A Systematic Review of the Effectiveness of Laser Therapy for Hypertrophic Burn Scars

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KEYWORDS

• Burn • Scar • Hypertrophic • Laser therapy • Scar management

KEY POINTS

- Hypertrophic scars are a common complication following a burn injury.
- Different lasers can be used to treat the symptomatic characteristics associated with hypertrophic scars.
- The aim of this systematic review is to assess the effectiveness of laser therapy for the treatment of hypertrophic scars resulting from a burn injury.

BACKGROUND

The World Health Organization has recognized that nonfatal burn injuries are a key contributor to morbidity.[1] The most common complication experienced by burn survivors is the development of hypertrophic scarring, with incidence rates ranging from 30% to >60%.[2,3] Hypertrophic scars occur when the normal healing process is disrupted, causing increased inflammation and excess collagen accumulation at the wound site.[4] As a result, hypertrophic scars appear thicker than normal scars and are associated with symptoms including redness, stiffness, pain, and pruritus. Over the last several decades, laser therapy has emerged as a therapeutic tool to improve the symptomatic characteristics associated with hypertrophic scars caused by serious burn injuries.[5] According to Anderson and colleagues,[5] the three main groups of lasers that can be used to improve scars include the following: (1) pulsed dye lasers (PDLs) and devices that use similar technology, (2) Q-switched Nd:YAG lasers, and (3) ablative and nonablative fractional lasers. In 2011, Vrijman and colleagues[6] conducted a systematic review that investigated the effectiveness of laser and intense pulsed light (IPL) therapy for hypertrophic scars resulting from any cause. After carrying out the review, the investigators concluded that they did not have adequate evidence to comment on the efficacy of the different lasers used. However, they noted that restricting the review to include scars from a single cause may reduce the risk of bias because response to treatment may differ among different types of scars (ie, burn, acne, surgical). Thus, the aim of this systematic review is to assess the effectiveness of laser therapy for the treatment of hypertrophic scars resulting from a burn injury.

The authors have nothing to disclose.

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METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist was used to carry out this systematic review.[7]

Objective

The objective of this systematic review is to assess the effectiveness of laser therapy for the treatment of hypertrophic burn scars.

Selection Criteria

Inclusion criteria

Peer-reviewed journal articles that were randomized controlled trials (RCTs), quasi-RCTs, observational studies, and case series $\geq$5 were considered for review. Only patients that were diagnosed with hypertrophic scars secondary to burn injuries were included. The treatment of the intervention group was limited to laser therapy only (without a co-intervention). If present, comparative control interventions consisted of another therapy or no treatment at all. Last, only studies that used objective and/or subjective scar assessment scales and/or patient/clinician-reported outcome measures were included.

Exclusion criteria

Studies that included other scar types or scars from other causes were excluded from this review unless the appropriate subgroup analysis was carried out (subgroup = hypertrophic burn scar $\geq$ 5 cases).

Search Strategy

In conjunction with the principal author, an expert medical librarian from the authors' institution developed the search strategy for this review by updating and adapting the search strategy used by Vrijman and colleagues.[6] The databases MEDLINE (1946 to December 2016), EMBASE (1947 to December 2016), CENTRAL (inception to December 2016) on the Ovid platform, and Web of Science (1900 to December 2016) were searched. Search terms included database subject headings and text words for the concepts "hypertrophic scars" and "laser therapy." When appropriate, truncation symbols were used to capture variations in the endings of the text word search terms. The search was limited to human studies only and those published in English. The reference lists of relevant studies were then hand-searched to identify additional studies.

Study Selection

After all duplicate articles were removed, two review authors (J.Z. and N.Z.) independently examined study titles and abstracts to determine which articles should be included for further review. Full-text versions of the agreed upon articles were then reviewed according to the above-mentioned selection criteria. Authors of articles with unclear selection criteria were contacted for further clarification. Disagreements between reviewers regarding study eligibility were resolved by the third author (J.F.). The overall process for study selection is depicted in **Fig. 1**.

Data Extraction

The two reviewers (J.Z. and N.Z.) used a customized data extraction form designed (E.S. Ho and colleagues, unpublished observations, 2016) that was based on the Cochrane Consumers and Communication Review Group's data extraction template.[8] Disagreements between reviewers regarding data extraction were resolved by the third author (J.F.).

Risk of Bias and Quality Assessment

Evaluation of risk of bias and methodological quality were informed by the Risk of Bias in Nonrandomised Studies of Interventions (ROBINS-I) tool, and Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines.[7,9–12] Using a template designed by Ho and colleagues, study biases were categorized as (+) low risk, (−) high risk, or (?) unclear, whereas the reporting and rigor of study quality components were evaluated as (Y) yes, (N) no, (?) unclear.

RESULTS

Selected Studies

The search strategy and hand-searched references generated 960 studies for potential inclusion in this review (refer to **Fig. 1**). After duplicate records were removed, 331 records remained. Two hundred seventy-one articles were subsequently excluded after reviewing titles and abstracts, leaving 60 articles eligible for full-text review. Twelve studies met the selection criteria and were included in this review (justifications for exclusions are detailed in **Fig. 1**).[13–24] More specifically, six studies used a pretest-posttest design in which each patient's scars were assessed before and after laser treatment,[14,18–21,23] whereas one study used a proxy pretest-posttest design in which patients were given a posttreatment questionnaire and asked to recall how they felt before receiving laser therapy.[17] In addition, five studies used a controlled clinical trial design, which included a matched untreated scar area for comparison.[13,15,16,22,24]

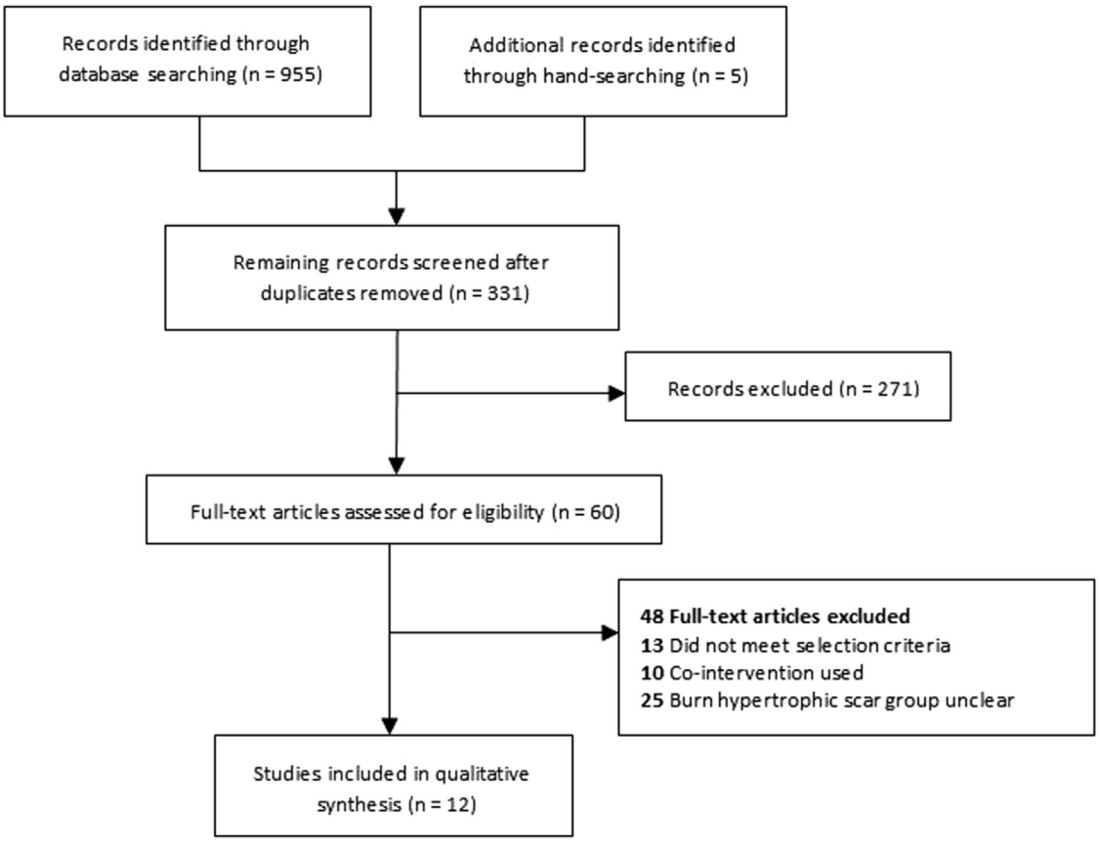

Fig. 1. Study selection process.

Study Characteristics

Details of the 12 included studies are summarized in **Table 1** including information regarding demographics, study protocol (design, treatment/control groups, duration of follow-up, outcome measures), and reported results. All studies assessed the effect of laser therapy to improve burn scars in children, adults, or both. Four different devices were used to carry out the procedures, including ablative 10,600-nm CO_2 lasers, a 585-nm PDL, a IPL device, and a 670-nm low-level laser (LLL). More than ten different outcome measures were used to evaluate the effects of treatment with high variability in duration of follow-up after laser treatment (range: 4 weeks to >1 year). Despite the many different outcome measures used, regression of burn scar symptoms was not reported in any study.

Quality and Risk of Bias Assessments

Quality and risk of bias assessments of the included studies are summarized in **Table 2**. Overall, the included studies were of low or unclear quality with a high or unclear risk of bias. More specifically, 11 of 12 studies were found to have a high risk of bias for confounding factors as well as measurement of outcomes according to the ROBINS-I assessment. As a result of these findings, the following evidence should be interpreted with caution.

Effectiveness of Laser Therapy

Ablative 10,600-nm CO_2 laser therapy

Eight of the included studies assessed the effect of 10,600-nm CO_2 laser therapy for hypertrophic burn scars.[13–20]

Vancouver Scar Scale All eight studies used the clinician-reported Vancouver Scar Scale (VSS) or a modified VSS for burn scar evaluation. All studies reported improvements in the mean total VSS score and/or VSS component scores (pliability, height, vascularity, pigmentation) with the exception of Zadkowski and colleagues,[20] who found no significant change in scar vascularity. In addition to using the clinician-reported VSS, their group also assessed scar changes using an unvalidated parent-reported VSS and obtained

Table 1
Summary table

Author	N, Gender, Mean Age, Age Range	Study Design	Intervention	Control	Follow-Up Duration (from Last Laser Session)	Outcome Measures	Results
Alster & Nanni,[21] 1998	N = 16, M/F = 15/1, NS y, 16–77 y	Pretest-Posttest	PDL, 585 nm; FS = 4.5–6.5 J/cm^2	NA	6 mo	1. Clinician + patient assessment 2. Clinician pliability assessment	1. All patients had improvements in the clinical appearance of their scars based on clinician and patient reports (*P* values not given) 2. "Significant" improvement in pliability scores (*P* values not given)
Blome-Eberwein,[13] 2016	N = 36, M/F = 20/16, 39 ± 15.6 y, NS y	Controlled clinical trial	AFCO$_2$, 10,600 nm; ES = 40–90 mJ	No therapy	4–6 wk	1. VSS 2. Pliability (cutometry) 3. Sensation (Semmes-Weinstein filaments) 4. Thickness (ultrasound) 5. Color: erythema + melanin (spectrometry) 6. POSAS (pain + pruritus)	1. Significant improvement in before-after: • Mean total VSS score (*P* = .006) • Sensation (*P* = .001). • Thickness (*P* = .001). • Erythema (*P* = .001) + Melanin (*P* = .004). 2. No significant improvements in: • Pain (*P* = .45) or pruritus (*P* = .288) • Before-after pliability R0 (*P* = .856) and R2 (*P* = .487)

Connolly et al,[14] 2014	N = 10, M/F = NS, NS y, NS y	Pretest-Posttest	$AFCO_2$, 10,600 nm; ES = 20–100 mJ	NA	2 months	1. VSS	1. Significant improvement in mean total VSS score (P = .002) 2. No significant improvement in average "erythema" score on VSS (P = .125)[a]
El-Zawahry et al,[15] 2015	N = 11, M/F = 1/10, 32.1 y, 16–58 y	Controlled clinical trial	$AFCO_2$, 10,600 nm; PS = 30 W	No therapy	3 months	1. VSS 2. POSAS	1. Significant improvement in before-after: • Mean total VSS score (P = .011) • Overall patient (P = .018) + observer POSAS scores (P = .017) 2. Significant improvement in treatment area vs control: • Mean total VSS score (P = .046) • Overall patient (P = .017) + observer POSAS scores (P = .017)
Gaida et al,[24] 2004	N = 19, M/F = 14/5, 38 ± 13.97 y, 18–77 y	Controlled clinical trial	LLLT 670 nm; FS = 4 J/cm^2	No therapy	UC	1. VSS 2. Visual Analogue Scale (pain + pruritus)	1. Improvement in before-after total VSS score (P values UC) 2. Improvement in pain + pruritus scores in treatment area (P values UC)

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Table 1
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Author	N, Gender, Mean Age, Age Range	Study Design	Intervention	Control	Follow-Up Duration (from Last Laser Session)	Outcome Measures	Results
Ghalambor & Pipelzadeh,[16] 2006	N = 320, M/F = NS, NS y, NS y	Controlled clinical trial	$AFCO_2$, 10,600 nm; PS = 4.5–9 W	No therapy	3 y	1. VSS (height + pliability) 2. Patient self-report	1. Specific VSS scores not reported. Scars <6 mo old had the best response to laser treatment in comparison to older scars (P<.001) 2. 76% of scars <6 mo old showed resolution in both pruritus and pain, in comparison to older scars (P<.001).
Hultman et al,[23] 2015	N = 20, M/F = 9/11, 35.4 y, 4–61 y	Pretest-Posttest	IPL, 560–650 nm; FS = 10–22 J/cm^2	NA	8 wk	1. Patient self-report	1. 16/20 patients had mild to significant improvement and reported 4.5/5 for efficacy and 4.4/5 for satisfaction (P values not given)

Levi,[17] 2016	N = 93, M/F = UC, UC y, UC y	Proxy Pretest-Posttest	$AFCO_2$, 10,600 nm; ES = 70–150 mJ	NA	≥2 mo	1. Patient-reported experience 2. Patient-reported pain, tightness, and pruritus 3. Short Form-36	1. Patient satisfaction with laser therapy was 96.7% (*P* values not given): • 94.6% reported improvements in scar thickness and pliability • 93.6% patients reported improvements in scar appearance 2. Significant improvements in pain, tightness, and pruritus (*P*<.0001) 3. Patients were classified within the "norm" for various health domains in Short Form-36
Ozog et al,[18] 2013	N = 10, M/F = 4/6, NS y, 20–53 y	Pretest-Posttest	$AFCO_2$, 10,600 nm; ES = 20–100 mJ	NA	2 mo	1. VSS 2. POSAS	1. Significant improvement in: • Mean total VSS score (*P* = .002) • Overall patient (*P* = .002) + observer POSAS scores (*P* = .004)
Qu et al,[19] 2012	N = 10, M/F = 5/5, 38.2 y, 24–58 y	Pretest-Posttest	$AFCO_2$, 10,600 nm; ES = 20–100 mJ	NA	2 mo	1. VSS 2. POSAS	1. Significant improvement in: • Mean total VSS score (*P* = .0002) • Overall patient (*P* = .0006) + observer POSAS scores (*P* = .00001)

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Table 1
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Author	N, Gender, Mean Age, Age Range	Study Design	Intervention	Control	Follow-Up Duration (from Last Laser Session)	Outcome Measures	Results
Sheridan et al,[22] 1997	N = 10, M/F = NS, 8.6 y, 0.5–17 y	Controlled clinical trial	PDL, 585 nm; FS = 6.75 J/cm^2	No therapy	5–58 wk	1. VSS	1. No significant improvement in any component of the VSS (*P* values not given)
Zadkowski et al,[20] 2016	N = 47, M/F = 21/26, 10.5 y, 7–16 y	Pretest-Posttest	AFCO$_2$, 10,600 nm; ES = 30–150 mJ	NA	8 mo	1. VSS (clinician + parent) 2. Thickness (ultrasound)	1. Significant improvement in: • Pigmentation component of VSS (*P*<.05) • Height component of VSS (*P*<.05) • Pliability component of VSS (*P*<.05) • Scar thickness (*P*<.05) 2. No significant improvement in vascularity component of VSS (*P*>.05)

Abbreviations: AFCO$_2$, ablative fractional carbon dioxide laser; ES, energy settings; FS, fluence settings; LLLT, low level laser therapy; NA, not applicable; NS, not specified; POSAS, Patient and Observer Scar Assessment Scale; PS, power settings; UC, unclear.

[a] VSS does not have erythema score: Assumption that the author is referring to pigmentation or vascularity.

Table 2
Quality and risk of bias assessment

	Quality				Risk of Bias (ROB)							
Author	Study Design	Inclusion + Exclusion Criteria	Hypothesis, Primary Outcome, Power Analysis	Reliable + Valid Outcome Measures	Confounding Factors	Participant Selection	Intervention Classification	Departures from Intended Intervention	Measurement of Outcomes	Attrition	Reporting	Overall Quality + ROB
Alster & Nanni,[21] 1998	No	No	No	No	–	?	?	+	–	+	–	–
Blome-Eberwein,[13] 2016	?	Yes	No	Yes	–	?	?	+	?	?	+	?
Connolly et al,[14] 2014	No	No	No	Yes	–	?	?	+	–	+	–	–
El-Zawahry et al,[15] 2015	?	Yes	No	Yes	–	?	+	+	–	–	+	?
Gaida et al,[24] 2004	?	No	No	Yes	–	?	+	+	–	+	?	?
Ghalambor & Pipelzadeh,[16] 2006	?	?	No	?	–	+	+	+	–	+	–	?
Hultman et al,[23] 2015	No	Yes	No	No	–	?	?	+	–	+	–	–
Levi,[17] 2016	No	?	No	No	–	+	?	+	–	–	?	–
Ozog et al,[18] 2013	No	No	?	Yes	–	?	?	+	–	–	+	?
Qu et al,[19] 2012	No	No	No	Yes	–	?	?	+	–	–	+	?
Sheridan et al,[22] 1997	?	?	No	Yes	–	?	+	+	–	?	?	?
Zadkowski et al,[20] 2016	No	Yes	No	?	–	?	?	+	–	+	?	?

Abbreviations: (–), high risk; (+), low risk; N, no; (?), unclear; Y, yes.

comparable results (no statistically significant differences between raters).

Patient and Observer Scar Assessment Scale The POSAS was used as an outcome measurement in 4 studies.[13,15,18,19] In all studies, statistically significant improvements in both the patient and the observer sections of the POSAS were reported after CO_2 laser treatment.

Objective assessments Blome-Eberwein and colleagues[13] used several objective scar assessment tools to evaluate the impact of CO_2 laser therapy, which included the following: (1) spectrometry to evaluate the change in scar color (measured by degree of erythema and melanin), (2) cutometry to measure scar elasticity, and (3) Semmes-Weinstein monofilaments to measure sensation in the scar.[13] Their study found significant improvements in laser-treated areas in scar color and sensation, but not in scar elasticity. In addition, both Blome-Eberwein and colleagues[13] and Zadkowski and colleagues[20] found significant improvement in scar thickness as measured by high-resolution ultrasonography following CO_2 laser treatment.

Miscellaneous assessments The Short Form-36 was used by Levi and colleagues[17] to evaluate health status among study participants. Aside from stating that participants were classified within the "norm" for various health domains, no further information or analysis was provided. In addition, their study used an unvalidated questionnaire to assess patient experience and outcomes related to scar symptoms before and after laser treatment. The questionnaire was completed by patients who were at least two months post laser treatment. Overall, 96.7% of patients were satisfied with laser treatment, and significant improvements in pain, pruritus, and scar tightness were noted. In addition, Ghalambor and Pipelzadeh[16] also used an unvalidated assessment to evaluate pain, pruritus, and vascularity following treatment with laser therapy and found younger scars (<6 months) responded better to treatment.

585-nm pulsed dye laser therapy

Two of the 12 included studies assessed the effect of 585-nm PDL therapy for hypertrophic burn scars.[21,22] In the study carried out by Alster and Nanni,[21] 2 physicians assessed scars before and after treatment using unvalidated Likert scales to evaluate clinical appearance (0 = no improvement to 3 = vast improvement) and scar pliability (0 = normal skin to 4 = banding that produces a rope of scar tissue with blanching). Study participants also used the same clinical appearance scale to rate their scars and were asked to provide information about their level of pain, pruritus, and burning sensation/tenderness at the scar site. Statistical analysis was not carried out; however, improvements in scar symptoms were reported. Conversely, Sheridan and colleagues[22] used the VSS for scar evaluation following treatment and found no significant change in any VSS component (pliability, height, vascularity, pigmentation) whatsoever.

Intense pulsed light therapy

Treatment with IPL therapy was investigated in one study.[23] Hultman and colleagues[23] used unvalidated Likert scales to assess overall improvement (1 = significantly worse to 5 = significantly improved) and patient satisfaction (1 = very unsatisfied to 5 = very satisfied) approximately 8 weeks after receiving IPL treatment. Overall, 16/20 patients reported mild to significant improvement in their scars (mean improvement score = 4.5; mean satisfaction score = 4.4).

Low-level laser therapy

The effect of LLL therapy for burn scars was investigated by Gaida and colleagues.[24] In addition to observing overall improvements in mean total VSS scores in treated areas compared with control areas, Gaida and colleagues also reported improvements in both pain and pruritus in all but one symptomatic patient using the Visual Analogue Scale.

DISCUSSION

This systematic review aimed to assess the effectiveness of laser therapy for the treatment of hypertrophic burn scars. Eleven of the 12 studies that met the selection criteria for this review reported improvements in overall scarring and/or specific scar symptoms, suggesting that laser therapy is a beneficial treatment of patients with burn scars.[13–21,23,24] Despite these positive findings, quality and risk of bias assessments revealed that all studies were of low or unclear quality with a high or unclear risk of bias. As a result, there is insufficient scientific evidence to determine the effectiveness of laser therapy for hypertrophic burn scars from this systematic review. Although some studies such as those carried out by Blome-Eberwein and colleagues[13] and El-Zawahry and colleagues[15] were more rigorous than others, quality and bias issues were found in all studies. More specifically, significant issues related to study methodology, outcome measurements, and the use laser protocols were identified during the review process.

Study Methodology

Given that there were no RCTs investigating laser therapy for hypertrophic burn scars that met the selection criteria for this review, all of the included studies used less rigorous designs. As a result, many of the studies included in this review had significant methodological problems, making it difficult to ascertain the reliability of the reported findings. First, most investigators did not provide adequate information regarding the scar assessment process, thereby introducing the potential for bias. In addition, information regarding the blinding of assessors was only provided in two studies.[13,20] Given that burn scars often appear heterogeneous (parts of the scar may be better or worse), it is crucial that the exact same area of the scar is measured before and after laser treatment. Moreover, the individual (patient and/or clinician) who is responsible for rating the scar must be blinded from previous measurements in order to prevent detection bias. Expert consensus has recommended that RCTs be carried out in order to optimize laser treatment.[5] Ultimately, the ideal study would use an RCT design in which scar assessments are carried out in a highly standardized manner to minimize bias and improve study quality. The same scarred area would be marked and photographed before and after treatment and would be evaluated by a blinded individual who is independent from the study team. In addition, statistical adjustments would be made for any confounding factors such as scar severity.

Outcome Measurements

Several issues related to outcome measurements were identified in this review, including the use of unvalidated scar assessments, a lack of objective scar assessment tools, and selective reporting. First, clinician and/or patient-reported scar assessment scales that have not been previously tested for validity and reliability in the burn patient population were used in several studies.[16,17,21,23] In the absence of appropriate psychometric validation, the authors cannot determine if these scales are able to adequately and consistently measure scar change over time. As a result, the findings from these studies are not reliable. Second, the absence of objective scar assessments in most studies must also be considered. The use of objective measures is particularly advantageous in scar research because the results can be easily quantified and cannot be skewed by patients' or clinicians' perception.[25] For example, a study carried out by Cheng and colleagues[26] compared clinician-reported VSS measurements of scar height against objective measurements taken by ultrasound and found that clinical assessment using the VSS had an accuracy rate of only 67%. Although many objective scar assessment tools currently exist, they were not used in most of the studies included in this review with the exception of Blome-Eberwein and colleagues[13] and Zadkowski and colleagues.[20] A final issue that arose in many of the included studies was the decision to only report the change in overall VSS scores as opposed to reporting each component (pigmentation, pliability, height, vascularity) separately.[13,15,18,19,24] This type of selective reporting is problematic because each scar component may respond differently to laser treatment. For example, PDLs are typically used to improve hypervascularity, whereas ablative fractional lasers are used to target scar thickness.[5,27] As a result, one would expect greater improvements in the VSS components that are specifically targeted by each laser (vascularity and height). Thus, each component must be reported separately in order to fully understand how laser therapy affects the scar.

Use of Laser Treatment Protocols

Nine of the 11 studies included in this review noted that a range of different laser settings were used to treat patients.[13,14,16–21,23] Although adjusting laser settings according to clinical opinion is appropriate for everyday practice, information regarding the exact laser settings used and how they were determined is required when carrying out a scientific study. For example, it is known that lower energy settings must be used when treating darker skin types with PDL therapy in order to prevent dyspigmenation.[28] However, information regarding how laser settings were adjusted for skin type was not provided in the included PDL studies.[21,22] Using a detailed treatment protocol is important because it ensures that the therapy is consistent for all patients and can be evaluated in a reliable manner. Moreover, it can help clinicians determine the timing and number of laser procedures required by each patient. In addition, it is essential that the person who is operating the laser is adequately trained so that treatment is delivered with a high level of integrity. Given that detailed information relating to the experience level of the laser operator was poorly detailed or not provided in most studies, it is impossible to determine if each patient received comparable interventions.

Limitations

This systematic review has several limitations that must be taken into consideration. First, by only

including English-language studies, potentially relevant articles may have been excluded. Second, because this review was limited to hypertrophic scars secondary to burn injuries, studies that also included other types of scars (keloid, surgical, and so forth) but did not distinguish them from one another in the analysis using subgroups were excluded. Last, because the intervention was limited to laser therapy only, seminal laser studies such as those carried out by Donelan and colleagues[29] and Hultman and colleagues[27] were excluded because of the use of cointerventions.

SUMMARY

Given that most of the studies included in this review were of low quality and had a high or unclear risk of bias, the authors were unable to draw definitive conclusions regarding the effectiveness of laser therapy for hypertrophic burn scars. The methodological flaws and biases that were present in the included studies highlight the need for more rigorous trials to be conducted in the future. RCTs that integrate both objective and subjective scar assessment measures will provide clinicians with the comprehensive information that is needed to strengthen the scientific evidence to support the use of laser therapy for hypertrophic burn scars.

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