A Systematic Review: Effect of Low Level Laser on Hypertrophic Scar Post Burn

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Abstract

Background: Burn scars are known to be difficult to treat because of their tendency to worsen with hypertrophy and contracture. Various experimental and clinical efforts have been made to alleviate their effects but the problem has not been solved. Since patients keep asking for Low Level Laser Therapy (LLLT) and believe in its effectiveness on burn scars, and since former studies show contradictory results of the influence of LLLT on hypertrophic scars, this study was designed to objectify the effects of LLLT on burn scars.

Aim of the Study: The purpose of this study is to systematically review the effects of low level laser therapy) He-Ne, Ga-As) on hypertrophic scar post burn.

Material and Methods: Systematic review of all published studies with all research designs except expert opinions. A search was made in PubMed, Cochrane library, Pedro and Google scholar.

Results: Seven studies met the inclusion criteria in this SR, two studies included in meta-analysis but the remaining studies is included in descriptive analysis in order not to exclude their results.

Conclusion: The current level of evidence to support the effectiveness of effect of low level laser therapy on hypertrophic scar post burn shows that LLLT has insignificant effect on hypertrophic scars post burn. The main limitations are the heterogeneity between included studies in meta-analysis and small number of the studies involved.

Key Words: Systematic review – Low level laser therapy – Burn scar – Bio stimulation and inhibition – He-Ne – Ga-As – Laser parameters.

Introduction

SYSTEMATIC reviews help overcoming limitation of primary research by testing its findings for consistency and whether they can be generalized across populations or not. Meta-analysis in particular increases the power and precision of estimates and treatment effects and exposure risks. Besides the explicit methods used in SR, it limits bias and improves reliability and accuracy in conclusions. In this way, SR and meta-analysis can help physicians, physical therapists, health care providers and policy makers to make informed decisions in health care [1].

Hypertrophic scar formation is a major clinical problem in the developing and industrialized worlds. Scar control is a major concern in burn wound management. When scarring occurs, the outcome may be associated with a loss of function or an undesirable cosmetic result, as once scars have formed; they are known to be difficult to treat because of their tendency to worsen with hypertrophy and contractures [2].

LLLT was used for the treatment of a pigmented hypertrophic scar. Laser irradiation was carried out with a Gallium-Aluminum-Arsenate (Ga-As) diode laser (980nm, 6W energy density of 6-10J/cm^2, He-Ne 630nm 1J/cm^2 and blue LED 450nm) with satisfactory results particularly on reducing pain, edema and hyperpigmentation. It is concluded that low level laser therapy can be used for the treatment of keloids and hypertrophic scars with remarkable improvement for the above mentioned complaint [3].

The analgesic effect of LLLT is another motivating factor for its application after burn induced damage on skin. Ga-As laser, one form of LLLT, reduces histological abnormalities, collagen concentration, and oxidative stress in damaged tissues. Reduction of fibrosis could be mediated by its beneficial effects on the oxidant/antioxidant [4-7].
Patients and Methods

Procedure of the systematic review was accomplished through the following items:

1- Search strategy for identification of studies:

- Data sources:
  - Google scholar website.
  - Science direct web site.
  - Physiotherapy Evidence Database (Pedro) http://www.pedro.org.au/”.
  - Wikipedia web site.

To systematically review studies published in English language which studies the effects of low level laser therapy on hypertrophic scar post burn.

Search was done for systematically review the randomized controlled trials and cohort study registered.

2- Study selection criteria:

- Types of studies: Randomized controlled trials and cases studies of low level laser therapy on hypertrophic scar.
- Types of participants: The review was included participants aged from 25 to 40 years.
- Types of interventions: This review was included studies which demonstrate the effects of low level laser therapy programs with reported findings for analysis of its effectiveness.

Inclusion criteria:

- Men and women from 25 to 40 years.
- Low level laser therapy.
- Physiotherapy alone.
- The randomized controlled trial.

Exclusion criteria:

- Any non-randomized controlled trial.
- Un related studies.
- Studies published in language other than English.
- Studies did not meet the inclusion and exclusion criteria.
- Studies that included the population which is younger than 20 years old and more than 45 years old.
- Unpublished studies.

3- Data extraction:

Three independent reviewers screened the abstracts of the publications found in the databases. If the abstracts were not available. The title of the publication was screened for acceptance. If reviewers felt that the abstract or title was potentially useful, copies of the article were obtained and were analyzed by all reviewers in accordance with the inclusion criteria. A copy of the published article was also obtained in cases where there was no consensus between the reviewers and the publication (evaluated through the abstract) potentially met the inclusion criteria. If there was inadequate information to make a decision, a copy of the published article was obtained as well. The reviewers analyzed all papers initially selected by the abstract or title for the inclusion/exclusion criteria. Each criterion was graded on a yes/no basis. The published paper had to provide enough information to meet the criterion. In order for papers to be evaluated at the next level, the critical appraisal, the paper had to meet all the inclusion criteria. When discrepancies occurred between reviewers in regard to whether a paper met a criterion, the rating forms were compared and the criterion discussed until a consensus was reached.

<table>
<thead>
<tr>
<th>Search strategy</th>
<th>PubMed results</th>
<th>Cochrane results</th>
<th>Pedro results</th>
<th>Google scholar results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect of (He-Ne, Ga-As) on hypertrophic scar</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5220</td>
</tr>
<tr>
<td>Effect of low level laser on hypertrophic scar</td>
<td>14</td>
<td>13</td>
<td>0</td>
<td>14300</td>
</tr>
<tr>
<td>Effect of low level laser on skin thickness</td>
<td>23</td>
<td>51</td>
<td>2</td>
<td>270000</td>
</tr>
<tr>
<td>Effect of low level laser on keloid</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>8100</td>
</tr>
<tr>
<td>Effect of low level laser on abnormal wound closure</td>
<td>5</td>
<td>15</td>
<td>0</td>
<td>23300</td>
</tr>
<tr>
<td>Low level laser and hypertrophic scar</td>
<td>49</td>
<td>13</td>
<td>0</td>
<td>13700</td>
</tr>
</tbody>
</table>
Ethics:
The protocol of this study was approved by the Ethical Committees of the Faculty of Physical Therapy, Cairo University, Egypt.

Results
Seven studies met the inclusion criteria in this SR, two studies included in meta-analysis but the remaining studies is included in descriptive analysis in order not to exclude their results.

After extracting data from each included study in this systematic review, data were compared and findings were represented. Two trials from seven were involved in meta-analysis for measuring the effect of low level laser on hypertrophic scars. Because information needed to carry out the meta-analysis was not mentioned in the full text article and different methods used to assess the measured outcomes so descriptive analysis was performed for describing them.

Meta-analysis was carried out on two studies which are Karin et al., 2004 and Weal Naeim et al., 2012 for the effect of low level laser on hypertrophic scars.

The result of the meta-analysis showed insignificant effect of LLLT on hypertrophic scars and represent in Fig. (1).

From the previous two studies the effect of LLLT on hypertrophic scars had shown an insignificant effect.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD Total</td>
<td>Mean SD Total</td>
<td>Weight</td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>Karin et al., 2004</td>
<td>4.86 2.05 19</td>
<td>5.4 2.66 19</td>
<td>48.9%</td>
<td>-0.54 (-2.05, 0.97)</td>
</tr>
<tr>
<td>Wael Naeim et al., 2012</td>
<td>4.06 1.38 15</td>
<td>7.66 1.95 15</td>
<td>51.1%</td>
<td>-3.60 (-4.81, -2.39)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>34</td>
<td>34</td>
<td>100.0%</td>
<td>-2.10 (-5.10, 0.89)</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² =4.19; Chi² =9.61, df=1 (p=0.002); CI² =90%
Test for overall effect: Z=1.38 (p=0.17)

Fig. (1): Forest plot of comparison between experimental and control groups regarding outcome.

Discussion
The purpose of the current systematic review was to evaluate the effect of the low level laser on post burn hypertrophic scar in a systematic way and to update the review of literature on the topic to determine if higher quality studies that might clarify the scientific basis for the use of low level laser on hypertrophic scar that have been recently conducted.

The research was applied in PubMed, the Cochrane library and PEDro using the words ("hypertrophic scar", "low level laser", "(He-Ne, GA-AS)", "systematic review" and "post burn"). The research was for the randomized control trails and cases studies dealing with men and women with age from 25-40 years old and use of low level laser as a method of intervention. The only outcome measure was scar thickness and pliability.
Seven studies met the inclusion criteria. Meta-analysis was done between two studies and descriptive analysis was done for 5 studies due to heterogeneity of the study and findings are presented qualitatively due to heterogeneity of the studies.

In the study of Karin et al., [8], seventeen out of 19 lesions showed macroscopic improvement after the treatment (expressed in points on the vancouver scar scale); two lesions did not improve. Before the treatment the scars that were to be radiated were classified on an average of 7.10±2.13 points on the VSS. This number decreased to 4.68 ±2.05 points after the treatment. The respective data of the control areas were 5.86±2.71 points before and 5.40±2.66 points after the treatment. None of the scars became worse.

A significant difference in improvement between burn scars younger and older than 12 months could be found in the VSS: Lesions deriving from a thermal trauma less than 12 months prior to LLLT showed better results. All but one of the patients, who had reported pain or pruritus before the treatment, experienced relief of their symptoms through LLLT. The mean on the VAS decreased from 3.89 ±3.07 to 1.42± 1.67 for pain and from 4.36±3.26 to 1.31± 1.88 for pruritus. Negative effects of LLLT were neither seen nor reported by the patients. This study included in meta-analysis study as it is considered randomized controlled study.

In the study of Cecelia and Mary, [9], the results of the experiments revealed that laser energy 2 of 880nm wavelength at 16mW and 2.4J/cm² had a very mild inhibitory effect on both the primary cell lines, HF derived from hypertrophic scar explants and NF from normal dermal biopsy explants. In experiment A, on days 1 to 4, the HF cell numbers as compared to controls were not significantly decreased except for day 5, when it was statistically significantly lower (p<0.05, Mann-Whitney, M-W, U-test) and in experiment B, the NF cell numbers were also lower and reached significance on days 4 and 5 (p<0.05, Mann-Whitney U-test). The results of experiments C and D after the cell lines were exposed to similar laser parameters but of an energy density of 4J/cm². The results of experiment C showed that HF cell numbers were lower but not significant on any of the 5 days. In experiment D, the NF cells were significantly lower on just day 5 (p<0.05, Mann-Whitney U-test). The percentage differences in cell numbers on each of the 5 days for all the experiments are presented in the legends of the charts it is objective study. The result is not included in meta-analysis and it is considered as descriptive study.

In the study of Naeim et al., [10], 30 patients (males and females) with acute post burn hypertrophic scar, aged from 20 to 45 years, are selected randomly from the out patients clinic at Faculty of Medicine, Cairo University. Patients were randomly subdivided into two groups, each group consisted of 15 patients, the first group was the study group who received He-Ne (632.8nm) laser therapy, and the second group was the control group who received routine physical therapy treatment. The treatment was applied every day after day for 8 weeks. All patients are approximately the same age, they had acute post burn scar. They have no associated disorders, pregnancy, immuno deficiency, HIV, AIDS, diabetes. Patients who had received oral retinoid within the past year, who had skin abnormalities as active skin disease within the treatment areas (i.e., psoriasis, cancer, or autoimmune disease), who had a history of photosensitivity, and had dark skin were excluded from the study. This study included in meta-analysis study as it is considered randomized controlled study.

The finding of this study indicated a considerable difference in measuring vancouver scar scale and scar thickness (by ultrasonography) between pre-treatment and post treatment within the two groups (control and experimental). Moreover, the Results of this study concerning the effect of (632.8nm-15J/cm²) for promoting hypertrophic scar in humans shows that LLLT has a beneficial effect on burn scars in human beings. In general, the scars became softer and more pliable. The irradiation gave them relief from pruritus and pain and sometimes improved the pattern of scars. The present study suggests that a planned regime of treatment with LLLT can have significant benefit for a considerable proportion of patients during their habilitation stage.

In the study of Carla et al., [11], the experimental group consisted of seven females and two males, and the placebo group consisted of six females and two males. There were no significant differences in the anthropometric measures in both the groups, 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. 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 values, 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 participants from the EG had clinically relevant improvements in pigmentation, while PG maintained all the values. This study had not mean and standard deviation so it was not included in meta-analysis.

In the study of Hamideh et al., [3], this study concluded that by using Vancouver Scar Scale (VSC) the patient responded significantly to the treatment after 4 weeks; pliability increased up to 50%, hyperpigmentation decreased by 100%; the subjective sensations including pain and itching were limited significantly to the wrist area, and the height of the keloid and hypertrophic scar diminished up to 90% in marginal area and up to 50% in central zone. This study not included in meta-analysis as it was case report.

In the study of Bin Shu et al., [12], the study showed that the irradiation group that received the power densities of 100 and 150mW/cm² showed decreases in the cell proliferation index, increases in the percentage of cells in the G0/G1 phase, and decreases in collagen synthesis and type I procollagen gene expression. The purpose of this study was to investigate the effect of high-power He-Ne laser irradiation on scar formation. It examined the relationship between the power density of the He-Ne laser, scar fibroblast growth and collagen. It explored the inhibitory effects of high-power He-Ne laser irradiation on hypertrophic scars. This study not included in these study meta-analysis.

In the study of Shunji et al., [13], this study concluded that low level laser therapy for treatment of hypertrophic scar and keloid is safe and effective method even for lesion resistant to conventional treatments of topical steroid and mechanical compression. The mechanism of laser treatment remains un clear but the authors believe that the anti-inflammatory effect of laser is the most of probable cause of regression of the lesions. Further basic studies are warranted for both low level laser and pathophysiology of hypertrophic scar and keloid scar. This study not included in meta-analysis as it was not randomized controlled trials study.

Conclusions:
The current level of evidence to support the effectiveness of low level laser therapy on hypertrophic scar post burn. Studies shows that LLLT has insignificant effect on hypertrophic scars post burn. The main limitations are the heterogeneity between included studies in meta-analysis and small number of the studies involved.

References
الملخص العربي

الهدف من البحث:
الهدف من هذه الدراسة هو تأثير الليزر منخفض الشدة على التدابير مسفرة الصنع بعد الحروق.

أسلوب البحث:
استخدام الدراسات التي تضمنت تجارب عملية تأثير الليزر منخفض الشدة على التدابير مسفرة الصنع بعد الحروق للذكور والنساء من سن 25 سنة إلى 40 سنة بمراكز المعلومات: PEDro و Cochrane و Pubmed و Pudmed و WK و AACPDM و Pedo و Cochrane. وتم مراجعة المقالات المماثلة المتعلقة بالوضوع، وتم تقييم جودة الدراسات للبحث باستخدام مقياس PEDro و Cochrane و AACPDM.

النتائج:
تضمنت هذه الدراسة:
تستعمل دراسات عملية، وتم اتخاذ دراسات في التحليل الإحصائي. وتبقي الدراسات تم تناولها بالشرح الموضوعي. أظهرت النتائج أن تأثير الليزر منخفض الشدة على التدابير مسفرة الصنع بعد الحروق مازال ضعيف.

التوصيات:
- نشر الوعي للاخصائي العلاج الطبيعي باهمية الممارسة العملية المبنية على الدليل في مجال العلاج الطبيعي بعد الحروق.
- يجب عمل التجارب التجريبيات المحكمة جيدة التصميم في المستقبل لبحث تأثير الليزر منخفض الشدة على التدابير مسفرة الصنع بعد الحروق.
- انجز المزيد من البحوث العلمية في الجوام بين تأثير الليزر منخفض الشدة ووسائل علاجية أخرى وتأثير كل منهما على التدابير مسفرة الصنع بعد الحروق.