J Acupunct Meridian Stud 2015;8(1):2—16

Available online at www.sciencedirect.com

Journal of Acupuncture and Meridian Studies

journal homepage: www.jams-kpi.com

REVIEW ARTICLE

Laser Acupuncture for Treating Musculoskeletal Pain: A Systematic Review with Meta-analysis

Dina Law [1,*], Suzanne McDonough [2], Chris Bleakley [2], George David Baxter [1], Steve Tumilty [1]

[1] *Centre for Health, Activity and Rehabilitation Research, School of Physiotherapy, University of Otago, Dunedin, New Zealand*
[2] *Centre for Health, Activity and Rehabilitation Technologies, University of Ulster, Londonderry, UK*

Available online 10 July 2014

Received: Jan 13, 2014
Revised: Jun 18, 2014
Accepted: Jun 25, 2014

KEYWORDS
acupuncture therapy;
low-level laser therapy;
pain;
review

Abstract
Laser acupuncture has been studied extensively over several decades to establish evidence-based clinical practice. This systematic review aims to evaluate the effects of laser acupuncture on pain and functional outcomes when it is used to treat musculoskeletal disorders and to update existing evidence with data from recent randomized controlled trials (RCTs). A computer-based literature search of the databases MEDLINE, AMED, EMBASE, CINAHL, SPORTSDiscus, Cochrane Library, PubMed, Current Contents Connect, Web of Science, and SCOPUS was used to identify RCTs comparing between laser acupuncture and control interventions. A meta-analysis was performed by calculating the standardized mean differences and 95% confidence intervals, to evaluate the effect of laser acupuncture on pain and functional outcomes. Included studies were assessed in terms of their methodological quality and appropriateness of laser parameters. Forty-nine RCTs met the inclusion criteria. Two-thirds (31/49) of these studies reported positive effects, were of high methodological quality, and reported the dosage adequately. Negative or inconclusive studies commonly failed to demonstrate these features. For all diagnostic subgroups, positive effects for both pain and functional outcomes were more consistently seen at long-term follow-up rather than immediately after treatment. Moderate-quality evidence supports the effectiveness of laser acupuncture in managing

* Corresponding author. Centre for Health, Activity and Rehabilitation Research, School of Physiotherapy, University of Otago, PO Box 56, Dunedin 9054, New Zealand.
E-mail: dinalawnp@gmail.com (D. Law).

pISSN 2005-2901 eISSN 2093-8152
http://dx.doi.org/10.1016/j.jams.2014.06.015

musculoskeletal pain when applied in an appropriate treatment dosage; however, the positive effects are seen only at long-term follow-up and not immediately after the cessation of treatment.

1. Introduction

Musculoskeletal disorders represent a significant cost to the health care system [1]. A recent report estimated that 1.7 billion individuals globally are affected by various kinds of musculoskeletal problems, and highlighted the considerable impact of chronic pain and disabilities upon individuals [2]. Coupled with the increasing risk factors such as obesity, sedentary lifestyles, and aging populations in the modern world [3,4], increasing prevalence of musculoskeletal disorders is foreseeable, exacerbating the health care burden.

Recent research confirms that treatments such as physical therapy, acupuncture, and massage remain popular with pain sufferers. A survey conducted in 16 European countries showed that 70% of participants who suffered from musculoskeletal pain sought other forms of treatment apart from medication [5]. Acupuncture is one of the most common types of alternative treatments for patients looking for long-term pain management [6], which is a relatively safe procedure with minimal side effects. Growing demand for, and provision of, acupuncture services have been seen in different countries [5,7,8], resulting an interest in, and rapid development of, acupuncture research in order to establish a more solid evidence-based practice [9].

Such research development extends to other forms of acupuncture apart from the traditional needling method. The use of low-level laser to stimulate acupuncture points is suggested to be a safer technique due to its noninvasive nature and its acceptability to people with needle phobia [10]. Laser acupuncture is considered to be an effective alternative to traditional needling, is useful in patients who are needle phobic, or can be used at acupuncture points that require complicated application of the needle [10,11].

Ever since laser acupuncture studies were conducted in the 1970s [12,13], researchers have focused on the underlying mechanism of laser acupuncture to build the scientific basis for clinical practice. Controversy remains concerning the mechanisms of laser acupuncture, which, being free from any mechanical stimulation, do not share similar pain modulation pathways to those of traditional needling acupuncture [10]. Rather than producing a "needling sensation," the acupuncture point irradiated by the laser needs to receive sufficient energy to elicit the physiological effect at the cellular level, based upon the wider principle of "photobiomodulation" [14—16]. A key point to determine the effectiveness of laser acupuncture is the dosage applied: this issue has been stressed in several recent papers [16,17]. The development of dosage guidelines for laser acupuncture is confounded by the lack of a clear understanding of the mechanisms underpinning such treatment, as dosage dependency is normally explored during the stage of *in vitro* and animal studies [10]. At present, the World Association for Laser Therapy guidelines for low-level laser therapy published in 2010 provide recommendations for general laser treatment for different conditions only; no specific guidelines have been developed for laser acupuncture [18,19]. Hence, selection of laser parameters and dosage is often subjective or based on clinical experience. Studies may involve the use of an inappropriate dosage or report the parameters inadequately; hence, the results of these studies would be difficult to replicate or provide data to formulate the most efficacious dose [20—22].

More recent evidence supports the physiological effects of laser acupuncture, including anti-inflammatory [23] and antinociceptive effects [24]. Such studies highlight the potential effect of laser acupuncture under well-controlled conditions; however, whether or not these results can be extrapolated to the clinical setting remains unclear. It is critically important to understand the relevance of laser irradiation parameters, together with the appropriate selection of acupoints, to the effectiveness of laser acupuncture for musculoskeletal conditions.

Despite the growth of evidence in the field of laser acupuncture, its effectiveness for musculoskeletal condition remains unclear because of inconclusive results from different studies [14,20,22]. This expansion may suggest a shift in the evidence base; therefore, it is timely to review the results from recent studies to confirm the current evidence base for laser acupuncture. A systematic review with meta-analysis was, therefore, conducted to update the previous review in this area [17], with the following aims: (a) to assess the clinical effectiveness of laser acupuncture for relieving pain and improving functional outcomes when used for treating musculoskeletal conditions; (b) to explore the relationship between parameter choice and outcomes; and (c) to establish the level of evidence of the effectiveness of laser acupuncture with an update of the current literature.

2. Methods

2.1. Protocol and registration

This systematic review was conducted and reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline [25]; a pre-registered protocol was not used.

2.2. Selection criteria

Studies included for this review had to meet the following criteria.

2.2.1. Types of studies

Randomized controlled trials (RCTs) and controlled clinical trials published in peer-reviewed journals were included. In addition, studies published in databases since their inception to March 1, 2013 were included, in order not to miss any records and to update the findings of our previous systematic review [17] by the inclusion of more current publications. Due to resource limitations, this review excluded non-English-language publications.

2.2.2. Types of participants

Human participants with musculoskeletal diseases or injuries, and presenting with pain were included. Those with systemic illness and headache were not included. There were no restrictions based on age, gender, or physical activity status.

2.2.3. Types of intervention

Studies evaluating laser acupuncture as the primary intervention were included. Such intervention needed to include application of active low-level laser therapy to traditional Chinese medicine acupuncture points, trigger points, or tender points. Studies involving a primary intervention using needling or other forms of stimulation on acupuncture points, or those involving application of laser therapy to nonacupuncture points were not considered. In addition, those studies were included that compared laser acupuncture with one of the following as a control intervention: placebo or sham laser, no treatment, or other treatments, such as medication, exercise therapy, or other electrotherapy modalities.

2.2.4. Types of outcome measures

These studies included those that assessed pain or function using at least one of the following as primary outcomes: pain level (visual analog scale), global assessment of participants' improvement (subjective improvement, proportion of objective measures improvement, overall improvement), or a functional outcome measure (validated questionnaire or functional scale specific to the presenting condition).

2.2.5. Length of follow-up

No restriction was applied to the length of follow-up.

2.3. Search strategy

Studies were identified by an electronic search of the following databases: MEDLINE (from 1946 to March 1, 2013), AMED (from 1985 to March 1, 2013), EMBASE (from 1947 to March 1, 2013), CINAHL (from 1981 to March 1, 2013), SPORTSDiscus (from 1960 to March 1, 2013), Cochrane Library, PubMed (from 1950 to March 1, 2013), Current Contents Connect (from 1998 to March 1, 2013), Web of Science (from 1900 to March 1, 2013), and SCOPUS (from 1960 to March 1, 2013). The same search strategy was used in subject-based databases, as shown in Appendix 1. In addition, Google Scholar (from January 1, 2013 to March 1, 2013), Physiotherapy Evidence Database (PEDro; from 1966 to March 1, 2013), and two key journals (*Lasers in Surgery and Medicine*, from 2005 to March 1, 2013; and *Photomedicine and Laser Surgery*, from 2005 to March 1, 2013) were searched manually to cover recent studies, which may have not been included in other databases. Two independent reviewers ran the search independently on March 1, 2013.

2.4. Selection of studies

Two independent reviewers assessed the eligibility of all studies independently by screening the titles and abstracts with the above selection criteria. Full-text articles were retrieved if there was any uncertainty. When there was a disagreement between the two reviewers, the study was reassessed using the selection criteria as a basis for consideration of its eligibility until consensus was achieved. Relevant studies were retrieved as full-text articles, either from the databases or from the study authors, for final assessment of inclusion or exclusion. Reference lists of retrieved articles were checked for any missing relevant articles.

2.5. Assessment of methodological quality

All included studies were assessed for methodological quality using the PEDro scale [26]. Two reviewers performed the assessment independently in a standardized manner; they were not blinded to the details of the studies. Disagreements between reviewers were resolved by consensus, and a third reviewer was consulted if disagreements persisted. Methodological qualities of the included studies were rated from 1 to 10 on a 10-item PEDro scale. All included studies were also assessed for their level of risk of bias by two independent reviewers. The risk of bias assessment helps identify any major methodological flaws from different domains of the included studies [27]. Further subgroup analyses related to bias assessment were planned where appropriate.

2.6. Data extraction

Two independent reviewers extracted data from included studies. Disagreements were resolved by discussion; if no agreement could be reached, a third reviewer was available for cross-referral.

Data were extracted from each included trial on: study population; details of interventions; types of outcome measures; and laser acupuncture dosage (including parameters recommended by the World Association for Laser Therapy [28] or calculation of missing data if possible).

2.7. Outcome measures

Data from included studies were pooled for further meta-analysis where appropriate. If available, means and standard deviations for outcome measures were extracted or calculated using published relevant data with Review Manager (RevMan) software, version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012 [29]. Unpublished data were not sought from authors because of time limitations. Data were categorized and analyzed based on the following parameters, (1) Pain score—using a visual analogue scale and expressing the raw score on a 0—10 scale. Change in scores (difference between various time points in a study) were also considered but grouped separately. (2) Pressure pain threshold—algometric measurement expressed in kg/cm^2. (3) Functional score—using validated functional scales, measuring grip strength, or comparing the difference in functional scores prior to and after the intervention.

2.8. Statistical analysis

Dichotomous outcomes were expressed as relative risks, and continuous outcomes were expressed as the standardized mean difference (SMD); both were presented with 95% confident intervals [27]. A negative SMD was defined to indicate favorable effects of laser acupuncture to the control intervention and vice versa. Magnitudes of the overall effect size were classified as small (0.2–0.5), moderate (0.5–0.8), and large (>0.8) according the value of SMD using the Cohen's categories [30]. Qualitative analysis was performed if studies failed to provide data to be pooled for analysis. Studies were assessed for heterogeneity using the Chi-square test to decide whether a random or fixed effect model was used; Chi-square test with a $p \geq 0.05$ indicates a significant heterogeneity [27]. I^2 value quantifies the degree of heterogeneity: moderate ($I^2 > 30\%$), substantial ($I^2 > 50\%$), and considerable ($I^2 > 75\%$) [27].

2.9. Subgroup and sensitivity analyses

Subgroup analyses were conducted to evaluate the following overall effects: (1) diagnosis; (2) control intervention; (3) follow-up period—measures taken immediately at the end of the intervention (short-term effect) or from 6 weeks to 26 weeks postrandomization (long-term effect); and (4) site of laser acupuncture application—acupuncture point, trigger point, or tender point.

Sensitivity analyses were conducted for testing the robustness of the pooled effect size. Effects were examined according to risk of bias, to ensure that the analysis was not biased by any study with a large number of methodological flaws.

2.10. Risk of bias across studies

The risk of publication bias was assessed by analyzing the symmetry of the funnel plots generated by RevMan (The Cochrane Collaboration). Symmetrical funnel plots represented lower risk of bias, whereas higher risk of bias was demonstrated by increased asymmetry [31].

2.11. Quality of evidence

The Grading of Recommendations Assessment, Development, and Evaluation approach was used to judge and categorize the quality of evidence for the primary outcomes [32]. This reflects the extent of confidence of the estimated effects by considering the study design and other confounding factors that may affect the judgment. The following quality grades used were used. (1) High quality: "We are very confident that the true effect lies close to that of the estimate of the effect". (2) Moderate quality: "We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different". (3) Low quality: "Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect". (4) Very low quality: "We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect".

3. Results

3.1. Study selection

Fig. 1 depicts the process of study selection with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. The search was conducted on March 1, 2013, and a total of 2093 potential relevant records were retrieved. After adjusting for duplicates, 1432 records remained. One additional study was retrieved from Google Scholar. A total of 49 studies met the inclusion criteria and were included in the current review.

3.2. Study characteristics

Table 1 [33–81] summarizes the characteristics of all 49 included studies. All studies were RCTs published in English. A total of 2360 participants, aged $\geq$ 18 years, were involved. All trials were conducted in either a primary or a secondary health care setting. Participants received from three to 15 treatment sessions over a period of 1–12 weeks. Laser acupuncture was performed by physiotherapists or other trained health care professionals in most of the trials; however, half of the studies failed to report this clearly.

3.3. Quality assessment of included studies

Appendix 3 shows the methodological assessment of the included studies using the PEDro scale [26]. Thirty studies (61%) were considered to be of high methodological quality with a moderate cut-off score of 6 [82]. The most common flaws were inadequate allocation concealment (78%), lack of blinded therapists (63%), and lack of intention-to-treat analysis (71%). Despite the possible bias related to these flaws, other criteria were adequately addressed to minimize the risk of bias. Almost all the studies (94%) performed adequate randomization, thereby reducing possible selection bias. In most of the studies, patients (81%) and assessors (63%) were blinded successfully. Almost three-quarters (73%) of the studies provided adequate follow-up data with $< 15\%$ dropout rate; therefore, attrition bias was lowered. Inter-rater agreement was at an acceptable level, and disagreements were resolved by consensus.

Evaluation of the included studies using the risk of bias assessment tool provided by the Cochrane collaboration [27] showed similar results to that using the PEDro score (see Fig. 2). Risks of selection bias and performance bias were mixed, as risks of some of the studies were unclear due to insufficient description. Other domains remained at low risk in all the included studies, except for 20% of the studies that exhibited high risk in attrition due to high dropout rates or nondescription of reasons for withdrawals.

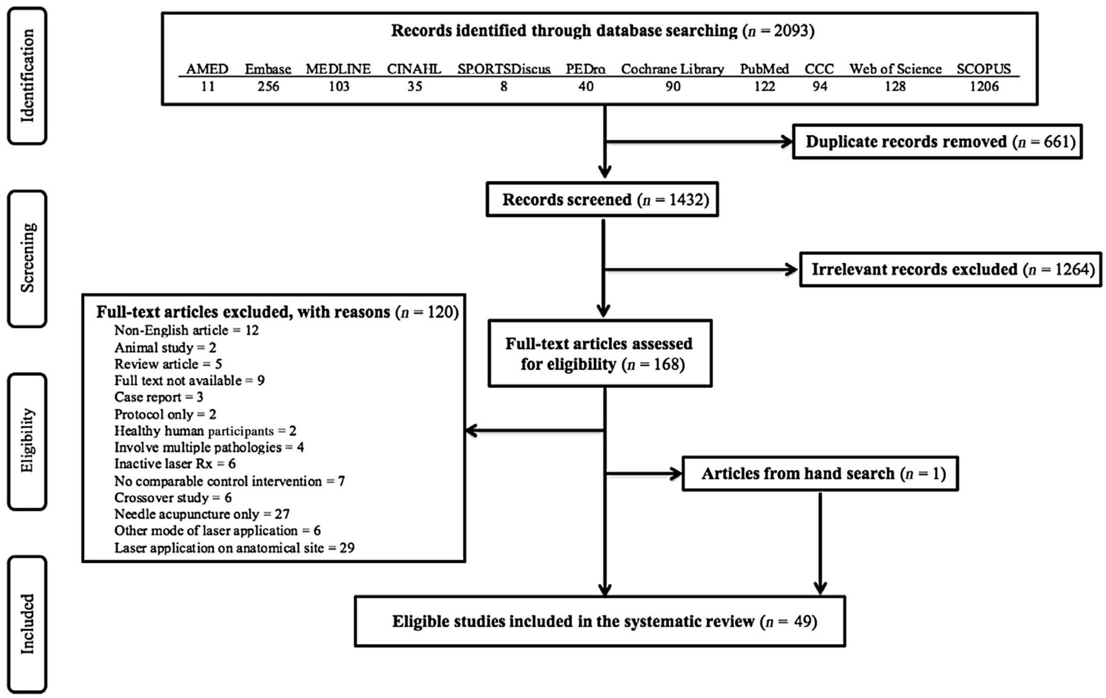


Figure 1 PRISMA flow diagram. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

3.4. Effects of laser acupuncture

Thirty-three studies provided sufficient data to calculate effect sizes for key outcome measures using RevMan (The Cochrane Collaboration) and were included in the meta-analysis. These studies showed mixed results, as reported by the authors, with two-thirds reporting positive effects favoring laser acupuncture, and one-third inconclusive or no effect.

3.4.1. Pain

All 33 studies assessed pain as one of the primary outcome measures. However, due to the heterogeneous characteristics of studies, results for pain scores were subcategorized into laser acupuncture versus placebo or laser acupuncture versus other interventions. To account for possible variation among different studies, the random effects model was used and the pooled effects were expressed as the SMD.

When compared with the placebo intervention, the overall effect for pain favored laser acupuncture, both at the end of intervention (SMD −0.43; −0.74 to −0.12) and at the follow-up period (SMD −0.61; −1.12 to −0.10). The pooled effect sizes of laser acupuncture for pain were considered to be small at short-term follow-up, but showed a moderate effect at long-term follow-up (see Appendix 4). Other studies [40,41,44,47,48,50,54,57,61,62,74,80] expressed the pain change scores from baseline, and showed a similar effect on pain relief at both short-term (SMD −0.53; −0.95 to −0.10) and long-term follow-ups (SMD −0.77; −1.25 to −0.29). When compared with other interventions, results of pain scores were mixed. Laser acupuncture failed to show significant favorable effects on pain scores at any time point compared to the control treatment (SMD −0.23; −1.00—0.54; SMD −1.43; −3.84—0.98).

Nine studies investigated pain by measuring the pressure pain threshold [36,38,39,43,51,58,59,64,69]. A positive effect indicates the beneficial effects of laser acupuncture as compared to control interventions. Similarly, compared with a placebo group, results showed a strong positive effect in favor of the experimental group at the end of intervention (SMD 1.02; 0.72—1.33) and during the follow-up period (SMD 0.91; 0.30—1.53). Comparing laser acupuncture to other interventions, no short- (SMD 0.35; −0.01—0.71) or long-term effects (SMD 0.20; −0.26—0.66) were found on the pressure pain threshold (see Appendix 4).

In the studies measuring pain with a visual analogue scale, subgroup analysis of pain scores was performed for the three most common diagnoses—myofascial pain or musculoskeletal trigger point syndrome, lateral epicondylitis, and temporomandibular joint pain (Fig. 3). The subgroup differences were not significant at the end of intervention and during the follow-up period ($p > 0.05$). The overall effect on pain in the short term moderately favored laser acupuncture (SMD −0.49; −0.79 to −0.18). Effects calculated from long-term follow-up almost doubled, which suggested that laser acupuncture has a strong beneficial effect on pain (SMD −0.95; −1.55 to −0.35).

3.4.2. Myofascial pain/musculoskeletal trigger points

Among 13 studies investigating the effectiveness of laser acupuncture for myofascial pain or musculoskeletal trigger points, only six showed favorable effects at the end of intervention [61,63,64,66,67,77]. During the follow-up period, four out of six studies demonstrated a positive effect in favor of laser acupuncture [39,59,63,77]. In most of the studies showing no significant effect of laser acupuncture, laser parameters were reported inadequately [34,45,50,52,58,69]. The overall effect of laser acupuncture on pain was positive, with a moderate effect at short

Table 1 Characteristics of the included studies.*

Authors	Year	Diagnosis	*n*	Interventions	Follow-up
Ferreira et al [33]	2013	Temporomandibular joint disorder	40	Laser acupuncture (20) versus placebo (20)	Monthly until intervention completed
Kannan [34]	2012	Myofascial pain	45	Ultrasound (15) versus laser (15) versus ischemic compression (15)	End of intervention
Lin et al [35]	2012	Low back pain	60	Laser acupuncture (21) versus placebo (21)	After each session
Sattayut and Bradley [36]	2012	Temporomandibular joint disorder	30	Low-energy-density laser (10) versus high-energy-density laser (10) versus placebo (10)	After each session
Skorupska et al [37]	2012	Lateral epicondylitis	80	LLLT (40) versus ultrasound (40) (trigger point application versus anatomical site application; 20 in each subgroup)	End of intervention; 12 mo
Lee and Han [38]	2011	Myofascial trigger point pain	24	Laser (12) versus placebo (12)	End of intervention
Rayegani et al [39]	2011	Myofascial pain	49	Laser (17) versus ultrasound (16) versus placebo laser (16)	6 wk
Emanet et al [40]	2010	Lateral epicondylitis	47	Laser acupuncture (24) versus placebo (23)	End of intervention; 12 wk after intervention
Glazov [41]	2010	Low back pain	100	Laser acupuncture (45) versus placebo (45)	After each session; 6 wk after intervention; 6 mo after intervention
Katsoulis et al [42]	2010	Tendomyopathy	11	Laser (7) versus placebo (4)	3 mo after intervention
Öz et al [43]	2010	Myofascial pain	40	Laser (20) versus occlusal splint (20)	End of intervention
Zhao et al [44]	2010	Knee osteoarthritis	40	Laser on acupuncture point (19) versus laser on sham point (17)	2 wk; 4 wk
Carrasco et al [45]	2009	Myofascial pain	60	Laser (30) versus placebo (30)—three-parameter groups; 10 in each group	After four sessions; after eight Rx; 15 d after intervention; 1 mo after intervention
Glazov et al [46]	2009	Low back pain	100	Laser acupuncture (45) versus placebo (45)	After each session; 6 wk after intervention; 6 mo after intervention
Shen et al [47]	2009	Knee osteoarthritis	40	Laser acupuncture (20) versus placebo (20)	2 wk; 4 wk
Shirani et al [48]	2009	Myofascial pain	16	Laser acupuncture (8) versus placebo (8)	After first session; 1 wk; the day with complete pain relief
Shen et al [49]	2008	Knee osteoarthritis	48	Laser acupuncture (24) versus placebo (24)	2 wk; 4 wk
Dundar et al [50]	2007	Myofascial pain	64	Laser acupuncture (32) versus placebo (32)	4 wk
Lam and Cheing [51]	2007	Lateral epicondylitis	39	Laser acupuncture (21) versus placebo (18)	After five sessions; end of intervention; 3 mo after intervention
Matsutani et al [52]	2007	Fibromyalgia	20	Laser (10) versus no laser (10)	End of intervention
Mazzetto et al [53]	2007	Temporomandibular joint disorder	48	Laser (24) versus placebo (24)	After four sessions; after eight sessions; 30 d after intervention
Yurtkuran et al [54]	2007	Knee osteoarthritis	55	Laser (27) versus placebo (25)	2 wk; 12 wk
Aigner et al [55]	2006	Whiplash injury	50	Laser acupuncture (23) versus placebo (22)	After each session; end of intervention; 8—12 mo after injury
Armagan et al [56]	2006	Fibromyalgia	32	LLLT (16) versus placebo (16)	End of intervention; 6 mo after intervention

(*continued on next page*)

Table 1 (*continued*)

Authors	Year	Diagnosis	*n*	Interventions	Follow-up
Chow et al [57]	2006	Chronic neck pain	90	Laser (45) versus placebo (45)	7 wk; 12 wk
Kiralp et al [58]	2006	Myofascial pain	43	Laser (23) versus trigger point injection (20)	End of intervention; 6 mo after intervention
Altan et al [59]	2005	Myofascial pain	53	Laser (23) versus placebo (25)	2 wk; 12 wk after intervention
Tam [60]	2005	Periarthritis of shoulder	60	Corticosteroid injection (20) versus LLLT (21) versus wait-and-see policy (18)	3 wk; 6 wk; 12 wk; 26 wk; 52 wk
Ceylan et al [61]	2004	Myofascial pain	46	Laser (19) versus placebo (20)	End of intervention
Chow et al [62]	2004	Chronic neck pain	20	Laser (10) versus placebo (10)	7 wk; 12 wk
Gur et al [63]	2004	Myofascial pain	60	Laser (30) versus placebo (30)	2 wk; 3 wk; 12 wk
Ilbuldu et al [64]	2004	Trigger point pain	60	Placebo laser (20) versus dry needling (20) versus laser (20)	End of intervention; 6 mo
Al-Shenqiti and Oldham [65]	2003	Rotator cuff tendinitis	55	Laser (26) versus placebo (29)	End of intervention; 3 mo
Hakgüder et al [66]	2003	Myofascial pain	62	Laser (31) versus no laser (31)	End of intervention; 3 wk after intervention
Gür et al [67]	2002	Fibromyalgia	40	Laser (20) versus placebo (20)	End of intervention
Wong et al [68]	2001	Carpal tunnel syndrome	12	Laser (12) versus placebo (12)	End of intervention
Chen et al [69]	1997	Myofascial pain	21	Placebo (5) versus continuous laser (7) versus pulsed laser (9)	End of intervention
Conti [70]	1997	Temporomandibular joint disorder	20	Laser (10) versus placebo (10)	After each session
Laasko et al [71]	1997	Myofascial trigger point pain	41	Red laser (15) versus IR laser (16) versus placebo (10)	Prior to each session; after each session
Lögdberg-Andersson et al [72]	1997	Tendinitis and myofascial pain	176	Laser (92) versus placebo (84)	End of intervention; 4 wk after intervention
Papadopoulos et al [73]	1996	Lateral epicondylitis	29	Laser (14) versus placebo (15)	After four sessions; after six sessions
Vecchio et al [74]	1993	Rotator cuff tendinitis	35	Laser (19) versus placebo (16)	2 wk; 4 wk; 8 wk
Haker and Lundeberg [75]	1991	Lateral epicondylitis	60	Laser (29) versus placebo (29)	End of intervention; 3 mo; 6 mo; 12 mo
Haker and Lundeberg [76]	1990	Lateral epicondylitis	49	Laser acupuncture (23) versus placebo (26)	End of intervention; 3 mo; 12 mo
Ceccherelli et al [77]	1989	Myofascial pain	27	Laser (13) versus placebo (14)	End of intervention; 3 mo after intervention
Snyder-Mackler et al [78]	1989	Myofascial trigger point pain	24	Laser (13) versus placebo (11)	Prior to each session; after each session
Waylonis et al [79]	1988	Fibromyalgia/chronic myofascial pain	55	Placebo versus laser acupuncture	6 wk after each round of intervention; 60 d; 120 —d
Lundeberg et al [80]	1987	Lateral epicondylitis	57	Placebo (19) versus GaAs laser (19) versus HeNe laser (19)	Every 2 wk; end of intervention; 3 mo; 6 mo
Snyder-Mackler et al [81]	1986	Musculoskeletal trigger point pain	27	Laser (13) versus placebo (11)	Prior to each session; after each session

*See Appendix 2 for the outcome measures and summarized results of individual studies.
IR = infrared; LLLT = low-level laser therapy.

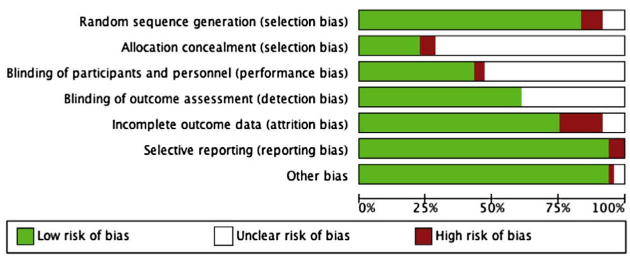


Figure 2 Risk of bias—graphical distribution of the judgments across all included studies.

term (SMD −0.49; −0.83 to −0.16) and a strong effect at long term (SMD −0.95; −1.68 to −0.23).

3.4.3. Lateral epicondylitis

Two studies examined the effect of laser acupuncture on lateral epicondylitis and showed conflicting results [40,51]. The overall effects did not suggest any favorable result of laser acupuncture at any time point. The study by Emanet et al [40] reported a positive conclusion during the follow-up period; yet the effect was not significant (SMD −0.42; −1.00—0.16). Again, the laser parameters employed in this study were unclear and incomplete; thus, it is not possible to estimate whether or not the dosage was appropriate.

3.4.4. Temporomandibular joint pain

Two studies [33,36] compared laser acupuncture with placebo in treating temporomandibular joint pain at the end of intervention. Mixed results were obtained: one was positive [33] and the other one was inconclusive [36]. The latter study involved two laser acupuncture groups receiving different dosages. The group that received a higher dosage showed a better effect of laser acupuncture compared with the group receiving a lower dosage; however, neither of them have a significant effect on pain. During the follow-up period, only one study [42] provided data; hence, outcome effect was not estimated.

3.4.5. Functional outcome

Most of the studies assessed functional improvement using a wide range of scales. Each study could involve multiple results from different functional scales; hence, an estimated overall effect size across the studies was not possible. Studies were more likely to report positive effects during the follow-up period rather than at the end of the intervention. Only two out of 11 studies [51,63] reported a positive short-term effect on functional outcomes, while six out of eight studies [39,40,51,57,62,63] showed positive effects at long term (see Appendix 4).

Two studies [40,51] investigated lateral epicondylitis; the pooled effect sizes of handgrip strength strongly favored laser acupuncture at both time points, but were significant only during the long-term follow-up period (MD5.16; 1.14—9.19). In regard to the small number of studies analyzed, it is important not to overlook this significant pooled effect (see Appendix 4).

Sensitivity analyses were conducted to explore whether or not the above mentioned main findings were affected by any studies with high risk of bias in certain domains. We exclude studies with any of the following: high risk of attrition bias, selection bias, and performance bias. No significant difference was found after excluding high-risk studies.

3.5. Appropriateness of laser acupuncture treatment

All included studies were analyzed for the appropriateness of laser parameters used. They were grouped separately into those reporting positive effects and those reporting inconclusive or no effects, and are displayed, along with the parameters used, in Tables 2 and 3[33—81], respectively. It is notable that four studies [52,59,74,80] reported no significant difference between groups; by contrast, their calculated effect sizes from RevMan (The Cochrane Collaboration) analysis favored laser acupuncture.

Almost 70% of studies reporting positive results used the clinically appropriate dosage suggested by Baxter et al [17]. Their systematic review stated that laser acupuncture would be effective when irradiation is applied at a minimum average output power of 10 mW and an energy dose of at least 0.5 J per point.

By contrast, studies reporting inconclusive or no effect of laser acupuncture either failed to describe the parameters comprehensively or applied an inappropriate dosage.

Half of these negative studies are deemed of low methodological quality, with PEDro scores of < 6.

3.6. Application site

The most common sites for the application of laser acupuncture were trigger points (39%). Subgrouping to perform another analysis to examine any difference of the effects on pain with different application sites was performed. No significant difference was observed between the subgroups at the end of intervention and during the follow-up period ($p > 0.05$). However, only the application at trigger points showed a positive effect in favor of laser acupuncture; this was not seen in case of application at acupuncture points or tender points. (see Appendix 5).

3.7. Risk of bias across studies

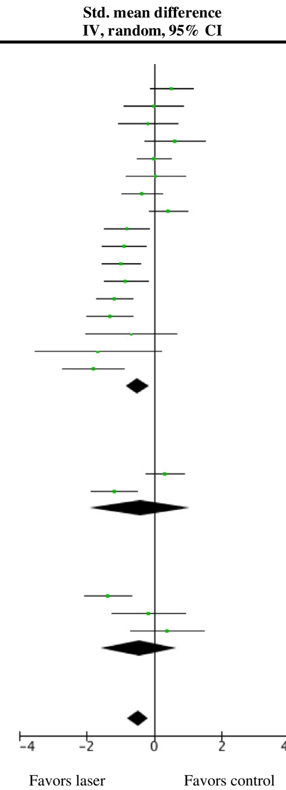
Considering the heterogeneity of the studies, funnel plots were drawn according to different outcome measures. Visual assessment of funnel plots did not show any considerable asymmetry, indicating a comprehensive coverage of publications. Hence, publication-related bias was low in this review.

4. Discussion

This systematic review investigated the clinical effectiveness of laser acupuncture, focusing on its effects on pain and functional outcomes while treating musculoskeletal disorders. The current findings strengthen the evidence from a previous systematic review [17]. The key findings in the current review support the continued use of laser acupuncture for treating musculoskeletal pain. Results from the meta-analysis suggest that the effect of laser acupuncture on pain and functional outcomes tended to be

A **Pain measured at the end of intervention**

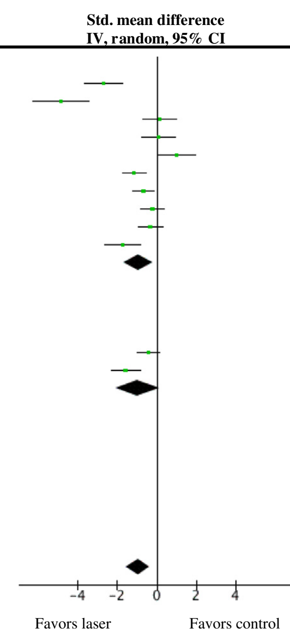
Study or subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std.mean difference IV, random, 95% CI
i. Myofascial pain/ musculoskeletal trigger point								
Kannan 2012	2.66	1.23	15	2.18	0.7058	30	5.1%	0.52 [-0.11, 1.15]
Carrasco 2009 (1)	6.73	1.65	10	6.75	1.49	10	4.2%	-0.01 [-0.89, 0.86]
Carrasco 2009 (2)	6.4	2.32	10	6.8	1.74	10	4.2%	-0.19 [-1.07, 0.69]
Carrasco 2009 (3)	7.04	1.72	10	5.97	1.6	10	4.2%	0.62 [-0.29, 1.52]
Dundar 2007	3.2	2.5	32	3.2	2.3	32	5.6%	0.00 [-0.49, 0.49]
Matsutani 2007	4.7	2.9	10	4.6	2.0	10	4.2%	0.04 [-0.84, 0.92]
Kiralp 2006	2.18	1.63	23	2.77	1.57	20	5.2%	-0.36 [-0.97, 0.24]
Altan 2005	4.13	0.58	23	3.92	0.42	25	5.3%	0.41 [-0.16, 0.98]
Ceylan 2004	34.54	23.5	19	54.96	25.89	20	5.0%	-0.81 [-1.46, -0.15]
Ilbuldu 2004 (4)	2.05	1.43	20	3.65	2.03	20	5.0%	-0.89 [-1.55, -0.24]
Gur 2004	3.11	2.29	28	5.79	3.12	26	5.3%	-0.97 [-1.54, -0.40]
Ilbuldu 2004 (5)	2.05	1.43	20	3.71	2.33	20	5.0%	-0.84 [-1.49, -0.19]
Hakguder 2003	3.41	2.0	31	5.77	2.0	31	5.4%	-1.17 [-1.71, -0.62]
Gur 2002	1.27	0.76	20	2.44	0.98	20	4.9%	-1.31 [-2.00, -0.62]
Chen 1997 (6)	1.94	1.87	9	3.25	1.32	3	2.9%	-0.68 [-2.03, 0.67]
Chen 1997 (7)	0.83	1.29	7	3.25	1.32	2	1.9%	-1.66 [-3.54, 0.21]
Ceccherelli 1989	9.46	13.17	13	37.42	16.58	14	4.1%	-1.80 [-2.72, -0.89]
Subtotal (95% CI)			**300**			**303**	**77.7%**	**-0.49 [-0.83, -0.16]**
Heterogeneity: Tau-square = 0.34; Chi-square = 59.18, df = 16 (p < 0.00001); I^2 = 73%								
Test for overall effect: Z = 2.87 (p = 0.004)								
ii. Lateral epicondylitis								
Emanet 2010	1.13	0.94	23	0.83	0.88	24	5.3%	0.32 [-0.25, 0.90]
Lam 2007	3.05	1.77	21	5.39	2.12	18	4.9%	-1.18 [-1.87, -0.49]
Subtotal (95% CI)			**44**			**42**	**10.2%**	**-0.42 [-1.89, 1.06]**
Heterogeneity: Tau-square = 1.03; Chi-square = 10.84, df = 1 (p = 0.0010); I^2 = 91%								
Test for overall effect: Z = 0.55 (p = 0.58)								
iii. Temporomandibular joint pain								
Ferreira 2013	0.05	0.22	20	2.75	2.71	20	4.9%	-1.38 [-2.07, -0.68]
Sattayut 2012 (8)	4.5	2.58	10	5.0	3.38	5	3.6%	-0.17 [-1.24, 0.91]
Sattayut 2012 (9)	6.1	2.29	10	5.0	3.38	5	3.6%	0.39 [-0.70, 1.47]
Subtotal (95% CI)			**40**			**30**	**12.0%**	**-0.45 [-1.57, 0.67]**
Heterogeneity: Tau-square = 0.74; Chi-square = 8.43, df = 2 (p = 0.01); I^2 = 76%								
Test for overall effect: Z = 0.79 (p = 0.43)								
Total (95% CI)			**384**			**375**	**100.0%**	**-0.49 [-0.79, -0.18]**
Heterogeneity: Tau-square = 0.37; Chi-square = 79.89, df = 21 (p < 0.00001); I^2 = 74%								
Test for overall effect: Z = 3.12 (p = 0.002)								
Test for subgroup differences: Chi-square = 0.01, df = 2 (p = 0.99), I^2 = 0%								



(1) Laser dose: 105J/cm^2; (2) Laser dose: 60J/cm^2; (3) Laser dose: 25J/cm^2; (4) vs. placebo; (5) vs. dry needling; (6) Pulsed laser; placebo group data divided ; (7) Continuous laser; placebo group data divided; (8) High energy laser; placebo group data divided; (9) Low energy laser; placebo group data divided

B **Pain measured during the follow-up period (6 to 26 wks)**

Study or subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std.mean difference IV, random, 95% CI
i. Myofascial pain/ musculoskeletal trigger point								
Rayegani 2011 (1)	20.5	4.1231	17	30.7	3.2	16	7.8%	-2.69 [-3.66, -1.71]
Rayegani 2011 (2)	20.5	4.1231	17	40.7	4.0	16	6.4%	-4.85 [-6.27, -3.43]
Carrasco 2009 (3)	7.14	2.68	10	6.75	2.45	10	8.1%	0.15 [-0.73, 1.02]
Carrasco 2009 (4)	5.67	2.99	10	5.4	3.06	10	8.1%	0.09 [-0.79, 0.96]
Carrasco 2009 (5)	6.91	2.24	10	4.63	2.1	10	7.9%	1.01 [0.06, 1.95]
Altan 2005	3.17	0.58	23	3.8	0.51	25	8.9%	-1.14 [-1.75, -0.52]
Gur 2004	4.18	2.65	28	6.29	3.52	26	9.1%	-0.67 [-1.22, -0.12]
Ilbuldu 2004 (6)	2.12	1.9	20	2.59	2.18	20	8.9%	-0.23 [-0.85, 0.40]
Ilbuldu 2004 (7)	2.12	1.9	20	2.89	2.63	20	8.9%	-0.33 [-0.95, 0.30]
Ceccherelli 1989	8.46	10.76	13	35.57	18.28	14	8.1%	-1.74 [-2.64, -0.83]
Subtotal (95% CI)			**168**			**167**	**82.4%**	**-0.95 [-1.68, -0.23]**
Heterogeneity: Tau-square = 1.18; Chi-square = 78.58, df = 9 (p < 0.00001); I^2 = 89%								
Test for overall effect: Z = 2.58 (p = 0.01)								
ii. Lateral epicondylitis								
Emanet 2010	0.29	0.47	23	0.57	0.79	24	9.0%	-0.42 [-1.00, 0.16]
Lam 2007	1.48	1.36	21	4.28	2.11	18	8.6%	-1.57 [-2.30, -0.84]
Subtotal (95% CI)			**44**			**42**	**17.6%**	**-0.97 [-2.10, 0.15]**
Heterogeneity: Tau-square = 0.55; Chi-square = 5.87, df = 1 (p = 0.02); I^2 = 83%								
Test for overall effect: Z = 1.70 (p = 0.09)								
iii. Temporomandibular joint pain								
Katsoulis 2010	3.25	2.248	7	2.65	0.7362	4		Not estimable
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**212**			**209**	**100.0%**	**-0.95 [-1.55, -0.35]**
Heterogeneity: Tau-square = 0.95; Chi-square = 84.78, df = 11 (p < 0.00001); I^2 = 87%								
Test for overall effect: Z = 3.09 (p = 0.002)								
Test for subgroup differences: Chi-square = 0.00, df = 1 (p = 0.97), I^2 = 0%								



(1) vs. ultrasound; (2) vs. placebo; (3) Laser dose: 105J/cm^2; (4) Laser dose: 25J/cm^2; (5) Laser dose: 60J/cm^2; (6) vs. dry needling; (7) vs. placebo

Figure 3 Forest plot comparison of different diagnoses. CI = confidence interval; SD = standard deviation.

more significant during long-term follow-up periods rather than at the end of intervention. These results indicate that laser acupuncture may be effective in treating musculoskeletal pain and improving function if an adequate dosage is used, and that the effects are long lasting, as evidenced by the increase in effect sizes demonstrated in the meta-analysis at 6–26 weeks postrandomization. It is important to stress that results from the included studies were dependent upon the appropriateness of laser parameters used. Studies with higher methodological quality, which

Table 2 Studies reporting positive effect of laser acupuncture.[a]

Authors	Average output (mW)	Power density (mW/cm^2)	Dose (J)	PEDro
Studies included in meta-analysis				
Chow et al [62]	300	670	9	10
Chow et al [57]	300	670	9	10
Glazov [41]	10	50	0.2	9
Yurtkuran et al [54]	4	10	0.48	8
Armagan et al [56]	50	75	2	8
Gur et al [63]	11.2	11.2	2	8
Ceccherelli et al [77]	5	?	0.1 or 1	8
Shen et al [47]	36 and 200	?	?	7
Öz et al [43]*	300	1071	3	7
Lam and Cheing [51]	25	208	0.275	7
Shirani et al [48]	17.3 or 1.76	17.3 or 1.76	7.2	6
Hakgüder et al [66]	5	25.5	0.98	6
Gür et al [67]	11.2	11.2	2	6
Ferreira et al [33]	50	1250	4.5	6
Sattayut and Bradley [36]	60 or 300	333 or 1666	4 or 20	6
Zhao et al [44]	36 and 200	36 and 100	163.2	6
Rayegani et al [39]*	1100	?	?	6
Emanet et al [40]	?	?	?	5
Lin et al [35]	40	50	12	4
Kannan [34]*	2.4	2.4	0.074	4
Ceylan et al [61]	8	40	1.44	3
Chen et al [69]	15 or 1.5	?	18 or 1.8	2
Studies not included in meta-analysis				
Al-Shenqiti and Oldham [65]	100	800	4	8
Conti [70]	100	?	4	7
Tam [60]*	27	135?	3 to 4	6
Snyder-Mackler et al [78]	0.95	0.95	0.02	6
Laasko et al [71]	10 or 25	278 or 893	1 or 5	5
Snyder-Mackler et al [81]	0.95	0.95	0.014	5
Lögdberg-Andersson et al [72]	8	8	0.5 to 1	5
Wong et al [68]	30	107	5.4	5
Mazzetto et al [53]	70	8750	0.72	4

*Laser acupuncture compared to other interventions.
PEDro = physiotherapy evidence database.
[a] The symbol '?' indicates insufficient details for calculating the missing parameters.

also reported dosages properly, showed a more consistent result, with a favorable effect of laser acupuncture on both pain and functional outcomes.

To the best of our knowledge, there has been no further evaluation of the latest literature on laser acupuncture since a previous systematic review [17]. It concluded that laser acupuncture was an effective treatment for myofascial pain, based on a moderate level of evidence from 18 RCTs that were published prior to 2005. A massive growth in publications in recent years has provided further evidence on the effectiveness of laser acupuncture. Not surprisingly, a large number of clinical trials were identified from the current literature, most of which were published during the past decade. The total number of eligible studies included in this systematic review was more than twofold that of the past review [17].

4.1. Primary outcomes

The majority of studies reported positive findings on the effects of laser acupuncture on both pain and functional outcomes; by contrast, one-third of reviewed studies reported no benefit. Given the heterogeneity of included studies, meta-analyses were performed using subgroups of studies according to their study populations and follow-up time point. The three most common diagnoses were analyzed separately in order to have a minimum of two studies for each analysis. Sensitivity analyses excluded studies comparing laser acupuncture with other active treatments, as the primary scope of this review was to evaluate whether or not laser acupuncture is effective, rather than comparing its effectiveness with other active treatments.

4.1.1. Myofascial pain/musculoskeletal trigger points

Ten studies showed positive effects of laser acupuncture on myofascial pain or pain at trigger points: four studies [34,50,52,58] had an individual effect size that did not favor the laser group. Coincidently, all these studies did not include follow-up assessments to investigate possible long-term effects. Given the increased effect sizes at follow-up, as highlighted here, it is possible that these researchers

Table 3 Studies reporting inconclusive or no effect of laser acupuncture.

Authors	Average output (mW)	Power density (mW/cm^2)	Dose (J)	PEDro
Studies included in meta-analysis				
Glazov et al [46]	10	50	0.2	9
Vecchio et al [74]	30	429	3	9
Dundar et al [50]	58	58	7	9
Ilbuldu et al [64]*	?	?	2	8
Altan et al [59]	?	?	?	7
Carrasco et al [45]	50 or 60 or 70	?	?	6
Lundeberg et al [80]	1.56 or 0.07	?	0.09 or 0.004	5
Lee and Han [38]	450	6428	27 or 54 or 135	5
Kiralp et al [58]*	?	?	?	5
Matsutani et al [52]	30	?	?	4
Katsoulis et al [42]	40	1000	1.6–2.4	2
Studies not included in meta-analysis				
Skorupska et al [37]*	0–400	?	?	8
Haker and Lundeberg [75]	12	?	0.36	7
Papadopoulos et al [73]	50	400	3	6
Haker and Lundeberg [76]	?	?	0.6	5
Shen et al [49]	?	?	?	5
Waylonis et al [79]	1	?	0.02	4
Aigner et al [55]	5	5	0.08	4

*Laser acupuncture compared to other interventions.
PEDro = physiotherapy evidence database.
The symbol '?' indicates Insufficient details for calculating the missing parameters.

might have overlooked a potential effect in the longer term; another study [59] found positive effects only during the follow-up period, but not at the end of intervention.

4.1.2. Lateral epicondylitis

Emanet et al [40] showed more favorable effects in the short term than in the long term. However, the individual effect size (for pain) from the forest plot crossed zero at the long-term time point, indicating a lack of statistical significance. Although the pooled effects from another study [51] did not suggest any favorable outcome for treatment with laser acupuncture to reduce pain in lateral epicondylitis, results for handgrip assessment yielded some interesting findings. Both studies investigated the effectiveness of laser acupuncture by evaluating pain and functional outcomes, and appeared to be more homogeneous, so the mean difference was used as the pooled effect result. Again, the estimated effect size for functional outcome (handgrip) favored laser acupuncture, especially during the follow-up period. However, it should be stressed that this analysis is based on two studies examining laser acupuncture, and the result may not be generalized to other conditions.

4.1.3. Temporomandibular joint pain

The three studies reviewed showed mixed results, and only one of these reported outcomes at long term. At short term, the effect was inconclusive. No further analysis was carried out to compare the effects at different time points.

4.2. Increased long-term follow-up effects

Findings related to the three different diagnoses showed a consistent trend of better pain-relieving effects during the follow-up period. Pooled effect sizes were doubled during the follow-up period compared to those at the end of intervention. This phenomenon may account for the conflicting results from some of the negative studies. Without taking into consideration the possibility of delayed or long-lasting effects, their conclusions of lack of effectiveness may be flawed. Results from our analyses included both short- and long-term follow-up data; these data were separated into similar time points to allow more comparable subgroup analyses.

4.3. Weaknesses of negative studies

The five studies [38,42,46,50,74] that found no significant benefit of laser acupuncture had a number of shortcomings. In one study [74], a mismatch was found between the calculated individual effect and the authors' conclusion. Although the effect size (expressed in the SMD) for pain favored laser acupuncture, Vecchio et al [74] reported no benefit. This apparent error was also highlighted by another systematic review [83], which suggested a flaw in their analysis. In another study on back pain, Glazov and colleagues [41] performed a *post hoc* analysis on their data, which challenged the results of their original study [46]. They suggested that the randomization failed to create comparable groups and resulted in an imbalanced baseline characteristic that responded differently to the intervention. The PEDro quality rating of the study by Katsoulis et al [42] was exceptionally low (2 out of a PEDro score of 10), representing a major performance bias. The remaining two studies [38,50] applied laser acupuncture around the neck and upper trapezius muscles area. The parameters selected in both studies were similar to the other two positive studies [57,66] targeting the neck region, but the authors' conclusions were based on results measured only at short term. Consequences of these apparent methodological flaws may be an underestimation of the true effect of laser acupuncture from these studies.

5. Clinical relevance of the laser parameter

Variation in application of the laser acupuncture intervention can very likely account for a certain degree of difference in outcomes. Such clinical heterogeneity should be considered when evaluating the effectiveness of a therapy. Laser acupuncture has been suggested to be a dosage-dependent modality [16,21]; these sources suggest that the energy delivered to the target point by laser acupuncture has to reach a threshold in order to produce a desired effect. Thus, the dosages reported in the included studies may explain the observed difference in outcomes. Characteristics of the laser beam and the application site of the laser would directly affect the actual energy received by the target point [10,14]. Although detailed discussion of the potential mechanisms of laser acupuncture is beyond the scope of this review, the importance of selecting and reporting parameters accurately is paramount to understand and interpret the results of individual studies.

Unfortunately, the quality of reporting of parameters and dosages varied among the studies included in this review; five studies stated neither the power density nor the irradiated area [40,58,59,64,75]. This brings into question whether or not an appropriate dosage was applied. Reporting of these parameters is essential, as recommended by the World Association for Laser Therapy guidelines [28], to determine the appropriateness of the dosage. In addition, unclear reporting of parameters was more commonly seen among studies with negative or inconclusive results (Tables 2 and 3).

It is challenging to draw meaningful conclusions regarding an effective dosage window from these studies due to the variation in the application of laser acupuncture and the wide dosage range employed. This systematic review covered different musculoskeletal conditions, and each condition may have required a distinct parameter and dosage regime for clinical effectiveness. Site of application is a key factor in the selection of parameters, given that there may be a specific acupuncture point for a particular diagnosis. In this review, the point of application was not limited to acupuncture points only, but included trigger and tender point applications as well, because a wide range of evidence suggests overlapping of acupuncture points [84–86]. It seems unwise to exclude those studies using trigger points or tender points even though the existence of these specific points is still controversial [85,87,88]. A subgroup analysis based on different application sites was performed; however, no obvious difference could be seen between groups. Application on acupuncture, trigger, and tender points appeared equally effective.

6. Quality of included studies in our review

The number and proportion of trials rated to be of high methodological quality doubled in this review, compared to a previous review [17]. Over two-thirds of the 49 RCTs included in this review were high-quality studies, whereas in the previous review less than one-third of the studies were of high quality. Considering this growth in the number of higher-quality studies in this body of literature, the findings of this systematic review were expected to be more robust.

There was an apparent relationship between levels of methodological quality and reported results. Two-thirds of high-quality (PEDro score $\geq$6) studies reported beneficial effects of laser acupuncture, which is similar to the proportion for all included studies. Lower-quality studies appeared to show more conflicting results, with equal numbers of studies reporting benefits ($n = 9$) or no benefits ($n = 9$). This methodological heterogeneity should be considered when assessing the overall pooled effect in the meta-analysis. However, it should be stressed that the sensitivity analyses, excluding studies with high risk of bias in various domains, failed to show any differences in overall findings that conflicted with the effects estimated.

6.1. Limitations

The limitations of this review include potential bias related to heterogeneity and methodological quality of the included studies. These problems were anticipated while designing the methodology of this review, and so different subgroup analyses were initiated to address this limitation. Another limitation of this review is that some of the studies have a high risk of bias in some of the domains; however, the sensitivity analyses suggested no major effects upon the outcomes. Lastly, even though non-English publications were excluded, the funnel plot assessment did not detect any potential publication bias. Although this kind of visual assessment is considered to be prone to error [89], it is one of the most common methods adopted for detecting publication bias owing to its simplicity [31]. Given the large number of studies included in this meta-analysis, funnel plot should be able to detect possible bias.

6.2. Recommendations

Using the Grading of Recommendations Assessment, Development, and Evaluation system [90], the strength of recommendation is based on not only the quality of the evidence, but also other factors that should not outweigh the benefit of the treatment. Using pain and functional outcomes to assess the clinical effectiveness of laser acupuncture, most of the included studies were found to be high-quality RCTs, providing high-quality evidence. Yet the quality of evidence was downgraded (-2) due to inconsistency and imprecision of the results for both pain and functional outcome measures [32]. Owing to the possible dose response for pain-relieving effects, and a large effect from functional outcome, the quality of evidence was upgraded ($+1$). As a result, there is a moderate quality of evidence supporting the effectiveness of laser acupuncture for treating pain and improving functional outcomes in musculoskeletal disorders. It suggests with moderate confidence that the estimated effect from the meta-analysis is likely to be close to the true effect. Serious adverse events have seldom been reported for laser acupuncture, given its noninvasive nature; this is in keeping with the results of all the included studies. Based upon this systematic review, a strong recommendation can be made that laser acupuncture is effective for improving musculoskeletal pain and functional outcomes at 6–26 weeks.

7. Conclusion

Overall, the evidence is sufficiently robust to determine the effectiveness of laser acupuncture at long term for treating musculoskeletal conditions. In trials reporting negative or inconclusive results, neither enough evaluation was carried out nor were the participants followed up to a sufficient time point. These trials did not allow complete evaluation of pain and functional outcomes, and their conclusions were made based upon results measured at short term only. Hence, this review highlights the importance of providing a sufficient course of treatment to allow laser acupuncture to work effectively in the clinical situation.

Although the evidence does not allow us to determine an effective dosage window for laser acupuncture, the possible range of applications was largely adjusted and designed to fit specific musculoskeletal conditions. To foster the development of clinical guidelines, future research should carefully define the study population and provide rationale for the parameters chosen. This would facilitate not only pooling of data for meta-analysis, but also more precise analysis for a specific condition or application site. With the improvement in quality of evidence over time, more robust recommendations for clinical application of laser acupuncture can be anticipated in the future.

Disclosure statement

The authors declare that they have no conflicts of interest and no financial interests related to the material of this manuscript.

Appendix A Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jams.2014.06.015.

References

[1] World Health Organization. *Burden of Musculoskeletal Diseases at the Start of the Millennium: Report of a WHO Scientific Group*. Geneva: World Health Organization; 2003.
[2] Vos T, Aboyans V, Dherani M, Diaz-Torne C, Dolk H, Dorsey ER, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the global burden of disease study 2010. *Lancet*. 2012;380:2163–2196.
[3] Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. *Bull World Health Org*. 2003;81:646–656.
[4] Brooks PM. The burden of musculoskeletal disease—a global perspective. *Clin Rheumatol*. 2006;25:778–781.
[5] Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain*. 2006;10:287–333.
[6] Rickards LD. Therapeutic needling in osteopathic practice: an evidence-informed perspective. *Int J Osteopath Med*. 2009;12:2–13.
[7] Su D, Li L. Trends in the use of complementary and alternative medicine in the United States: 2002–2007. *J Health Care Poor Underserved*. 2011;22:296–310.
[8] Xue CC, Zhang AL, Lin V, Da Costa C, Story DF. Complementary and alternative medicine use in Australia: a national population-based survey. *J Altern Complement Med*. 2007;13:643–650.
[9] Han J-S, Ho Y-S. Global trends and performances of acupuncture research. *Neurosci Biobehav Rev*. 2011;35:680–687.
[10] Whittaker P. Laser acupuncture: past, present, and future. *Lasers Med Sci*. 2004;19:69–80.
[11] Litscher G. High-tech laser acupuncture is Chinese medicine. *Med Acupunct*. 2008;20:245–254.
[12] Plog FMW. Biophysical application of the laser beam. *Lasers Surg Med*. 1980;1:21–37.
[13] Zhou YC. An advanced clinical trial with laser acupuncture anesthesia for minor operations in the oro-maxillofacial region. *Lasers Surg Med*. 1984;4:297–303.
[14] Chang WD, Wu JH, Yang WJ, Jiang JA. Therapeutic effects of low-level laser on lateral epicondylitis from differential interventions of Chinese–Western medicine: systematic review. *Photomed Laser Surg*. 2010;28:327–336.
[15] Peplow PV, Chung TY, Baxter GD. Laser photobiomodulation of proliferation of cells in culture: a review of human and animal studies. *Photomed Laser Surg*. 2010;28(Suppl. 1):S3–S40.
[16] Litscher G, Opitz G. Technical parameters for laser acupuncture to elicit peripheral and central effects: state-of-the-art and short guidelines based on results from the Medical University of Graz, the German academy of acupuncture, and the scientific literature. *Evid Based Complement Alternat Med*. 2012;2012:697096.
[17] Baxter GD, Bleakley C, McDonough S. Clinical effectiveness of laser acupuncture: a systematic review. *J Acupunct Meridian Stud*. 2008;1:65–82.
[18] WALT. *Recommended treatment doses for low level laser therapy—laser class 3B, 904 nm GaAs lasers*. World Association for Laser Therapy; 2010 [updated Apr 2010; cited Feb 13, 2013]. Available at: http://waltza.co.za/wp-content/uploads/2012/08/Dose_table_904nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf [Date accessed: Feb 13, 2013].
[19] WALT. *Recommended treatment doses for low level laser therapy—laser class 3 B, 780–860nm GaAlAs lasers*. World Association for Laser Therapy; 2010 [updated Apr 2010; cited 2013 Feb 13]. Available at: http://waltza.co.za/wp-content/uploads/2012/08/Dose_table_780-860nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf [Date accessed: Feb 13, 2013].
[20] Chow RT, Johnson MI, Lopes-Martins RAB, Bjordal JM. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. *Lancet*. 2009;374:1897–1908.
[21] David Baxter G. Laser acupuncture: effectiveness depends upon dosage. *Acupunct Med*. 2009;27:92.
[22] Jang H, Lee H. Meta-analysis of pain relief effects by laser irradiation on joint areas. *Photomed Laser Surg*. 2012;30:405–417.
[23] Lorenzini L, Giuliani A, Giardino L, CalzÃ L. Laser acupuncture for acute inflammatory, visceral and neuropathic pain relief: an experimental study in the laboratory rat. *Res Vet Sci*. 2010;88:159–165.
[24] Erthal V, da Silva MD, Cidral-Filho FJ, Santos AR, Nohama P. ST36 laser acupuncture reduces pain-related behavior in rats: involvement of the opioidergic and serotonergic systems. *Lasers Med Sci*. 2013;28:1345–1351.
[25] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting

systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med*. 2009;151:W65—94.
[26] PEDro Scale. *Physiotherapy Evidence Database*; 1999 [updated June 21, 1999; cited Feb 13, 2012]. Available at: http://www.pedro.org.au/wp-content/uploads/PEDro_scale.pdf [Date accessed: Feb 13, 2013].
[27] Shuster JJ, Green S. *Review: Cochrane handbook for systematic reviews for interventions, version 5.1.0*. The Cochrane Collaboration; 2011 [updated Mar 2011]. Available at: http://www.cochrane-handbook.org/ [Date accessed: Feb 13, 2013].
[28] WALT. *Consensus agreement on the design and conduct of clinical studies with low level laser therapy and light therapy for musculoskeletal pain and disorders*. World Association for Laser Therapy; 2010 [updated Nov 2004; cited Apr 1, 2013]. Available at: http://waltza.co.za/wp-content/uploads/2012/08/walt_standard_for_conduct_of_randomized_controlled_trials.pdf [Date accessed: Apr 1, 2013].
[29] Review Manager (RevMan) [Computer program]. *Version 5.2*. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2012.
[30] Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. New Jersey: Lawrence Erlbaum Associates; 1988.
[31] Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629—634.
[32] Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. Grade guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64:401—406.
[33] Ferreira LA, de Oliveira RG, Guimarães JP, Carvalho AC, De Paula MV. Laser acupuncture in patients with temporomandibular dysfunction: a randomized controlled trial. *Lasers Med Sci*. 2013;28:1549—1558.
[34] Kannan P. Management of myofascial pain of upper trapezius: a three group comparison study. *Glob J Health Sci*. 2012;4:46—52 [Clinical Trial Comparative Study].
[35] Lin ML, Wu HC, Hsieh YH, Su CT, Shih YS, Lin CW, et al. Evaluation of the effect of laser acupuncture and cupping with Ryodoraku and visual analog scale on low back pain. *Evid Based Complement Alternat Med*. 2012;2012:521612.
[36] Sattayut S, Bradley P. A study of influence of low intensity laser therapy on painful temporomandibular disorder patients. *Laser Ther*. 2012;21:183—192.
[37] Skorupska E, Lisinski P, Samborski W. The effectiveness of the conservative versus myofascial pain physiotherapy in tennis elbow patients: double-blind randomized trial of 80 patients. *J Musculoskelet Pain*. 2012;20:41—50.
[38] Lee JH, Han JT. The dose-dependent effect of an 830-nm, 450-mW low-level laser therapy on the myofacial trigger point of the upper trapezius muscle: a randomized, double-blinded, clinical trial. *J Phys Ther Sci*. 2011;23:933—935.
[39] Rayegani SM, Bahrami MH, Samadi B, Sedighipour L, Mokhtarirad MR, Eliaspoor D. Comparison of the effects of low energy laser and ultrasound in treatment of shoulder myofascial pain syndrome: a randomized single-blinded clinical trial. *Eur J Phys Rehabil Med*. 2011;47:381—390.
[40] Emanet SK, Altan LI, Yurtkuran M. Investigation of the effect of GaAs laser therapy on lateral epicondylitis. *Photomed Laser Surg*. 2010;28:397—403.
[41] Glazov G. The influence of baseline characteristics on response to a laser acupuncture intervention: an exploratory analysis. *Acupunct Med*. 2010;28:6—11.
[42] Katsoulis J, Ausfeld-Hafter B, Windecker-Gétaz I, Katsoulis K, Blagojevic N, Mericske-Stern R. Laser acupuncture for myofascial pain of the masticatory muscles. A controlled pilot study. *Schweiz Monatsschr Zahnmed*. 2010;120:213—225.
[43] Öz S, Gökçen-Röhlig B, Saruhanoglu A, Tuncer EB. Management of myofascial pain: low-level laser therapy versus occlusal splints. *J Craniofac Surg*. 2010;21:1722—1728.
[44] Zhao L, Shen X, Cheng K, Deng H, Ding G, Tan M, et al. Validating a nonacupoint sham control for laser treatment of knee osteoarthritis. *Photomed Laser Surg*. 2010;28:351—356.
[45] Carrasco TG, Guerisoli LD, Guerisoli DM, Mazzetto MO. Evaluation of low intensity laser therapy in myofascial pain syndrome. *Cranio*. 2009;27:243—247.
[46] Glazov G, Schattner P, Lopez D, Shandley K. Laser acupuncture for chronic non-specific low back pain: a controlled clinical trial. *Acupunct Med*. 2009;27:94—100.
[47] Shen X, Zhao L, Ding G, Tan M, Gao J, Wang L, et al. Effect of combined laser acupuncture on knee osteoarthritis: a pilot study. *Lasers Med Sci*. 2009;24:129—136.
[48] Shirani AM, Gutknecht N, Taghizadeh M, Mir M. Low-level laser therapy and myofacial pain dysfunction syndrome: a randomized controlled clinical trial. *Lasers Med Sci*. 2009;24:715—720.
[49] Shen XY, Ding GH, Wu F, Wang LZ, Zhao L, Wang M, et al. Effects of 650 nm—10.6 μm combined laser acupuncture—moxibustion on knee osteoarthritis: a randomized, double-blinded and placebo-controlled clinical trial. *J Acupunct Tuina Sci*. 2008;6:315—317.
[50] Dundar U, Evcik D, Samli F, Pusak H, Kavuncu V. The effect of gallium arsenide aluminum laser therapy in the management of cervical myofascial pain syndrome: a double blind, placebo-controlled study. *Clin Rheumatol*. 2007;26:930—934.
[51] Lam LKY, Cheing GLY. Effects of 904-nm low-level laser therapy in the management of lateral epicondylitis: a randomized controlled trial. *Photomed Laser Surg*. 2007;25:65—71.
[52] Matsutani LA, Marques AP, Ferreira EAG, Assumpção A, Lage LV, Casarotto RA, et al. Effectiveness of muscle stretching exercises with and without laser therapy at tender points for patients with fibromyalgia. *Clin Exp Rheumatol*. 2007;25:410—415.
[53] Mazzetto MO, Carrasco TG, Bidinelo EF, Andrade Pizzo RC, Mazzetto RG. Low intensity laser application in temporomandibular disorders: a phase I double-blind study. *Cranio [serial on the Internet]*; 2007:3. Available at: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/304/CN-00611304/frame.html [Date accessed: Mar 2, 2013].
[54] Yurtkuran M, Konur S, Ozcakir S, Bingol U. Laser acupuncture in knee osteoarthritis: a double-blind, randomized controlled study. *Photomed Laser Surg*. 2007;25:14—20.
[55] Aigner N, Fialka C, Radda C, Vecsei V. Adjuvant laser acupuncture in the treatment of whiplash injuries: a prospective, randomized placebo-controlled trial. *Wien Klin Wochenschr*. 2006;118:95—99.
[56] Armagan O, Tascioglu F, Ekim A, Oner C. Long-term efficacy of low level laser therapy in women with fibromyalgia: a placebo-controlled study. *J Back Musculoskelet Rehabil*. 2006;19:135—140.
[57] Chow RT, Heller GZ, Barnsley L. The effect of 300 mW, 830 nm laser on chronic neck pain: a double-blind, randomized, placebo-controlled study. *Pain*. 2006;124:201—210.
[58] Kiralp MZ, Ari H, Karabekir I, Dursun H. Comparison of low intensity laser therapy and trigger point injection in the management of myofascial pain syndrome. *Pain Clin*. 2006;18:63—66.
[59] Altan L, Bingöl U, Aykaç M, Yurtkuran M. Investigation of the effect of GaAs laser therapy on cervical myofascial pain syndrome. *Rheumatol Int [serial on the Internet]*; 2005:1. Available at: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/915/CN-00510915/frame.html [Date accessed: Mar 2, 2013].
[60] Tam G. *Effects of LLLT on the Periarthritis of the Shoulder: a Clinical Study on Different Treatments with Corticosteroid*

Injections or a Wait-and-see Policy. Progress in Biomedical Optics and Imaging—Proceedings of SPIE. 2005. Florence.
[61] Ceylan Y, Hizmetli S, Siliğ Y. The effects of infrared laser and medical treatments on pain and serotonin degradation products in patients with myofascial pain syndrome. A controlled trial. *Rheumatol Int [serial on the Internet]*; 2004: 5. Available at: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/365/CN-00502365/frame.html. http://link.springer.com/article/10.1007%2Fs00296-003-0348-6.
[62] Chow RT, Barnsley L, Heller GZ, Siddall PJ. A pilot study of low-power laser therapy in the management of chronic neck pain. *J Musculoskelet Pain*. 2004;12:71—81 [Date accessed: Mar 2, 2013].
[63] Gur A, Sarac AJ, Cevik R, Altindag O, Sarac S. Efficacy of 904 nm gallium arsenide low level laser therapy in the management of chronic myofascial pain in the neck: a double-blind and randomize-controlled trial. *Lasers Surg Med*. 2004;35: 229—235.
[64] Ilbuldu E, Cakmak A, Disci R, Aydin R. Comparison of laser, dry needling, and placebo laser treatments in myofascial pain syndrome. *Photomed Laser Surg*. 2004;22: 306—311.
[65] Al-Shenqiti A, Oldham J. *The Use of Low Level Laser Therapy (LLLT) in the Treatment of Trigger Points That Are Associated with Rotator Cuff Tendonitis. Window on the Laser Medicine World*. Bellingham: SPIE-Int Society for Optical Engineering; 2003.
[66] Hakgüder A, Birtane M, Gürcan S, Kokino S, Turan FN. Efficacy of low level laser therapy in myofascial pain syndrome: an algometric and thermographic evaluation. *Lasers Surg Med [serial on the Internet]*; 2003:5. Available at: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/820/CN-00469820/frame.html [Date accessed: Mar 2, 2013].
[67] Gür A, Karakoç M, Nas K, Çevik R, Saraç J, Demir E. Efficacy of low power laser therapy in fibromyalgia: a single-blind, placebo-controlled trial. *Lasers Med Sci*. 2002;17:57—61.
[68] Wong W, Xiao S, Ip WY, Guo X, eds. *Effects of a Laser Acupuncture Therapy on Treating Pain. Proceedings of SPIE—The International Society for Optical Engineering*. 2001. Florence.
[69] Chen SM, Lin CP, Kuan TS, Chen JT, Hong CZ. *Cold Laser Therapy on Myofascial Trigger Points. 8th World Congress of the International Rehabilitation Medicine Association*. Bologna: Monduzzi Editore; 1997:605—610.
[70] Conti PCR. Low level laser therapy in the treatment of temporomandibular disorders (TMD): a double-blind pilot study. *Cranio*. 1997;15:144—149.
[71] Laakso EL, Richardson C, Cramond T. Pain scores and side effects in response to low level laser therapy (LLLT) for myofascial trigger points. *Laser Ther*. 1997;9:67—72.
[72] Lögdberg-Andersson M, Mützell S, Hazel Å. Low level laser therapy (LLLT) of tendinitis and myofascial pains—a randomized, double-blind, controlled study. *Laser Ther*. 1997;9: 79—85.
[73] Papadopoulos ES, Smith RW, Cawley MID, Mani R. Low-level laser therapy does not aid the management of tennis elbow. *Clin Rehabil*. 1996;10:9—11.
[74] Vecchio P, Cave M, King V, Adebajo AO, Smith M, Hazleman BL. A double-blind study of the effectiveness of low-level laser treatment of rotator cuff tendinitis. *Br J Rheumatol*. 1993;32:740—742.
[75] Haker EHK, Lundeberg TCM. Lateral epicondylalgia—report of noneffective midlaser treatment. *Arch Phys Med Rehabil*. 1991;72:984—988.
[76] Haker E, Lundeberg T. Laser treatment applied to acupuncture points in lateral humeral epicondylalgia. A double-blind study. *Pain*. 1990;43:243—247.
[77] Ceccherelli F, Altafini L, Lo Castro G, Avila A, Ambrosio F, Giron GP. Diode laser in cervical myofascial pain: a double-blind study versus placebo. *Clin J Pain*. 1989;5:301—304.
[78] Snyder-Mackler L, Barry AJ, Perkins AI, Soucek MD. Effects of helium—neon laser irradiation on skin resistance and pain in patients with trigger points in the neck or back. *Phys Ther*. 1989;69:336—341.
[79] Waylonis GW, Wilke S, O'Toole D, Waylonis DA, Waylonis DB. Chronic myofascial pain: management by low-output helium—neon laser therapy. *Arch Phys Med Rehabil*. 1988;69: 1017—1020.
[80] Lundeberg T, Haker E, Thomas M. Effect of laser versus placebo in tennis elbow. *Scand J Rehabil Med*. 1987;19: 135—138.
[81] Snyder-Mackler L, Bork C, Bourbon B, Trumbore D. Effect of helium—neon laser on musculoskeletal trigger points. *Phys Ther*. 1986;66:1087—1090.
[82] Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther*. 2003;83:713—721.
[83] Tumilty S, Munn J, McDonough S, Hurley DA, Basford JR, Baxter GD. Low level laser treatment of tendinopathy: a systematic review with meta-analysis. *Photomed Laser Surg*. 2010;28:3—16.
[84] Birch S. Trigger point—acupuncture point correlations revisited. *J Altern Complement Med*. 2003;9:91—103.
[85] Ahn AC, Colbert AP, Anderson BJ, Martinsen OG, Hammerschlag R, Cina S, et al. Electrical properties of acupuncture points and meridians: a systematic review. *Bioelectromagnetics*. 2008;29:245—256.
[86] Melzack R, Stillwell DM, Fox EJ. Trigger points and acupuncture points for pain: correlations and implications. *Pain*. 1977;3:3—23.
[87] Wick F, Wick N, Wick MC. Morphological analysis of human acupuncture points through immunohistochemistry. *Am J Phys Med Rehabil*. 2007;86:7—11.
[88] Han J-S. Acupuncture analgesia: areas of consensus and controversy. *Pain*. 2011;152:S41—S48.
[89] Terrin N, Schmid CH, Lau J. In an empirical evaluation of the funnel plot, researchers could not visually identify publication bias. *J Clin Epidemiol*. 2005;58:894—901.
[90] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924—926.