational variables and the marginal homogeneity test for nominal variables were used (41).

Results

The EG consisted of seven females and two males, and the PG consisted of six females and two males. There were no significant differences in the anthropometric measures in both the groups (Table I).

Table 1 - Sample's anthropometric characteristics

| | Experimental group (n = 9) | | Placebo group (n = 8) | | p | U |
|-------------|----------------------------|-------------------------|-----------------------|-------------------------|-------|--------|
| | Median | Interquartile deviation | Median | Interquartile deviation | | |
| Age (years) | 21 | 1 | 19.5 | 2.5 | 0.942 | 35.000 |
| Weight (Kg) | 65 | 4.5 | 67.5 | 8.5 | 0.284 | 24.500 |
| Height (m) | 1.68 | 5.5 | 1.72 | 6 | 0.353 | 26.000 |

In the seventeen participants, whose skin scars that were analyzed in this study, approximately 58.8% of the scars were located in the trunk and 41.2% in extremities. Regarding the age of scars analyzed, it was found that 17.6% were less than six months old, and the same percentage were between 12 and 24 months old. Approximately, 29.4% and 35.6% of the target population of this study had scars between 6 and 12 months and older than 24 months, respectively. There were no significant differences in the localization and in the age of scars between EG and PG.

Inter-group analysis

After 5 weeks of ILLT application, there were no statistically significant differences in the studied variables between the two groups.

Intra-group analysis –Thickness

When comparing EG and PG, MI and M2 thickness decreased significantly in both the groups, respectively $Z = -2.666$ ($p = 0.002$) and $Z = -2.313$ ($p = 0.012$).

Taking in account MDC thickness, participants in both the groups improved clinically (decreased thickness). Nevertheless, a greater scar's thickness improvement in EG's older scars was observed after 5 weeks of LLLT (Figure 2)

Intra-group analysis –Vancouver Scar Scale (VSS)

The EG's total VSS score improved after 5 weeks (verified by a decreased score) ($Z = -2.673$ to $p = 0.003$). Therefore, analyzing VSS individual items, only the color and the elasticity were significantly better after 5 weeks, respectively, as follows: MH = 18.000 ($p = 0.004$) and MH = 17.000 ($p = 0.016$). When analyzing MDC VSS items by group, 55.6% of the

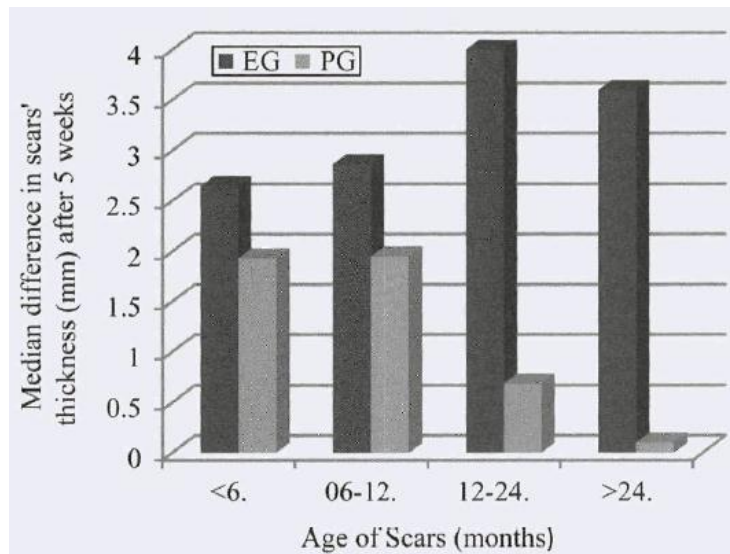


Figure 2 - Median difference in scars' thickness after 5 weeks of LLLT

Intervention. EG: experimental group; PG: placebo group.

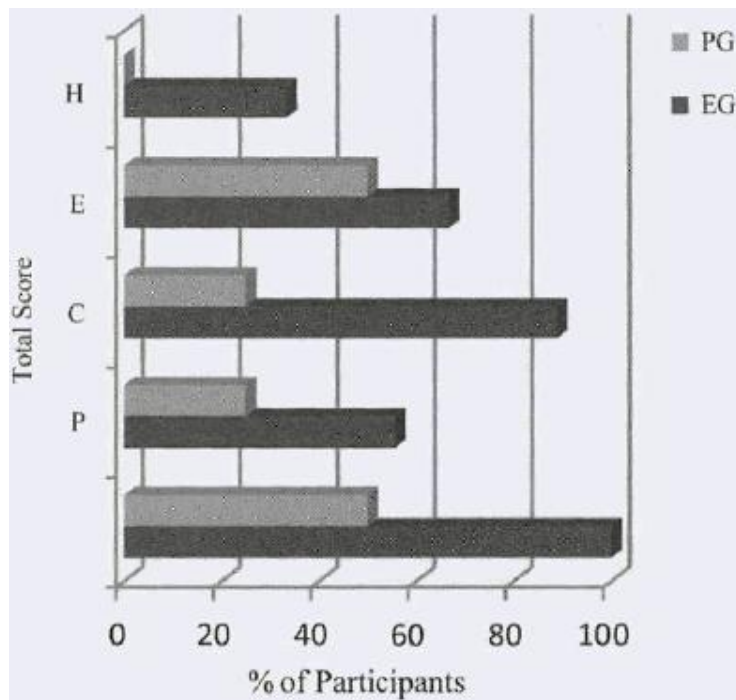


Figure 3 - Positive clinical results of the intervention (MDC), in the total score and in the four items from the Vancouver Scar Scale. EG: experimental group; PG: placebo group; H: height; E: elasticity; C: color; P: pigmentation

participants from the EG had clinically relevant improvements in pigmentation, while PG maintained all the values (Figure 3).

Intra-group analysis – Pain threshold

After 5 weeks of ILLT, both the groups showed a significant decrease in the pain threshold: for EG, $Z=-2.666$ ($p=0.002$), and for PG, $Z=-2.380$ ($p=0.008$). According to MDC pain threshold values, it was found that most of the participants in EG and PG had relevant clinical improvements (Figure 4).

Intra-group analysis – Length, width, itching, and pain perception

Even though after 5 weeks, there were no significant improvements in length, width, pain perception, and itching in EG, it is important to refer that MDC showed 22.2% clinical improvement for scars' length and 44% for scars' width. It was found that most individuals in both the groups had a clinical improvement in pain perception (Figure 4).

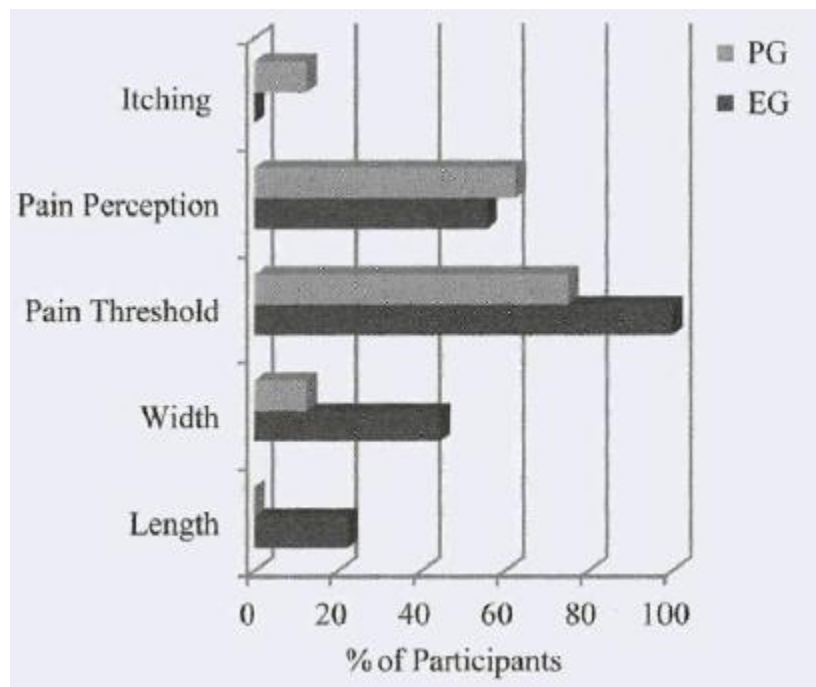


Figure 4 - Positive clinical results of the intervention (MDC), in scars' length, width, pain threshold, pain perception and itching.

EG: experimental group; PG: placebo group.

Discussion

This study analyzed the effect of LLLT 5-week treatment on scars' thickness, macroscopic aspect, length, width, itching, pain threshold, and pain perception. In fact, it cannot be said for sure that LLLT has influence in all the studied variables as there were no significant differences between experimental and placebo groups, mainly due to the reduced sample.

Nevertheless, when observing the groups independently, EG had a significant decrease in the VSS total score, after 5 weeks of LLLT, revealing an improvement in the macroscopic appearance of the scars as it was found by Gaida and colleagues (2004), in 19 patients with burn scars. These authors used laser therapy with similar power, energy density, and duration (4).

According to Huang and colleagues (2009), an energy density between 3 and 5 J/cm² has a best positive results in wound healing in vivo (24), supporting the use of 4 J/cm² in the present investigation. Energy density appears to be the only treatment parameter with predictable dose dependent treatment effect according to Woodruff and colleagues (2004). These authors have no doubt that LLLT is an effective modality for treating wounds. Nevertheless, they also found that the result may be dependent on wave length, pulse duration, irradiance, pulse repetition rate, treatment time, treatment repetition rate, or a combination of all these factors (23).

Despite the lack of evidence on using VSS by item, the researcher chose to use them independently in order to observe differences in specific aspects. Scar's elasticity and color (as VSS items) improved significantly in EG, with an improvement in MCD pigmentation. Height item VSS results suggested a ceiling effect. Brussaers and colleagues (2010), in a systematic review of different scars' scales, show some advantages in using scales, as they are the advantages in the clinical setting, given their low-cost and expenditure of time, they are easy to include in the clients' files. The same authors pointed the importance of their validity, reliability and practical application (38). However, the same authors in another study questioned scales as they are subjective to evaluate scars, depending on who applies them (42). This aspect was partially controlled as evaluations were done by the same researcher.

Scars' thickness was measured using an echography as ultrasound high frequency assesses not only the distance to the surface of the scar skin, but also in-depth fibrosis (42). There was a significant decrease in scars' thickness (conjunctive tissue) in both the groups. In fact, the reduced thickness can be explained by a decrease in myofibroblasts' density and an extracellular matrix alteration (43). These changes may be due to natural wound-healing process until 24 months, as most of the scars of this study are in the remodeling phase (17). However, EG thickness improvement on scars older than 24 months, despite the lack of statistical significance, can be seen as a possible favorable effect of laser action on old scars. These results are in agreement with Lucas and colleagues (2000), who found that scientifically LLLT had poor positive effects in human studies but acceptable clinical results (22). The problem of sorting out optimum treatment characteristics for LLLT may be difficult as there are a large number of variables (22, 23). Results concerning old scars' thickness improvements using LLLT are not supported by any evidence being relevant to explore it in future investigations.

Pain threshold measured by an algometer decreased in both the groups. Therefore, it cannot be forgotten that the relationship between participant and researcher can influence pain threshold improvement. In fact, personal relations during 5 weeks, thrice a week, can lead to participant's sense of well-being, which leads to a release of opioids by limbic system closing the gate control and preventing pain to ascend to the cortex, where it is recognized (44).

Pain perception only had clinical results, where improvements were observed in most subjects, in both the groups. These results suggest that digital pressure algometry may be more objective quantifying the pain in scars than VAS.

Laser application did not change scars' length and width in the intervention group when compared with those in the control group. However, Hopkins and colleagues (2004) in a randomized controlled trial, in the first two phases of wound healing, found significant improvements in the scars when comparing the groups, but only in superficial scars (abrasions) (3).

The limitations of this study were the lack of researcher impartiality as well as the limited sample.

For future studies, it is suggested the comparison of the effects of laser with those of other forms of assistance: ultrasound, massage therapy, or pressure therapy. It is also suggested that the effects of laser therapy should be studied in scars older than 24 months.

Conclusion

The intervention with LLLT appears to have a positive effect on the macroscopic appearance on old scars, and on old scars thickness, in the studied sample. However, it cannot be said for sure that LLLT has influence on scar tissue.

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