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Lasers in Medical Science

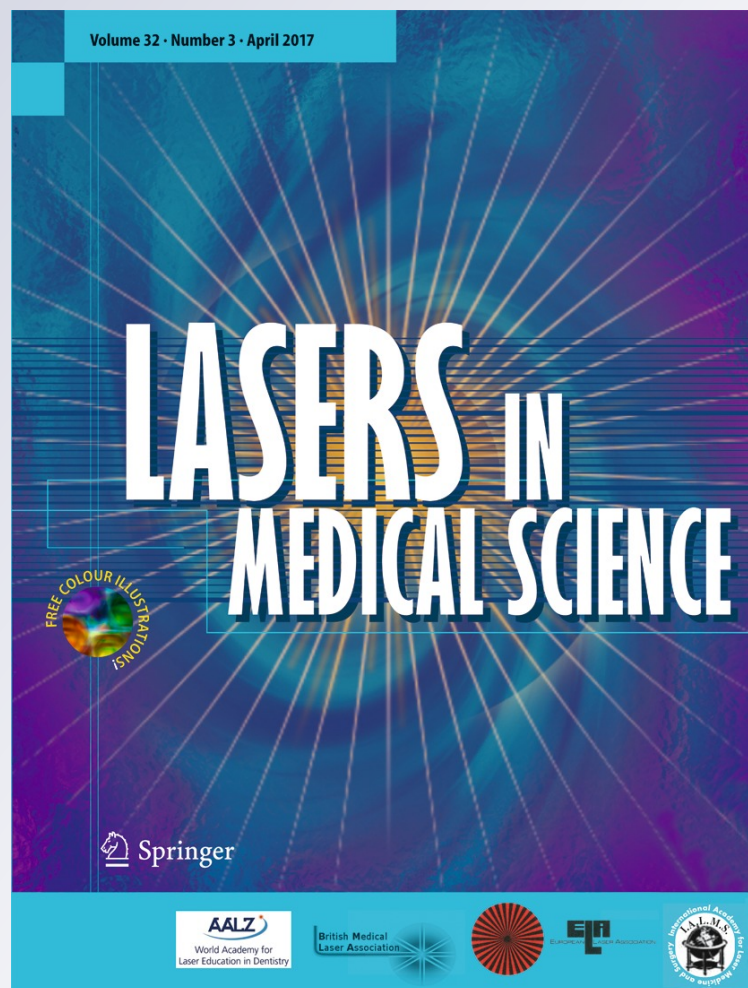
ISSN 0268-8921

Volume 32

Number 3

Lasers Med Sci (2017) 32:693-701

DOI 10.1007/s10103-017-2172-3



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Long-term effects of pulsed high-intensity laser therapy in the treatment of post-burn pruritus: a double-blind, placebo-controlled, randomized study

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Received: 28 October 2016 / Accepted: 9 February 2017 / Published online: 23 February 2017
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Abstract We assessed the long-term effects of pulsed high-intensity laser therapy (HILT) in post-burn pruritus treatment. A total of 49 adult burn patients with mean age of 31.53 ± 10.14 years participated, with 24 patients randomly assigned to the active laser group (ALG) and 25 in the placebo laser group (PLG). The ALG received HILT three times per week for 6 weeks, while the PLG received placebo HILT. Both groups received 10-mg cetirizine tablets twice daily and 10 mg at bedtime. All patients were advised to massage their burn scars with coconut oil for 5 min four times daily. The outcomes measured were the itch severity scale (ISS), impairment of pruritus-related quality of life (QoL), pain level by the visual analog scale (VAS), hand grip strength by handheld dynamometer, and daily cetirizine intake. Repeated-measures ANOVA was used to compare the baseline and post-treatment measurements and after 12 weeks of follow-up. Statistical significance was set at $P < 0.05$. ISS decreased significantly in the ALG after 6 weeks of treatment and after 12 weeks of follow-up compared with the PLG. The QoL results showed a significant improvement in the ALG compared with the PLG, which continued after 12 weeks. VAS results significantly decrease, hand grip strength significantly improved, and cetirizine intake significantly decreased post-treatment in the ALG relative to the PLG. HILT combined with cetirizine seems more effective in patients with post-burn pruritus than a placebo laser procedure with cetirizine.

Keywords Post-burn pruritus · HILT · ISS · Pain · QoL · Antihistamine

Introduction

Most burn trauma leads to persistent and severe discomfort from itching as the wounds heal, and itching continues for many months after complete wound healing [1]. Pruritus (from the Latin *prurio*, meaning “to itch”) is an aberrant sensation that leads to a desire to scratch. It is disabling and a common feature during stages of both healing and healed burn wounds. The incidence of severe itching is as high as 100% in pediatric burns and 87% in adult burn victims [2]. Pruritus impacts activities in daily living and the quality of life (QoL) of burn patients, and it becomes more intense in the evening [3]. Pruritus is also associated with a reduction in health-related QoL, impaired sleep quality, sleep disturbances, and psychological symptoms such as negative mood and depression [4].

Pruritus is classified into four categories according to the cause. Pruritogenic pruritus occurs due to inflammation, dryness, or damage of the skin, while neurogenic pruritus originates centrally without clues regarding the neurological pathology. Neuropathic pruritus includes any disease affecting any point of the afferent neurological pathway, and psychogenic pruritus is connected with mostly psychiatric conditions. The pruritus associated with burn trauma is considered to be pruritogenic, but it is increasingly considered to involve neuropathic factors in its nature and pathophysiology [5].

Similar to the pain pathway, the pathway for itching sensation engages the spinothalamic tracts and unmyelinated C fibers, and it may be related to descending modulation. Because of the congruity between the itching and pain pathways, it is possible that itching could be susceptible to treatments used

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for neuropathic pain control [6], such as transcutaneous electrical nerve stimulation (TENS) and laser treatment. Many of the affordable treatments for decreasing itching can only be used during wound healing, such as oatmeal baths, colloid, anesthetic creams, massage, doxepin cream, antihistamines, anticonvulsant drugs, gabapentin, and pregabalin [7–9]. Other interventions may include psychological counseling, relaxation techniques, behavioral modification strategies such as meditation or hypnosis, and biofeedback. Complementary therapies that may help include hydrotherapy, reflex therapy, nutritional therapy, and herbal remedies [7, 10].

Laser treatment is non-invasive, painless, very safe, and can be easily applied in primary care for a variety of conditions [11]. Laser stimulation enhances the production and release of endorphins and significantly decreases pain sensation in many conditions, such as postoperative pain, median nerve entrapment, fibromyalgia, acute and chronic osteoarthritis, post-mastectomy pain syndrome (PMPS), and shoulder pain [12, 13]. Pulsed Nd:YAG laser is a form of high-intensity laser therapy (HILT) that is used in physical therapy and rehabilitation. Many patients report significant pain reduction after using a pulsed Nd:YAG laser [14]. Studies have validated the anti-inflammatory, anti-edematous, pain relief, and analgesic effects of Nd:YAG laser [15]. Little research has been conducted to evaluate the effects of therapeutic modalities and non-pharmacological treatment on post-burn pruritus. Therefore, this study investigates the long-term effects of pulsed Nd:YAG HILT on itching according to the itch severity score (ISS), pain, QoL, antihistaminic intake, and hand grip strength in victims with post-burn pruritus.

Patients and methods

This double-blind, placebo-controlled, randomized study was carried out on adult patients in Alnour Hospital, Makkah, Saudi Arabia. Measurements were obtained at baseline (0 weeks), after 6 weeks, and after 12 weeks. The study group comprised 49 adult outpatients in the post-burn healing phase (wounds healed in 1 month or less than 1 month in the early remodeling phase) with complaints of moderate to severe itching and were randomized into either the active laser group (ALG) or placebo laser group (PLG). All of the patients were able to complete the questionnaires and received the same medical, occupational, and physical rehabilitation program during the hospitalization period. Informed consent was obtained from all individuals for participation and publication of results.

The inclusion criteria were age between 15 and 50 years old, total body surface area (TBSA) of burns >10%, deep second-degree burn on upper extremities (mainly the forearm) and wounds that are either in the healing phase (>80% of the wounds have epithelialized) or had healed completely within

1 month prior to the study period, visual analog scale (VAS) score for itching ranging from moderate to severe (VAS 6–10) [8], and the capability to complete the entire assessment questionnaire. The exclusion criteria were age less than 15 years old (due to the difficulty of assessing VAS in children), diabetes, hand deformity, skin diseases, kidney diseases, pregnancy, lactation, refusal to be part of the trial, split skin grafting, wounds taking more than 1 month to heal, and the use of other topical treatments to relieve itching.

Power analysis

Microsoft G-Power 3.1 (USA) was used for power analysis with $\alpha = 0.05$, a power of 0.90, and an expected effect size of 0.65. The results indicated that a sample size of 49 is desirable to avoid type II error. High effect size was used to obtain a sample size that would detect all major variations in the variables evaluated.

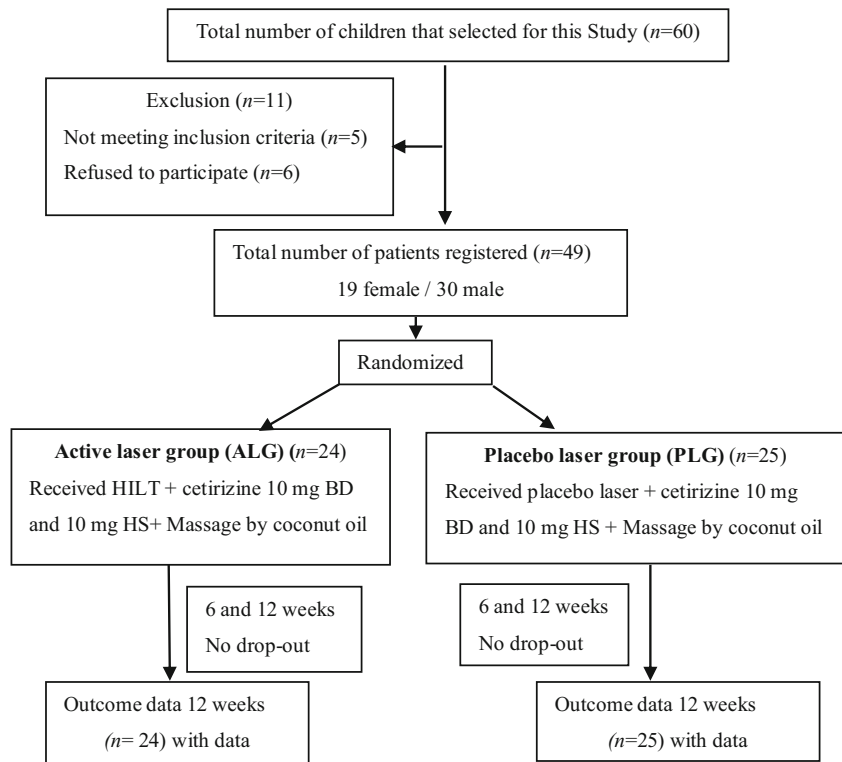
Randomization

Participants were randomized using SPSS software (IBM, Inc., USA) into the ALG, which includes 24 patients, and the PLG, which includes 25 patients. The patients and the research team were blinded to the group assignment. The ALG received HILT on the forearm and hand, while the PLG received placebo HILT on the forearm. Both groups received 10 mg of cetirizine twice daily and another 10 mg at bedtime. All participants were instructed to massage their burn scars using coconut oil for 5 min four times daily (Fig. 1). The study was ethically approved by the College of Applied Medical Science Departmental Council of Umm Al-Qura University.

Outcome measures

Itch

To evaluate the effectiveness of treatment, pruritus severity was measured by a modified version of the ISS, which is a self-reported questionnaire [16]. The modified ISS comprises 24 individual questions that cover 7 components: itch frequency, description, affected body surface area, effect on sleep, intensity, effect on mood, and effect on sexual desire/function. The net score of each component is computed by dividing the actual score by the maximum score, resulting scores ranging from 0.0 to 1.0. The total score is obtained by adding the component scores and multiplying them by 3, resulting in total scores ranging from 0 to 21.

Fig. 1 Flow diagram of the study

Quality of life

The impairment of pruritus-related quality of life (QoL) was evaluated by the modified dermatology life quality index (DLQI) [17]. Items 1, 2, and 10 were excluded, and the items measured included influence on work, social activities, and physical activities, among others. The total score ranged from 0 to 21.

Pain assessment

Pain intensity was assessed by using VAS, which is a simple, reliable, valid, and sensitive tool for measuring pain intensity. Pain intensity was evaluated using a 10-cm VAS ranging from 0 (no pain) and 10 (the worst imaginable pain). Higher scores denote greater pain intensity.

Hand grip strength

Hand grip strength was evaluated using a portable Jamar hand dynamometer (Lafayette Instrument Co., 78010 Hand Dynamometer, UK). This method is reliable for measuring handgrip strength. The evaluation was done with the patient in a sitting position in a chair with back support. The shoulder joint was adducted with 90° elbow flexion and neutral rotation of the forearm. The mean of three trials was computed, and the patient was allowed to rest for 20 s between each trial [18].

Cetirizine intake

The daily dose of cetirizine intake was evaluated in both groups at baseline, 6, and 12 weeks.

Intervention

Pulsed Nd:YAG laser therapy

Participants in the ALG and PLG received 18 treatment sessions over 6 consecutive weeks (3 sessions/week) of pulsed Nd:YAG laser (HIRO 3 machine, ASA Laser company, Italy) with a pulse emission of 1064 nm, very high peak power (3 kW), fluency/energy density of 510–1780 mJ/cm², low frequency (10–40 Hz), brief duration (120–150 μs), duty cycle of about 0.1%, probe diameter of 0.5 cm, and spot size of 0.2 cm² [19]. All participants received HILT with the handpiece in contact with and perpendicular to the treated area on the forearm and hand.

A total energy dose of 3000 J was applied in three phases. The initial phase was performed with fast manual scanning in transverse and longitudinal directions on the affected area for a total of 1300 J, and the laser fluency was divided into three successive subphases of 610, 710, and 810 mJ/cm². The intermediate phase was applied to 16 points of the itching area of the forearm and hand with 25 J each, a fluency of 610 mJ/cm², and duration of 14 s at each point for a total of 400 J. In the final phase, the HILT was applied in the same way as the

initial phase except that the scanning was done slowly with total energy of 1300 J. The total time for all phases was approximately 15 min. The energy received was calculated by the HILT device in each phase and the total energy received by the patients during the treatment session.

Outcome measures

The outcome measures were ISS, QoL, VAS, hand grip strength, and cetirizine intake.

Statistical analysis

The data were analyzed using SPSS version 22 (IBM, Inc.). The power calculations and sample size were analyzed by Microsoft G-Power 3.1. A paired *t* test was used to compare the patients' ages, percentage of burn, and duration from injury between both groups. An unpaired *t* test was used to analyze the differences in hand grip strength between groups at baseline and at 6 and 12 weeks after treatment. The group comparison of hand grip strength was done using repeated-measures analysis of variance (ANOVA). The Mann–Whitney test was used to compare the ISS, VAS, and QoL between groups at the three measurement intervals, and Friedman's test was used to compare the within-group results. For all measures, the significance was set at an alpha level of 0.05, and the data are presented as means and standard deviations (SDs).

Results

We considered 60 adult burn patients as possible participants (Fig. 1), of which 5 did not meet the study criteria and 6 declined to participate. A final total of 49 patients participated in the study, who had a mean \pm SD age of 31.53 ± 10.14 years, mean percentage of burn of $21.34 \pm 7.42\%$, mean duration from injury of 34.55 ± 3.44 days, and a mean VAS score of 7.98 ± 1.20 . The ALG (HILT + cetirizine) consisted of 24 patients, and the PLG (placebo HILT + cetirizine) consisted of 25 patients. The socio-demographic data of all participants in each group are shown in Table 1. There were no significant differences in homogeneity of variance in the subjects ages ($P = 0.5112$), percentage of burn ($P = 0.5788$), and duration from injury between participants in both groups ($P = 0.0905$) (Table 1). There were also no significant differences between participants in both groups in baseline ISS (Table 2), impairment of pruritus-related QoL, VAS, hand grip strength, and cetirizine intake (Table 3).

In comparison to the baseline values and those of the PLG, the ALG showed significantly lower post-treatment ISS scores, including the frequency, description, area, intensity, mood, effect on sexuality, sleep impairment, total area, sensory, and affective scores (Table 2). The impairment of pruritus-related QoL results showed a considerable difference and lower values in post-treatment (6 and 12 weeks) in the ALG compared with baseline values and the PLG (Table 3 and Fig. 2).

Table 1 Socio-demographic characteristics of patients at baseline

	Active laser group ($n = 24$)	Placebo laser group ($n = 25$)	<i>P</i> value	<i>t</i> value
Age (year)	30.25 \pm 12.05	32.45 \pm 11.21	0.5112 ^a	0.6620
Percentage of burn (%)	19.33 \pm 6.40	20.45 \pm 7.55	0.5788 ^a	0.5590
Duration from injury (days)	33.46 \pm 3.38	34.67 \pm 2.45	0.0905 ^a	1.728
VAS score	7.91 \pm 1.24	8.08 \pm 1.22	0.6308 ^a	0.4837
Sex	9 female/16 male	11 female/15 male		
Area affected	Upper limbs and abdomen	Upper limbs and abdomen		
Degree				
Superficial 2nd degree	7	6		
Deep 2nd degree	17	19		
Marital status				
Married	16	18		
Single	8	7		
Occupation				
Unemployed	4	3		
Employed	15	16		
Housewives	5	6		
Affected upper limb (No)				
Dominant	19	20		
Non dominant	6	5		

Values are mean \pm SD

^a There were no statistically significant differences between both groups at baseline

Table 2 Values (mean \pm SD) of ISS components and ISS total scores for both groups at baseline, 6 weeks, and after 12 weeks

Pruritus severity component		Active laser group (<i>n</i> = 24)	Placebo laser group (<i>n</i> = 25)	<i>P</i> value	<i>t</i> value
ISS1 Frequency (min: 0; max: 1)	Baseline	0.81 \pm 0.24	0.80 \pm 0.26	0.8895 ^a	0.1397
	6 weeks	0.29 \pm 0.22	0.71 \pm 0.25	<0.0001 ^b	6.233
	12 weeks	0.25 \pm 0.23	0.73 \pm 0.24	<0.0001 ^b	7.143
	<i>P</i> value	<0.0001 ^c	0.4142 ^a		
ISS2 Description (min: 0; max: 1)	Baseline	0.52 \pm 0.21	0.53 \pm 0.23	0.8746 ^a	0.1587
	6 weeks	0.22 \pm 0.19	0.48 \pm 0.22	<0.0001 ^b	4.419
	12 weeks	0.17 \pm 0.22	0.47 \pm 0.26	<0.0001 ^b	4.351
	<i>P</i> value	<0.0001 ^c	0.6338 ^a		
ISS3 Area (min: 0; max: 1)	Baseline	0.44 \pm 0.23	0.45 \pm 0.24	0.8823 ^a	0.1488
	6 weeks	0.20 \pm 0.17	0.39 \pm 0.21	0.0011 ^b	3.472
	12 weeks	0.17 \pm 0.16	0.38 \pm 0.20	0.0002 ^b	4.048
	<i>P</i> value	<0.0001 ^c	0.4720 ^a		
ISS4 Intensity (min: 0; max: 1)	Baseline	0.77 \pm 0.20	0.79 \pm 0.21	0.7345 ^a	0.3411
	6 weeks	0.25 \pm 0.22	0.73 \pm 0.24	<0.0001 ^b	7.289
	12 weeks	0.20 \pm 0.23	0.71 \pm 0.25	<0.0001 ^b	7.423
	<i>P</i> value	<0.0001 ^c	0.4570 ^a		
ISS5 Mood (min: 0; max: 1)	Baseline	0.66 \pm 0.19	0.68 \pm 0.20	0.7215 ^a	0.3586
	6 weeks	0.25 \pm 0.20	0.62 \pm 0.22	<0.0001 ^b	6.152
	12 weeks	0.20 \pm 0.22	0.59 \pm 0.26	<0.0001 ^b	5.657
	<i>P</i> value	<0.0001 ^c	0.3695 ^a		
ISS6 Effect on sexuality (min: 0; max: 1)	Baseline	0.63 \pm 0.19	0.64 \pm 0.20	0.8585 ^a	0.1793
	6 weeks	0.21 \pm 0.18	0.58 \pm 0.22	<0.0001 ^b	6.428
	12 weeks	0.16 \pm 0.17	0.59 \pm 0.19	<0.0001 ^b	8.337
	<i>P</i> value	<0.0001 ^c	0.5395 ^a		
ISS7 Sleep impairment (min: 0; max: 1)	Baseline	0.50 \pm 0.20	0.51 \pm 0.21	0.8653 ^a	0.1706
	6 weeks	0.21 \pm 0.19	0.46 \pm 0.23	0.0001 ^b	4.139
	12 weeks	0.17 \pm 0.20	0.47 \pm 0.22	<0.0001 ^b	4.988
	<i>P</i> value	<0.0001 ^c	0.6982 ^a		
ISS Total with area (min: 0; max: 21)	Baseline	12.99 \pm 2.41	13.2 \pm 2.50	0.7661 ^a	0.2992
	6 weeks	4.89 \pm 1.20	11.91 \pm 2.53	<0.0001 ^b	12.324
	12 weeks	3.96 \pm 1.75	11.88 \pm 2.59	<0.0001 ^b	12.489
	<i>P</i> value	<0.0001 ^c	0.1182 ^a		
ISS2a (sensory) (min: 0; max: 1)	Baseline	0.53 \pm 0.25	0.55 \pm 0.23	0.7719 ^a	0.2916
	6 weeks	0.22 \pm 0.24	0.50 \pm 0.22	<0.0001 ^b	4.260
	12 weeks	0.16 \pm 0.23	0.51 \pm 0.24	<0.0001 ^b	5.205
	<i>P</i> value	<0.0001 ^c	0.7197 ^a		
ISS2b (affective) (min: 0; max: 1)	Baseline	0.81 \pm 0.26	0.83 \pm 0.24	0.7807 ^a	0.2800
	6 weeks	0.24 \pm 0.23	0.77 \pm 0.22	<0.0001 ^b	8.245
	12 weeks	0.19 \pm 0.22	0.76 \pm 0.26	<0.0001 ^b	8.268
	<i>P</i> value	<0.0001 ^c	0.5412 ^a		

Significant values are shown in italic

Values are mean \pm SD

^a Non-significant difference in baseline mean values

^b Significant difference in the same measurement interval between both groups ($P < 0.05$)

^c Significant difference between the measurement intervals (baseline, 6, and 12 weeks) in both groups ($P < 0.05$)

The VAS scores decreased markedly after 6 weeks for both groups, but those of the ALG were considerably lower than

those of the PLG at 6 and 12 weeks (Table 3 and Fig. 3). Hand grip strength increased noticeably after 6 and 12 weeks of

Table 3 Values (mean \pm SD) of impairment of pruritus-related QoL, VAS hand grip strength, and cetirizine intake for both groups at baseline, 6 weeks, and after 12 weeks

		Active laser group ($n = 24$)	Placebo laser group ($n = 25$)	<i>P</i> value	<i>t</i> value
Impairment of pruritus-related QoL.	Baseline	10.3 \pm 4.9	9.5 \pm 4.8	0.566 ^a	0.577
	6 weeks	5.6 \pm 3.5	8.6 \pm 4.5	<i>0.0125</i> ^b	2.597
	12 weeks	3.1 \pm 3.4	8.2 \pm 4.2	<i><0.0001</i> ^b	4.660
	<i>P</i> value	<i><0.0001</i> ^c	0.5818 ^a		
VAS	Baseline	8.55 \pm 2.65	8.45 \pm 3.55	0.9118 ^a	0.1114
	6 weeks	3.58 \pm 3.35	7.43 \pm 3.76	<i>0.0004</i> ^b	3.779
	12 weeks	4.44 \pm 4.21	7.67 \pm 3.55	<i>0.0055</i> ^b	2.908
	<i>P</i> value	<i><0.0001</i> ^c	0.5838 ^a		
Hand grip strength	Baseline	19.88 \pm 3.15	20.21 \pm 2.44	0.6830 ^a	0.4110
	6 weeks	25.25 \pm 4.26	22.45 \pm 3.56	<i>0.0159</i> ^b	2.501
	12 weeks	26.56 \pm 3.33	22.55 \pm 3.67	<i>0.0002</i> ^b	4.000
	<i>P</i> value	<i><0.0001</i> ^c	0.0208 ^c		
Cetirizine intake (mg/day)	1st to 3rd week	30 mg (BD + HS)	30 mg (BD + HS)		
	4th to 6th week	20 mg (OD + HS)	30 mg (BD + HS)		
	7th to 12th week	20 mg (OD + HS)	30 mg (BD + HS)		

VAS visual analog scale (score:0–10) measures the intensity of pain (a higher were indicated higher pain intensity)

Significant values are shown in italic

OD once daily, BD twice daily, HS at bedtime

^a Non-significant difference in baseline mean values

^b Significant difference in the same measurement interval between both groups ($P < 0.05$)

^c Significant difference between the measurement intervals (baseline, 6, and 12 weeks) in both groups ($P < 0.05$)

follow-up for both groups, but the significance was higher in the ALG than the PLG (Table 2 and Fig. 4). The participants in the ALG showed a considerable decrease in daily cetirizine dose after 6 and 12 weeks in comparison with the PLG (Table 3 and Fig. 5). Our results indicate that pulsed Nd:YAG laser therapy decreases ISS score, improves QoL, and decreases pain and cetirizine intake compared with placebo laser treatment.

Discussion

The main outcome of this study is that pulsed HILT decreases ISS score, pain, and antihistamine intake, while it improves QoL and increases grip strength in adult patients with post-burn pruritus. Furthermore, the advantage is maintained after the discontinuance of the HILT application for up to 12 weeks. This randomized controlled study is the first trial to assess the QoL in burn patients with post-burn pruritus treated by HILT therapy using a QoL questionnaire. The results indicate that moderate to severe post-burn pruritus (VAS score 6–10) can be effectively controlled for a long period by HILT, antihistamine, and massage, but a complete cure may be attained by centrally mediated drugs or combination of pharmacological and non-pharmacological agents.

Most single agents used for the treatment of post-burn pruritus are most likely to be ineffective for complete remission of post-burn itching, so combinations of treatments are needed for relief in a majority of post-burn pruritus patients [1, 20]. Currently, antihistamines are prescribed as a standard routine therapy for post-burn pruritus, but they never provide full relief on their own for patients with moderate to severe post-burn itch. Such patients produce excessive histamine, and antihistamines do not act by desensitizing or inhibiting the itch receptors, so sufficient relief from itching is not attained [9]. Massage is used as a supplementary treatment for all post-burn antipruritic

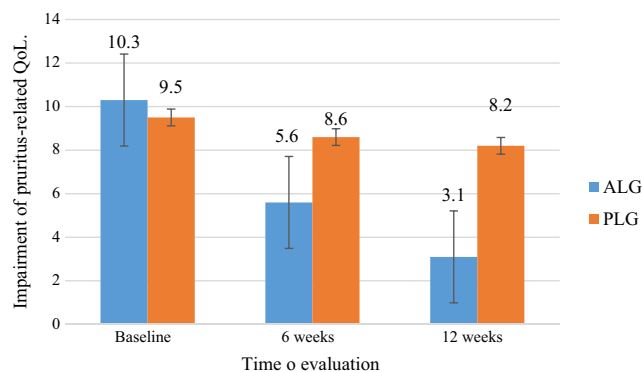


Fig. 2 Mean values of impairment of pruritus-related QoL for both groups

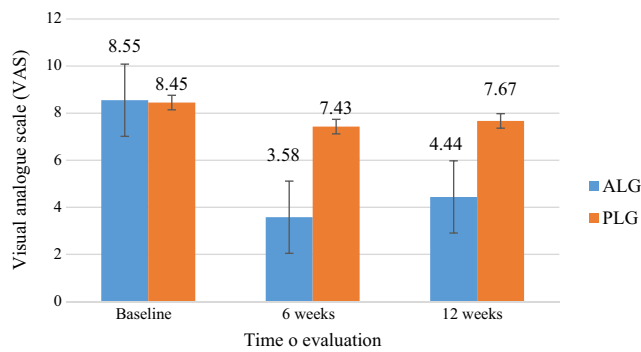


Fig. 3 Mean values of VAS score for both groups

therapy. When used alone, there is a significant improvement for mild to moderate itching, but results are unsatisfactory for severe itching [9]. Thus, we used coconut oil massage as an adjunct to HILT and antihistamine in our protocol.

Low-intensity laser therapy is effective for severe pruritus during the process of healing after burn injury, and the improvements remained at 6 and 12 months after treatment. The symptomatic relief might be due to the beneficial effects of the laser on microcirculation and the pruritogenic chemicals found in scar tissue [21]. Vashghani et al. applied low-level laser therapy in rats with second-degree cutaneous burns during the inflammatory and proliferative phases of healing. The treatment significantly increased the number of intact mast cells, but laser application during the remodeling phase decreased the total number of mast cells. These results may have considerable significance for the treatment of wound healing in humans, as well as for reducing the composition of immoderate fibrotic tissue in keloids and scars [22].

Laser therapy provides direct biostimulative light energy to the body's cells and enhances anti-inflammatory action [23]. The anti-inflammatory effect results from decreased levels of pro-inflammatory cytokines such as interleukin-1 alpha (IL-1 α) and IL-1 beta (IL-1 β), as well as increased levels of anti-inflammatory cytokines and growth factors. It also reduces swelling produced by inflammation and encourages nerve regeneration and immunological processes [24].

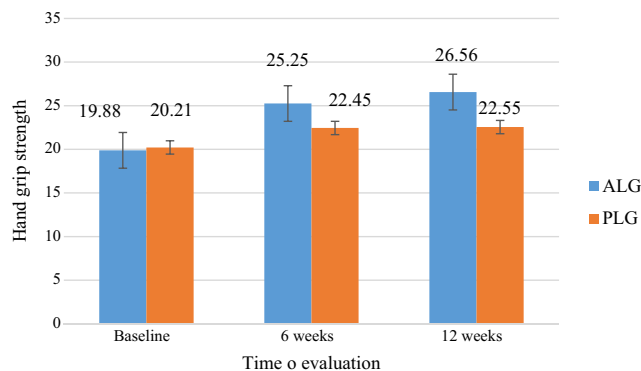


Fig. 4 Mean values of hand grip strength for both groups

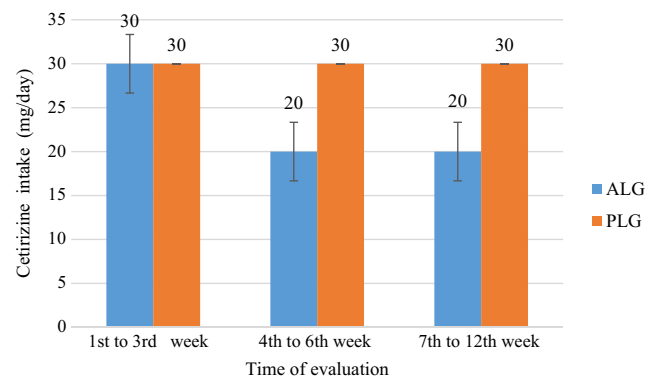


Fig. 5 Mean values of cetirizine intake for both groups

Laser treatment inhibits the release of cyclooxygenase (Cox) 2, prostaglandins, and cytokine levels, and it accelerates collagen synthesis and cell proliferation. It also decreases pain levels, improves tissue repair, and inhibits A δ and C fiber transmission due to its effect on nerve structures and functional disability [15, 25–27]. Recently, pulsed HILT has been used for a broad range of conditions and has been proven in the treatment of many musculoskeletal diseases, including wound repair in diabetic and neuropathic foot ulcers [28], anti-edematous treatment, shoulder pain, knee arthritis [29, 30], PMPS [12], chronic ankle pain, and low back pain [15, 31].

The effectiveness of laser treatment depends on many factors, such as the treatment dose, wavelength, duration, depth, and site of target tissue. Some preliminary studies indicate that HILT is more potent than low-level laser therapy (LLLT) due to its higher intensity and the greater depth reached by the laser [19, 29]. Studies conducted on the profile of dose response of laser therapy suggest that the particular penetration abilities through human skin depend on the different wavelengths used [32].

The wavelength in HILT ranges from the visible to the infrared range of the light spectrum, which can cause stimulation as well as inhibition of different organisms [33]. High-power pulsed Nd:YAG laser works using a specific wavelength (1046 nm) and high peak power (3 kW) with ordinary peaks of elevated amplitude values and low duty cycle. HILT is deemed a non-invasive regenerative therapy that is non-painful and non-invasive, and it quickly reduces pain symptoms and inflammation [19, 29]. The analgesic effect of HILT on pain is based on different mechanisms of action, including an ability to decrease or block the transmission of the pain stimulus and to increase the output of morphine-mimetic substances in the body [19].

Assessing QoL in burn patients is very important since the condition might affect the treatment amenability and cause poor overall QoL. QoL measurements have been widely recognized in clinical practice and research, and many QoL questionnaires have been developed [34]. Our study confirmed that there should be more consciousness among healthcare providers regarding the need to evaluate QoL in post-burn pruritus, which may assist in medical treatment and diagnosis. A

few studies correlate the relation between QoL and laser application, which comparisons are difficult. Ebid et al. [12] evaluated the long-term influence of HILT therapy on QoL in PMPS patients and observed an upward trend in QoL, decreased pain, and improved range of motion. Wong et al. [35] noticed an improvement in patient QoL after LLLT, and another study showed that overall QoL was enhanced in patients suffering from oral mucositis and pain during LLLT and after [36].

Our results agree with the outcomes of many studies indicating that active laser therapy has a better effect than placebo laser on curing disability, relieving pain, and improving QoL according to VAS and QoL questionnaire results [12, 13]. In this study, the effect of combined HILT with antihistamine was greater than that of placebo HILT with antihistamine. Most physicians report that placebo treatment is ethically permissible and an important tool that can be used by the medical community to complement regular therapies [37], but it remains controversial in medical practice [38]. Post-burn itching is considered to compromise patients' QoL, physical activity, and social wellbeing. The present study indicates that HILT with antihistamine and massage are clinically able to decrease itching, relieve pain, improve QoL, and improve hand grip strength, and these positive effects last for up to 3 months.

Conclusion

Pulsed Nd:YAG laser is a potent physiotherapy modality that provides better outcomes for post-burn pruritus. Its effect lasts for a longer period after treatment than placebo laser in terms of decreased ISS score, pain level, antihistamine intake, along with improved QoL, and increased hand grip strength for up to 12 weeks post-treatment.

Acknowledgements We would like to thank all the study participants and team members in the burn unit, as well as the physiotherapy staff and outpatient clinic for general and technical support.

Compliance with ethical standards

Funding There was no funding source.

Conflict of interest The authors declare that they have no conflict of interest.

References

- Vitale M, Fields-Blache C, Luterman A (1991) Severe itching in the patient with burns. *J Burn Care Rehabil* 12:330–333
- O'Donoghue M, Tharp MD (2005) Antihistamines and their role as antipruritics. *Dermatol Ther* 18:333–340
- Goutos I (2010) Burns pruritus—a study of current practices in the UK. *Burns* 36:42–48
- Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL (2000) The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. *Br J Dermatol* 143:969–973
- Twycross R, Greaves MW, Handwerker H, Jones EA, Libretto SE, Szepietowski JC, Zyllicz Z (2003) Itch: scratching more than the surface. *QJM* 96:7–26
- Wheeler DS, Vaux KK, Dan T (2000) Use of gabapentin in the treatment of childhood reflex sympathetic dystrophy. *Pediatr Neurol* 22(3):220–221
- Bell PL, Gabriel V (2009) Evidence based review for the treatment of post-burn pruritus. *J Burn Care Res* January/February. 55–61, doi: 10.1097/BCR.0b013e318191fd95.
- Rajeev BA, Rajat G, Gaurav G, Prabhat S (2011) A comparative analysis of cetirizine, gabapentin and their combination in the relief of post-burn pruritus. *Burns* 37:203–207
- Ahuja RB, Gaurav K (2013) Gupta. A four arm, double blind, randomized and placebo controlled study of pregabalin in the management of post-burn pruritus. *Burns* 39:24–29
- Yosipovitch G (2005) How to treat that nasty itch. *Exp Dermatol* 14(6):478–479
- Brown AW, Weber DC (2000) Physical agent modalities. In: Braddom RL (ed) *Physical medicine and rehabilitation*. WB Saunders, Harcourt Health Sciences Company, London, pp 440–458
- Ebid AA, El-Sodany AM (2015) Long-term effect of pulsed high-intensity laser therapy in the treatment of post-mastectomy pain syndrome: a double blind, placebo-control, randomized study. *Lasers Med Sci* 8:29–35. doi:10.1007/s10103-015-1780-z
- Gur A, Karakoc M, Nas K, Cevik R, Sarac J, Demir E (2002) Efficacy of low power laser therapy in fibromyalgia: a single-blind, placebo-controlled trial. *Lasers Med Sci* 17(1):57–61. doi:10.1007/s101030200010
- Santamato A, Solfrizzi V, Panza F, Tondi G, Frisardi V, Leggin BG, Ranieri M, Fiore P (2009) Short-term effects of high-intensity laser therapy versus ultrasound therapy in the treatment of people with subacromial impingement syndrome: a randomized clinical trial. *Phys Ther* 89(7):643–652
- Saggini R, Bellomo RG, Cancelli F (2009) Hilterapia and chronic ankle pain syndromes. Abstract from Energy for Health; International journal of information and scientific culture 3(3):22–25:38.
- Majeski CJ, Johnson JA, Davison SN (2007) Itch Severity Scale: a self-report instrument for the measurement of pruritus severity. *Br J Dermatol* 156:667–673
- Zachariae R, Zachariae C, Ibsen H, Mortensen JT, Wulf HC (2000) Dermatology life quality index: data from Danish inpatients and outpatients. *Acta Derm Venereol* 80:272–276
- Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S (1985) Grip and pinch strength: normative data for adults. *Arch Phys Med Rehabil* 66:69
- Zati A, Valent A (2006) Physical therapy: new technologies in rehabilitation medicine (translated to English). Edizioni Minerva Medica, pp 162–185.
- Goutos I, Eldardiri M, Khan AA, Dziewulski P, Richardson PM (2010) Comparative evaluation of anti-pruritic protocols in acute burns. The emerging value of gabapentin in the treatment of burns pruritus. *J Burn Care Res* 31:57–63
- Allison KP, Kiernan MN, Waters RA, Clement RM (2003) Pulsed dye laser treatment of burn scars. Alleviation or irritation? *Burns* 29: 207–213
- Vasheghani MM, Bayat M, Rezaei F, Bayat A, Karimipour M (2008) Effect of low-level laser therapy on mast cells in second-degree burns in rats. *Photomed Laser Surg* 26(1):1–5. doi:10.1089/pho
- Arora H, Pai KM, Maiya A, Vidyasagar M, Rajeev A (2008) Efficacy of He-Ne Laser in the prevention and treatment of radiotherapy-induced oral mucositis in oral cancer patients. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 105(2):180–186

24. Peplow PV, Chung TY, Baxter GD (2010) Application of low level laser technologies for pain relief and wound healing: overview of scientific bases. *Phys Ther Rev* 15(4):253–285
25. Gur A, Karakoc M, Cevik R, Nas K, Sarac AJ, Karakoc M (2003) Efficacy of low power laser therapy and exercise on pain and functions in chronic low back pain. *Lasers Surg Med* 32(3):233–238
26. Chow R, Armati P, Laakso EL, Bjordal JM, Baxter GD (2011) Inhibitory effects of laser irradiation on peripheral mammalian nerves and relevance to analgesic effects: a systematic review. *Photomed Laser Surg* 29(6):365–381
27. Lim W, Lee S, Kim I, Chung M, Kim M, Lim H, Park J, Kim O, Choi H (2007) The anti-inflammatory mechanism of 635 nm lightemitting-diode irradiation compared with existing COX inhibitors. *Lasers Surg Med* 39(7):614–621
28. Ebid AA, El-Kafy EM, Alayat MS (2013) Effect of pulsed Nd:YAG laser in the treatment of neuropathic foot ulcers in children with spina bifida: a randomized controlled study. *Photomed Laser Surg* 31(12):565–570. doi:10.1089/pho.2013.3533
29. Zati A, Fortuna D, Benedetti E, Zaghini I, Bigotta TW (2006) HILT Therapy in the treatment of knee osteoarthritis: the first clinical cases and protocol for a multicenter double-blind randomized trial. Proceedings 1st National Conference Dominate Energy, Scientific Report.
30. Stiglić-Rogoznica N, Stamenković D, Frlan-Vrgoc L, Avancini-Dobrović V, Vrbanić TS (2011) Analgesic effect of high intensity laser therapy in knee osteoarthritis. *Coll Antropol* 35(2):183–185
31. Fiore P, Panza F, Cassatella G, Russo A, Frisardi V, Solfrizzi V, Ranieri M, Di Teo L, Santamato A (2011) Short-term effects of high-intensity laser therapy versus ultrasound therapy in the treatment of low back pain: a randomized controlled trial. *Eur J Phys Rehabil Med* 47(3):367–373
32. Nussbaum EL, Van Zuylen J (2007) Transmission of light through human skinfolds: effects of physical characteristics, irradiation wavelength and skin-diode coupling relevant to phototherapy. *Physiother Can* 59:194–207
33. Schaffer M, Sroka R, Fuchs C, Schrader-Reichardt U, Schaffer PM, Busch M, Diihmke E (1997) Biomodulative effects induced by 805nm laser light irradiation of normal and tumor cells. *J Photochem Photobiol B Biol* 40:253–257
34. Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R (2002) Quality of life measurement: bibliographic study of patient assessed health outcome measures. *BMJ (Clin Res Ed)* 324(7351):1417
35. Wong S-F, Wilder-Smith P (2002) Pilot study of laser effects on oral mucositis in patients receiving chemotherapy. *Cancer J* 8(3):247–254
36. Simoes A, Eduardo FP, Luiz AC, Campos L, Sa PH, Cristofaro M, Marques MM, Eduardo CP (2009) Laser phototherapy as topical prophylaxis against head and neck cancer radiotherapy-induced oral mucositis: comparison between low and high/lowpower lasers. *Lasers Surg Med* 41(4):264–270. doi:10.1002/lsm.20758
37. Tilburt JC, Emanuel EJ, Kaptchuk TJ, Curlin FA, Miller FG (2008) Prescribing “placebo treatments”: results of national survey of US internists and rheumatologists. *BMJ* 337:a1938
38. Miller FG, Colloca L (2009) The legitimacy of placebo treatments in clinical practice: evidence and ethics. *Am J Bioethics* 9:39–47