

Review Article

Efficacy of high intensity laser therapy in the management of foot ulcers: a systematic review

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Abstract. [Purpose] The aim of this systematic review was to assess the efficacy of high intensity laser therapy (HILT) on wound surface area in patients with foot ulcers. [Methods] Four databases including PubMed, MEDLINE, the Cochrane library, and the Physiotherapy Evidence Database (PEDro) were searched up to the end of April 2018 to identify relevant studies. Studies were included if they met the following criteria: randomised controlled trial (RCT), assessed the efficacy of HILT in patients with foot ulcers, evaluated wound surface area, and written in English language with available full text. The PEDro scale was used to evaluate the quality of studies. [Results] A total of three RCTs met the inclusion criteria, with two studies of the efficacy of HILT in adult patients with diabetic foot ulcers and one in spina bifida children with neuropathic foot ulcers. According to the PEDro scale assessment, all three studies were rated as a fair quality. All studies found that HILT provided significantly better outcomes compared to sham laser or standard medical therapy. [Conclusion] This systematic review suggests that HILT is an effective modality for wound healing in patients with foot ulcers, but further large-scale studies are required to confirm its efficacy.

Key words: High intensity laser therapy, Foot ulcers, Diabetes

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INTRODUCTION

Foot ulcers are considered as a serious health problem and a complication frequently observed in diabetic patients¹⁾. Often patients with diabetes have lower-limb amputations preceded by foot ulceration²⁾, thus, appropriate management of foot ulcers is a priority. Annually, more than 2% of patients with diabetes develop new foot ulcers³⁾, with the costs to treat an adult male with a new foot ulcer during the two years after diagnosis estimated to be \$28 thousand⁴⁾. As there are multifactorial causes and high risk of recurrence, treating patients with foot ulcers is challenging, impacting on the health care system and community^{5, 6)}. It has been reported that ulceration is caused by multiple factors working together such as neuropathy, peripheral vascular disorders, callus, oedema, and deformity⁷⁾, therefore, proper prevention strategies and low-cost interventions are required.

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High intensity laser therapy (HILT) provided by many devices such as Nd: YAG (neodymium-doped yttrium aluminium garnet) is considered as a safe and an effective intervention modality. It has a high peak power (3 kW) and a wavelength of 1,064 nm which assists to provide its thermal, chemical and mechanical effects⁸. Many studies have reported the therapeutic effects of HILT in treating numerous musculoskeletal and some neurological disorders. It has been reported that HILT can relieve pain in patients with shoulder⁹, neck¹⁰ and lower back deriders¹¹, as well as improve the quality of life in knee osteoarthritis patients¹². In addition, some studies reported its efficacy in nerve recovery¹³, wound healing¹⁴, decreasing prostaglandin levels in blood¹⁵, bone density¹⁶ and reducing adhesions¹⁷. Although numerous studies have investigated the effects of HILT, no systematic review has been conducted to assess its efficacy on foot ulcers. Therefore, the aim of this systematic review is to evaluate the efficacy of HILT in the management of patients with foot ulcers.

METHODS

This study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under number CRD42018093849. Four databases were searched up to the end of April 2018 including PubMed, MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), and the Physiotherapy Evidence Database (PEDro). In addition, the reference lists of all included studies were searched for any further relevant studies. Search terms were determined based on the inclusion and exclusion criteria. Table 1 shows the search terms and method used in PubMed.

Studies were eligible for inclusion in this study if they met the following criteria: the design of the study must be an RCT assessing the effectiveness of HILT in patients with foot ulcers and the protocol of HILT should be clearly explained, studies must have primary outcome measure of wound surface area (WSA), and all included studies must be written in English language with available full text. Studies were excluded if they were observational and non-randomised studies or used low level laser therapy (LLLT), foot pain without ulcers, did not use wound surface area as outcome measures, were non-English language studies and without available full text.

The titles and abstracts of articles were independently screened by two researchers to assess their eligibility against the defined inclusion and exclusion criteria. When an abstract did not include sufficient data regarding the inclusion and exclusion criteria, the full text was screened. EndNote software was used to delete any possible duplicates in the search results. All RCTs that met the inclusion and exclusion criteria were carefully assessed and a standardised form was used to extract relevant data from studies that met the inclusion criteria. The risk of bias (the methodological quality) of the included studies was rated using the PEDro scale by two independent reviewers (MAA and HA). The PEDro scale has 11 items (questions yes and no), and the total score ranges between zero and ten¹⁸. The quality of the included studies was rated as low quality (score=three or less), fair quality (score=four to five) or high quality (score=six or more).

RESULTS

A total of 445 articles were identified using healthcare database searches and other sources. Following the removal of duplicate articles, 251 articles were screened by reading the titles and abstracts. Seven articles were initially eligible and after full text assessment, only three studies¹⁹⁻²¹ met the inclusion criteria, while four articles were excluded because they used low level laser therapy (LLLT). Figure 1 shows a flow diagram of the study selection process.

Table 1. Search terms and method (PubMed)

Step	Search terms and method
#1	Search randomized controlled trial [Publication Type] OR randomised controlled trial [Publication Type]
#2	Search foot ulcer [Title/Abstract] OR foot pain [Title/Abstract] OR foot wound [Title/Abstract]
#3	Search laser therapy [Title/Abstract] OR high intensity laser therapy [Title/Abstract] OR high power laser therapy [Title/Abstract] OR Nd:YAG [Title/Abstract] OR class IV laser [Title/Abstract]
#4	Search low level laser therapy [Title/Abstract]
#5	1 and 2 and 3 NOT 4

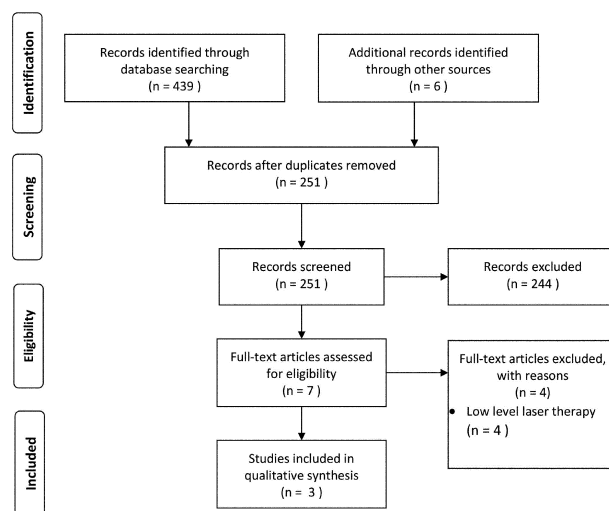


Fig. 1. Flow diagram of the study selection process.

Three studies^{19–21} with a total of 122 patients were included in this review, all of which were published during the last ten years. Two studies investigated the effect of HILT in patients with diabetic foot ulcers^{19, 20} and the third study was conducted on spina bifida children with neuropathic foot ulcers²¹. All studies assessed the efficacy of the intervention on WSA, while wound appearance (WA) was assessed in only one study²¹. All studies used HILT as the main intervention compared with sham laser in two studies^{20, 21}, while one study assessed HILT versus standard medical therapy¹⁹. In terms of the laser protocol, all studies used three phases during laser application, comprising an initial phase (manual scanning), intermediate phase (fixed points) and manual scanning (final phase). All studies used Nd-YAG laser. Table 2 summarises the main characteristics of the included studies.

As the heterogeneity was high and there were a low number of included studies, meta-analysis (quantitative) was not possible, so a qualitative synthesis of the main results was performed as shown in Table 2. When HILT was compared to placebo laser, two studies found that the combination of HILT with standard medical therapy provided better outcomes in terms of WSA^{20, 21} and WA²¹ than sham laser with standard medical therapy. Another study compared HILT alone to standard medical therapy and found that HILT was more effective ($p < 0.05$) than standard medical therapy in patients with chronic diabetic foot ulcers in terms of WSA improvement¹⁹. The quality of the included studies was assessed using the PEDro scale; all studies were rated as fair quality. All studies^{19–21} failed to meet some component of the PEDro scale involving the allocation concealment, blinding (participants, therapists or assessors) and intention to treat analysis. Table 3 demonstrates the risk of bias assessment of the included studies.

Table 2. Characteristics of included studies

Study	Population	Measured variables	Intervention	Summary of results (p value; mean \pm SD)
Ebid et al. ¹⁹	Chronic diabetic foot ulcer (n=40) Age (mean \pm SD): 58.17 \pm 9.83	WSA	Group 1 (n=20): HILT (Nd-YAG), 5 mm probe and energy density of 4 J/cm ² at a 1 cm distance from ulcer surface. P1: fast MS; P2: fixed points; P3: slow MS. 24 sessions (8 weeks), 3 days per week Group 2 (n=20): Standard medical therapy including hypoglycaemic medications such as insulin injections, systemic antibiotics, debridement, irrigation of the wound by normal saline solution, dressing, sterile gauze	HILT was more effective ($p < 0.05$) than standard medical therapy in patients with chronic diabetic foot ulcers (WSA was 0.65 \pm 0.58 for group 1 and 6.4 \pm 2.22 for group 2)
Basalamah et al. ²⁰	Chronic diabetic foot ulcer (n=43) Age (mean \pm SD): 55.14 \pm 6.52	WSA	Group 1 (n=22): HILT (Nd-YAG), 3 KW with an energy density of 510 mJ/cm ² , a wavelength of 1064 nm, probe was kept perpendicular at a 1 cm distance from the wound surface. P1: fast MS (510 mJ/cm ² , energy of 10 J/cm ² , and a total energy of 70–80 J); P2: 10 fixed points (10 J/point); P3: slow MS (510 mJ/cm ² , energy of 10 J/cm ² , and a total energy of 70–80 J), 3 sessions per week for 8 weeks, 8 mins at each treatment session Group 2 (n=21): Sham laser Both groups received standard medical treatment including good glycaemic control, adequate nutrition, off-loading (via bed rest or casts), local care (moist dressings and topical management), lessening of oedema, surgical debridement of devitalised wound tissue and antibiotic therapy	HILT group significantly ($p < 0.0001$) improved WSA (0.89 \pm 0.58 cm ²) more than placebo laser group (4.21 \pm 0.46 cm ²) after 8-weeks
Ebid et al. ²¹	Neuropathic foot ulcers in children with spina bifida (n=39) Age (mean \pm SD): 10.99 \pm 2.52	WSA & WA	Group 1 (n=19): HILT (Nd-YAG), 3 kW with an energy density of 510 mJ/cm ² , a wavelength of 1064 nm, probe was kept perpendicular at a 1 cm distance from the wound surface. P1: fast MS (510 mJ/cm ² , energy of 25 J/cm ² , and a total energy of 100–125 J); P2: 10 fixed points (10 J/point); P3: slow MS (510 mJ/cm ² , energy of 10 J/cm ² , and a total energy of 70–80 J), 3 sessions per week for 10 weeks, 10 mins at each treatment session Group 2 (n=20): Sham laser Both groups received pressure relief and protection for individuals with sensory impairment and compression therapy for persistent leg oedema, wound dressings (nonadherent gauze pads, hydrogels, hydrocolloids, and absorbent foam dressings), sharp debridement procedures (when needed), oral antibiotic therapy (when required)	The combination of HILT and standard wound care had significantly better outcomes in terms of WSA (0.29 \pm 0.25 cm ²) and WA (17.52 \pm 1.66) than the placebo group (3.24 \pm 0.44 cm ² and 38.11 \pm 3.17, respectively)

SD: standard deviation; WSA: wound surface area; WA: wound appearance; HILT: high intensity laser therapy; P: phase; MS: manual scanning.

Table 3. Risk of bias assessment of included studies

Items	Study		
	Ebid et al. ¹⁹⁾	Basalamah et al. ²⁰⁾	Ebid et al. ²¹⁾
Eligibility criteria	Yes	Yes	Yes
Random allocation	Yes	Yes	Yes
Concealed allocation	No	No	No
Baseline comparability	Yes	Yes	Yes
Blind participants	No	No	No
Blind therapists	No	No	No
Blind assessors	No	No	No
Adequate follow-up	No	Yes	Yes
Intention to treat analysis	No	No	No
Between-group comparisons	Yes	Yes	Yes
Point estimates and variability	Yes	Yes	Yes
Total score for each study	4	5	5

DISCUSSION

This review found that HILT can be considered as a safe treatment option for patients with foot ulcers. The combination of HILT and standard medical therapy significantly improved outcomes more than using sham laser with standard medical therapy in terms of WSA and WA. The risk of bias assessment indicated that all studies were rated as fair quality.

HILT is a class IV laser which has been reported to have anti-inflammatory, analgesic and wound healing effects that can assist in the management of patients with musculoskeletal disorders^{9–12, 14, 19–21}). Furthermore, laser therapy also has the ability to improve the local blood circulation, blood vessel permeability and cell metabolism²²). The results of this study are in consistent with a recent study conducted by Mahran et al.²³), who found that HILT had facilitating effects in reducing WSA in diabetic rats. According to a meta-analysis²⁴), laser therapy has beneficial healing effects such as accelerating inflammation, increasing collagen synthesis and tensile strength, reduction in healing time and decreasing wound size. Although this meta-analysis included 24 studies, they only investigated the efficacy of LLLT on wound healing.

HILT has been shown to be effective in treating patients with foot ulcers, however, there were some differences in HILT protocol (including parameters) and control treatments in the included studies, which may influence the quality of these studies. Only two^{20, 21}) out of three studies reported HILT parameters such as fluency (mJ/cm²), radiant exposure (mJ/cm²) and the total energy (J) used. In addition, these parameters were not similar between both studies (Table 2). This study has some limitations that may limit the generalisability of the results, only three available studies (with small sample size) were included and there were methodological issues (improper reporting of allocation concealment, lack of blinding of participants, therapists and assessors). This review did not include non-English language studies. In addition, heterogeneity was high, so meta-analysis was not conducted. In summary, HILT is considered as an effective modality for wound healing in patients with foot ulcers, however further high-quality studies with large sample sizes are required to confirm its efficacy.

Conflict of interest

The author declares that he has no competing interests.

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