Low-level laser therapy for chronic non-specific low back pain: a meta-analysis of randomised controlled trials

Gregory Glazov,1,2 Michael Yelland,3 Jon Emery4

ABSTRACT

Objective The efficacy of low-level laser treatment (LLLT) for chronic back pain remains controversial due to insufficient trial data. We aimed to conduct an updated review to determine if LLLT (including laser acupuncture) has specific benefits in chronic non-specific low back pain (CNLBP).

Methods Electronic databases were searched for randomised trials using sham controls and blinded assessment examining the intervention of LLLT in adults with CNLBP. Primary outcomes were pain and global assessment of improvement with up to short-term follow-up. Secondary outcomes were disability, range of back movement, and adverse effects. A random effects meta-analysis was conducted. Subgroup analyses were based on laser dose, duration of baseline pain, and whether or not laser therapy used an acupuncture approach.

Results 15 studies were selected involving 1039 participants. At immediate and short-term follow-up there was significant pain reduction of up to WMD (weighted mean difference) −1.40 cm (95% CI −1.91 to −0.88 cm) in favour of laser treatment, occurring in trials using at least 3 Joules (J) per point, with baseline pain <30 months and in non-acupuncture LLLT trials. Global assessment showed a risk ratio of 2.16 (95% CI 1.61 to 2.90) in favour of laser treatment in the same groups only at immediate follow-up.

Conclusions We demonstrated moderate quality of evidence (GRADE) to support a clinically important benefit in LLLT for CNLBP in the short term, which was only seen following higher laser dose interventions and in participants with a shorter duration of back pain. Rigorously blinded trials using appropriate laser dosage would provide greater certainty around this conclusion.

INTRODUCTION

Chronic non-specific low back pain (CNLBP) not attributable to a recognisable, known specific pathology is common, with an estimated prevalence in developed countries of approximately 23%.1 CNLBP is a major cause of medical expenses, absenteeism, and disability. There are concerns regarding the benefits and potential harms of medications such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), and opioids2,3 for the treatment of chronic back pain, and non-drug treatments including exercise and multidisciplinary and behavioural treatment have been demonstrated to be of benefit.4

Low-level laser therapy (LLLT) is a light source treatment that may act via non-thermal or photochemical reactions in cells. It includes laser acupuncture (LA), which involves focused irradiation at specific points, most commonly traditional acupuncture points, with a low intensity laser.5 LLLT for pain relief in medicine remains controversial with claims that apparent efficacy is due to the placebo effect.

Multiple mechanisms for LLLT analgesia may exist. There is experimental evidence suggesting that laser irradiation induces peripheral neural blockade, suppresses central synaptic activity, modulates neurotransmitters, reduces muscle spasm and interstitial oedema, and exerts anti-inflammatory effects.6 The World Association of Laser Therapy (WALT) has published guidelines for LLLT dosage described in Joules (J) per point for arthritis and tendinopathy.7

A number of meta-analyses since 2003 have reported pain relief from LLLT in painful musculoskeletal conditions.8–10 In 2008, a Cochrane systematic review of laser therapy focusing on non-specific low back pain (LBP)11 included seven trials, considered both acute and chronic pain, did not restrict controls to sham laser, and excluded LA trials. At that point, there
METHODS
This meta-analysis was performed in accordance with the guidelines of the Cochrane Back Review Group (CBRG) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The study protocol is provided in online supplementary data file appendix A.

Eligibility criteria
Studies were randomised controlled trials (RCTs) with blinded assessment of the outcome. Participants were non-pregnant adults with CNLBP. The primary intervention studied was LLLT, including LA. For the purposes of this review, LA studies were defined as those in which low intensity laser was applied to classical acupuncture points, tender points and/or trigger points, and where acupuncture intent was explicitly stated in the report; other studies were classified as non-acupuncture laser therapy. The comparison intervention needed to be sham laser therapy with similar appearance to the active treatment but without laser irradiation. Studies including co-interventions were allowed if applied equally to both laser and control groups. Crossover studies were excluded.

Outcomes
Primary outcomes were: (1) LBP measured by visual analogue scale (VAS) or numerical pain rating scale (NPRS); and (2) ‘global assessment’, which represented dichotomous categorical outcomes of overall improvement or satisfaction with the received intervention. These were measured immediately (<1 week post-treatment) and at short-term (1–12 weeks) follow-up.

Secondary outcomes included disability, quantified using the Oswestry Disability Index (ODI) or the Roland-Morris Disability Questionnaire (RMQ), as well as adverse effects, range of movement (ROM) of the back, and pain or global assessment at intermediate (~6 months) and long-term (~1 year) follow-up.

Search methods for identification of studies
Electronic databases (MEDLINE, PubMed, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Central Register of Controlled Trials (CENTRAL), Allied and Complementary Medicine Database (AMED), and Physiotherapy Evidence Database (PEDro)) were searched for RCTs of laser therapy or LA for the treatment of chronic LBP in which the control treatment used was sham laser. Publication reference lists were additionally examined to identify any missed studies. We used the Updated Search Strategies for CBRG, which included a generic search for RCTs and controlled clinical trials, combined with a specific search for ‘back’ conditions. We completed the search by adding terms related to the laser intervention, as detailed in the online supplementary data file appendix B.

Selection of studies, data extraction and management
Papers were initially screened at title and abstract level by one reviewer (GG) who removed duplicate reports and ineligible trials. There was no restriction of full text by language. Potentially eligible papers were reviewed by pairs of reviewers and data extracted independently. Authors were contacted if possible, to clarify further information. We used RevMan 5.3 (Cochrane Collaboration) for data management and statistical analysis.

Assessment of risk of bias in included studies
We adapted the Cochrane Collaboration tool for assessing risk of bias in 12 domains. Paired reviewers categorised domains as ‘high’, ‘low’ or ‘unclear’ risk of bias; disagreements were resolved by consensus. External reviewers assessed bias in one specific trial for which our reviewers were the authors. Trials were considered to be at ‘higher risk of bias’ if they contained more than six domains of ‘high’ and ‘uncertain’ risk.

Measures of treatment effect
For continuous data (pain intensity, disability, and ROM), treatment effects were expressed as a mean difference (MD) or standardised mean difference (SMD) together with 95% CIs. For global assessment we calculated the risk ratio (RR) and 95% CI. Meta-analysis was used to combine the results of trials using a random-effects model.

Unit of analysis issues
Different pain measurement scales (VAS and NPRS) were converted to a scale of 0–10 cm. In one trial that examined more than one laser dose, in order to avoid ‘double counts’, we split the sham laser control group into two equally sized groups to allow inclusion of two independent comparisons within the meta-analysis.

Missing data, assessment of heterogeneity and publication bias
We used the RevMan calculator to derive unreported statistical data. Where laser parameters were unreported, the following physical formula was used to calculate the dose:

\[
\text{Energy dose (J)} = \text{Watts (W)} \times \text{seconds (secs)};
\]

\[
\text{Energy density (J/cm}^2\text{)} = \text{W} \times \text{secs/area of treated surface or probe tip (cm}^2\text{)};
\]

\[
(\text{W/cm}^2\text{)} = \text{W/area of treated surface or probe tip (cm}^2\text{)}
\]

Heterogeneity was assessed and interpreted as described in the Cochrane Handbook. I² values of

0–40%, 30–60%, and 50–90% were considered to represent ‘unimportant’, ‘moderate’, and ‘substantial’ heterogeneity, respectively. Publication bias was addressed by examination of funnel plots for primary outcomes.

Data synthesis
We conducted meta-analysis for outcomes at immediate and short-term follow-up except where outcomes were reported for two studies or less, in which case results were presented narratively, together with the longer term follow-up. Decisions for conducting subgroup analyses were made at protocol stage based on: (1) acupuncture/non-acupuncture laser therapy; and (2) laser dosage. A post-hoc decision regarding the cut-off value for laser dose and a subgroup analysis for baseline pain duration was guided by consideration of the review findings. A sensitivity analysis was performed excluding trials considered at ‘higher risk of bias’.

Grading the quality of evidence
We followed the CBRG recommendation to adapt the GRADE approach for back reviews with the imprecision, and publication bias).

RESULTS
Search results
Electronic searches of databases from inception until August 2014, and screening reference lists, identified 15 studies that satisfied the inclusion criteria (figure 1). Three papers required translation into English from German and Japanese.

Characteristics of included studies
Participants
The selected trials included 1039 participants at randomisation (table 1). Participants were mostly recruited into trials from hospitals and rehabilitation clinics, except in the case of four trials that recruited via community newspapers. Some trials did not fully describe details of their inclusion criteria for chronicity or specificity. In trials where the mean baseline duration of pain was reported, this was categorised as ‘shorter’ (average range 4.6–27 months) or ‘longer’ (49 months to 13 years).

Interventions
Five trials were classified as LA studies (table 2). Three of these trials used smaller doses of 0.2–1.1 J/point. One trial used a ‘laser needle’ device to deliver 60–180 J/point irradiation, while another used 12 J/point. The remaining 10 trials were classified as non-acupuncture laser therapy studies. Two studies used ≤2.8 J/point, while much higher dosages were used in another two trials (239 and 1200 J/point, respectively). The remaining six trials used doses in the range of 3–25 J/point. Three trials used manual scanning to irradiate larger anatomically defined areas as well as irradiation of discrete points.

Controls
A variety of methods to achieve sham laser controls were reported including use of the same machine with on/off switch, or use of a separate machine and/or probe. Blinding methods included the use of opaque goggles, as well as a specific laser machine capable of blinding both patient and operator to treatment allocation (table 2). In some trials the description of the masking procedure was unclear or completely absent. Only three studies statistically analysed the success of the blinding technique used.

Outcomes
Only four trials defined predetermined primary outcomes. The majority of studies reported pain using a VAS; two studies used an NPRS. Participant based ‘global assessment’ was reported as a dichotomised categorical variable including ‘condition improved’ versus ‘same or worse’ and ‘good response’ versus ‘same or undecided’. Two trials only reported an arbitrary level of improvement on a pain scale (eg, >50% reduction of chronic pain on Von Korff Scale or ≥60% reduction pain on VAS scale). These dichotomous outcomes were combined during meta-analysis to determine the RR of ‘global improvement’. The majority of studies that reported disability used ODI; one trial reported only RMQ. Range of back movement was measured as flexion in centimetres (Schober’s test) or in degrees. Occurrence of adverse effects was briefly mentioned in five trials but quantitative comparisons were only undertaken in three. Most studies reported immediate and/or short-term outcomes; only three studies reported outcomes at longer-term follow-up.

Risk of bias in included studies
Figure 2 demonstrates the proportion of studies determined to be low risk for each domain. Under our criteria we found three trials that we considered to be at ‘higher risk of bias’.

Primary outcomes
Pain
Meta-analysis of data from 653 participants across 10 trials at immediate follow-up indicated a statistically significant reduction in total pain scores in laser versus control groups (WMD (weighted mean difference) −0.79 cm, 95% CI −1.22 to −0.36 cm; I²=70%), albeit with substantial heterogeneity (figure 3).

330

In our subgroup analyses, a significant reduction of pain (laser compared to control) was only seen for the trials in which participants had shorter mean baseline duration (<30 months) of LBP (WMD −1.39 cm, 95% CI −1.71 to −1.07 cm; I²=23%). Significant differences between laser and control were also seen in the higher dose trials (>3 J/point) (WMD −1.23 cm, 95% CI 11.61 to −0.84 cm; I²=51%) and non-acupuncture trials (WMD −1.17 cm, 95% CI −1.60 to 0.74 cm; I²=62%). At short-term follow-up, there were no significant differences and substantial heterogeneity in the total pain score was observed (see six trials, 391 participants; online supplementary data file appendix C). In subgroup analyses we observed a significant reduction of pain (for laser compared to control) with the largest effect seen in higher dose trials and in trials with shorter duration of back pain at baseline (WMD −1.40 cm, 95% CI −1.91 to −0.88 cm; I²=0%).

Global assessment
As illustrated in figure 4, pooling of categorical data at immediate follow-up from 416 subjects (five trials) showed a significant effect on global assessment (RR 1.5, 95% CI 1.10 to 2.04; I²=65%) in favour of laser treatment (substantial heterogeneity present) with a greater improvement in both non-acupuncture and higher dose subgroups (RR 2.16, 95% CI 1.61 to 2.90; I²=0%) with reduced heterogeneity. Pooled data for short-term follow-up showed no significant differences for three included LA trials, two of which used a ‘lower’ dose (see online supplementary data file appendix D).

Sensitivity analysis
Results were robust to exclusion of trials considered at ‘higher risk of bias’ with pain differences in favour of laser in the higher dose subgroup at immediate (WMD...
<table>
<thead>
<tr>
<th>Trial First author (year) (country)</th>
<th>Total group size (n)</th>
<th>Mean age (years)</th>
<th>(1) Clinical inclusion criteria</th>
<th>Baseline mean pain duration</th>
<th>Baseline mean pain intensity: (0–10 cm)</th>
<th>Baseline mean disability ODI (RMQ)</th>
<th>Other baseline variables reported</th>
<th>Outcomes measure (follow-up period(s) post-treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alayat24 (2014) (Saudi Arabia)</td>
<td>52</td>
<td>33</td>
<td>(1) Male patients with history of LBP for at least 1 year (2) Yes</td>
<td>13 months</td>
<td>8.3</td>
<td>34</td>
<td>Bodyweight</td>
<td>Pain, ODI, ROM (immediate, 12 weeks)</td>
</tr>
<tr>
<td>Ay25 (2010) (Turkey)</td>
<td>40</td>
<td>53.5</td>
<td>(1) LBP over 3 months duration due to lumbar disc herniation (2) Yes</td>
<td>49 months</td>
<td>6.3</td>
<td>24(15)</td>
<td>Education level</td>
<td>Pain, ODI, RMQ, ROM, GA (immediate)</td>
</tr>
<tr>
<td>Basford26 (1999) (USA)</td>
<td>63</td>
<td>48</td>
<td>(1) Non-radiating low back pain of &gt;30 days duration (2) Yes</td>
<td>10 months</td>
<td>3.6</td>
<td>23</td>
<td>Degeneration on lumbar X-ray, analgesic use, previous treatment</td>
<td>Pain, ODI, ROM (immediate, 4 weeks)</td>
</tr>
<tr>
<td>Djavid27 (2007) (Iran)</td>
<td>41</td>
<td>37</td>
<td>(1) LBP minimum 12 weeks duration (2) Yes</td>
<td>27 months</td>
<td>6.2</td>
<td>33</td>
<td>Education level, smoking status</td>
<td>Pain, ODI, ROM (immediate, 6 weeks)</td>
</tr>
<tr>
<td>Glazov28 (2009) (Australia)</td>
<td>100</td>
<td>51</td>
<td>(1) LBP at least 3 months duration (2) Yes</td>
<td>11 years</td>
<td>5.7</td>
<td>30</td>
<td>Multiple</td>
<td>Pain, ODI, GA (immediate, 6 weeks, 6 months)</td>
</tr>
<tr>
<td>Glazov18 (2014) (Australia)</td>
<td>144</td>
<td>54</td>
<td>(1) LBP at least 3 months duration (2) Yes</td>
<td>13 years</td>
<td>5.0</td>
<td>27</td>
<td>Multiple</td>
<td>Pain, ODI, GA (immediate, 6 months, 1 year)</td>
</tr>
<tr>
<td>Klein29 (1990) (USA)</td>
<td>20</td>
<td>42</td>
<td>(1) LBP at least 12 months duration (2) Yes</td>
<td>8.5 years</td>
<td>3.2</td>
<td>(5.6)</td>
<td>Nil other</td>
<td>Pain, RMQ, ROM (1 month)</td>
</tr>
<tr>
<td>Konstantinovic30 (2011) (Serbia)</td>
<td>56</td>
<td>69</td>
<td>(1) Geriatric patients with chronic LBP caused by degenerative changes without red flag symptoms (2) NR</td>
<td>4.6 months</td>
<td>6.8</td>
<td>31</td>
<td>Nil other</td>
<td>Pain, ODI, ROM (immediate)</td>
</tr>
<tr>
<td>Lin31 (2012) (Taiwan)</td>
<td>28</td>
<td>64</td>
<td>(1) LBP at least 3 months, recruited from a hospital. ‘Other complications like heart attack, kidney problem, pregnancy, excluded’ (2) NR</td>
<td>NR</td>
<td>5.2</td>
<td>NR</td>
<td>BMI</td>
<td>Pain (immediate)</td>
</tr>
<tr>
<td>Okamoto22 (1989) (Japan)</td>
<td>69</td>
<td>57</td>
<td>(1) ‘Patients admitted to hospital with LBP,… pregnant, lactating, recent surgery, immune suppressants, difficult to treat excluded’ (2) NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>Nil other</td>
<td>GA (immediate)</td>
</tr>
<tr>
<td>Ruth21 (2010) (Germany)</td>
<td>111</td>
<td>59</td>
<td>(1) LBP over 6 months duration (2) Yes</td>
<td>10 years</td>
<td>6.3*</td>
<td>NR</td>
<td>Employment status</td>
<td>GA (pain, disability)* (12 weeks)</td>
</tr>
<tr>
<td>Soriano32 (1998) (Argentina)</td>
<td>85</td>
<td>64</td>
<td>(1) LBP duration over 3 months (2) Yes</td>
<td>NR</td>
<td>8.0</td>
<td>NR</td>
<td>Nil other</td>
<td>GA (immediate)</td>
</tr>
</tbody>
</table>
Similar findings were shown in non-acupuncture and ‘short duration’ subgroups. There were no trials at ‘higher risk of bias’ that reported global assessment outcomes.

**Secondary outcomes**

Intermediate and long-term pain and global assessment

Two trials (both low dose LA) reported outcomes at 6 months and at 12 months. They found no significant difference between groups for pain or global assessment at these time periods. One trial reported less relapse of pain in the laser group at 6 months used an unvalidated outcome.

**Disability**

Analysis of data from 490 subjects (eight trials) at immediate follow-up found a small reduction in combined ODI score in laser versus control (WMD −2.5%, 95% CI −4.6% to −0.4%; $I^2=47%$; see online supplementary data file appendix F). Subgroup analyses showed greater benefit of laser in non-acupuncture trials (WMD −3.5%, 95% CI −6.0% to −1.5%; $I^2=33%$), and those applying higher dose treatment and/or including subjects with a shorter duration of back pain (WMD −3.6%, 95% CI −6.1% to −1.1%; $I^2=48%$). Combined data from 383 subjects (six trials) at short-term follow-up found no significant difference, but subgroup analyses found greater benefit up to a WMD of −5.9% (95% CI −8.9% to −2.8%; $I^2=64%$) in the same groups.

**Range of back movement**

ROM was measured only in the non-acupuncture trials.24–27, 29, 30 One trial found a significant difference of 4° flexion in favour of laser in the short-term.

**Adverse effects**

Brief reference to the absence of adverse effects was made in six trials.25, 26, 29, 32–34 Quantitative comparison (including flares of pain and other minor adverse effects) was undertaken in three studies that showed no significant difference between laser and control.

**Risk of publication bias**

We plotted the effect sizes from trials that reported pain at immediate or short-term follow-up against the inverse of their standard error (see online supplementary data file appendix G). Visual inspection of the funnel plot did not show asymmetry suggestive of ‘small study bias’.

**Quality of evidence**

We reached the conclusion that there was moderate quality evidence (GRADE profile) that laser therapy reduces pain in the immediate and short term in subjects with CNLBP if pain has been present for...
<table>
<thead>
<tr>
<th>Trial</th>
<th>Laser diode</th>
<th>Wavelength (nm)</th>
<th>Dose/point (J)</th>
<th>Mean laser power (mW)</th>
<th>Energy density (J/cm²)</th>
<th>Power density (W/cm²)</th>
<th>Sessions/weeks</th>
<th>Points treated</th>
<th>Time (s)</th>
<th>Co-intervention</th>
<th>Details of sham control</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Alayat</em> (2014)</td>
<td>Nd:YAG</td>
<td>1064</td>
<td>25</td>
<td>1786 (3 kW)</td>
<td>0.61</td>
<td>8.9</td>
<td>12/4</td>
<td>8</td>
<td>14</td>
<td>Exercise</td>
<td>No description of control device or if separate device used. Success of blinding not reported</td>
</tr>
<tr>
<td>Ay (2010)</td>
<td>GaAlAs</td>
<td>805</td>
<td>2.8</td>
<td>12 (100 mW)</td>
<td>40</td>
<td>1.4</td>
<td>15/3</td>
<td>2–4</td>
<td>240</td>
<td>Hot packs</td>
<td>Control used same machine without turning on device. Success of blinding not reported</td>
</tr>
<tr>
<td>†Basford (1999)</td>
<td>Nd:YAG</td>
<td>1060</td>
<td>239</td>
<td>2660</td>
<td>49</td>
<td>0.542</td>
<td>12/4</td>
<td>8</td>
<td>90</td>
<td>Nil</td>
<td>Control irradiated by the same but inactive probes. Not clear if separate machine used. Success of blinding not reported (there was a tendency for patients to experience ‘more warmth with active treatment’)</td>
</tr>
<tr>
<td>†Djavid (2007)</td>
<td>GaAlAs</td>
<td>810</td>
<td>&lt;7.5</td>
<td>50</td>
<td>27</td>
<td>8.2</td>
<td>12/6</td>
<td>8</td>
<td>150</td>
<td>Exercise</td>
<td>Control was irradiated with inactive probes. Not clear if separate machines used. Procedure to ensure masking not described, and success of blinding not reported</td>
</tr>
<tr>
<td>§Glazov (2009)</td>
<td>GaAlAs</td>
<td>830</td>
<td>0.2</td>
<td>10</td>
<td>1</td>
<td>0.05</td>
<td>10/10</td>
<td>8</td>
<td>20</td>
<td>Exercise</td>
<td>Control group had the same procedure as the laser group but without laser radiation. No other details given. Success of blinding not reported</td>
</tr>
<tr>
<td>§Glazov (2014)</td>
<td>GaAlAs</td>
<td>830</td>
<td>0.2</td>
<td>20</td>
<td>1, 4</td>
<td>0.1</td>
<td>8/8</td>
<td>9</td>
<td>10, 40</td>
<td>Nil</td>
<td>No description of control device or if separate device used. Success of blinding not reported</td>
</tr>
<tr>
<td>‡Klein (1990)</td>
<td>GaAs</td>
<td>904</td>
<td>1.3</td>
<td>5.4</td>
<td>1.3</td>
<td>0.005</td>
<td>12/4</td>
<td>50</td>
<td>240</td>
<td>Exercise</td>
<td>Machine was modified by manufacturer with a toggle switch with two settings, only one of which activated the laser. Single device used. Success of blinding not reported</td>
</tr>
<tr>
<td>Konstant-inovic (2011)</td>
<td>GaAs</td>
<td>905</td>
<td>3</td>
<td>100</td>
<td>3</td>
<td>0.1</td>
<td>15/3</td>
<td>4</td>
<td>60</td>
<td>Exercise</td>
<td>Two machines were used labelled A or B; one with active laser, another deactivated. Patients and therapist treating the patients could not distinguish which was active or control. Success of blinding not reported</td>
</tr>
<tr>
<td><strong>Lin</strong> (2012)</td>
<td>NR</td>
<td>808</td>
<td>12</td>
<td>20 (40 mW)</td>
<td>15</td>
<td>0.025</td>
<td>5/1</td>
<td>4</td>
<td>600</td>
<td>Soft cupping</td>
<td>Control group had the same procedure as the laser group but without laser radiation. No other details given. Success of blinding not reported</td>
</tr>
<tr>
<td>Okamoto (1989)</td>
<td>GaAlAs</td>
<td>830</td>
<td>18</td>
<td>30</td>
<td>143</td>
<td>0.24</td>
<td>10/3</td>
<td>1</td>
<td>600</td>
<td>Nil</td>
<td>Two machines of identical appearance used (A and B) corresponding to laser or placebo laser; each had decoy with light and sound. No other details given in paper. Success of blinding not reported</td>
</tr>
<tr>
<td>††Ruth (2010)</td>
<td>NR</td>
<td>680, 785</td>
<td>60–180</td>
<td>50–150</td>
<td>?</td>
<td>1–5</td>
<td>10/5</td>
<td>8</td>
<td>1200</td>
<td>Nil</td>
<td>Toggle switch on same machine operated by independent person according to randomisation list. Goggles on participants, and controls on machine covered by opaque black tape. Success of blinding confirmed by statistical analysis</td>
</tr>
<tr>
<td>†‡Soriano (1998)</td>
<td>GaAs</td>
<td>904</td>
<td>4</td>
<td>0.95</td>
<td>40</td>
<td>4.2</td>
<td>0.04</td>
<td>10/2</td>
<td>?</td>
<td>Nil</td>
<td>Used an activated laser and a deactivated laser but the electrical circuit, timer and alarm worked as usual. Not clear if separate devices used. Success of blinding not reported</td>
</tr>
</tbody>
</table>
## Table 2

Continued

<table>
<thead>
<tr>
<th>Trial</th>
<th>Laser diode</th>
<th>Pulse mode</th>
<th>Wavelength (nm)</th>
<th>Dose/point (J)</th>
<th>Mean laser power (mW) (peak power)</th>
<th>Energy density (J/cm²)</th>
<th>Power density (W/cm²)</th>
<th>Sessions/weeks</th>
<th>Points treated per session</th>
<th>Time (s)</th>
<th>Co-intervention</th>
<th>Details of sham control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umegaki²³ (1989)</td>
<td>GaAlAs</td>
<td>Continuous</td>
<td>830</td>
<td>18</td>
<td>30</td>
<td>143</td>
<td>0.24</td>
<td>10/3</td>
<td>2</td>
<td>30</td>
<td>Nil</td>
<td>Two machines of identical appearance used (A and B) corresponding to laser or placebo laser; each had decoy with light and sound. No other details given in paper. Success of blinding not reported</td>
</tr>
<tr>
<td>Vallone³³ (2014)</td>
<td>GaAlAs</td>
<td>Continuous</td>
<td>980</td>
<td>1200</td>
<td>2000</td>
<td>37.5</td>
<td>0.625</td>
<td>9/3</td>
<td>6</td>
<td>60</td>
<td>Exercise</td>
<td>Dials showing the on/off power setting of machine were not within view of subjects. Success of blinding not reported</td>
</tr>
<tr>
<td>Wallace³⁴ (1996)</td>
<td>GaAlAs</td>
<td>Continuous</td>
<td>830</td>
<td>1.1</td>
<td>37</td>
<td>2.64</td>
<td>0.09</td>
<td>5/5</td>
<td>8</td>
<td>30</td>
<td>Nil</td>
<td>Independent assistant operated and covered the coded switch on laser machine determining if laser on or off. Appearance of machine the same regardless of laser output. Success of blinding not reported</td>
</tr>
</tbody>
</table>

Entries in bold were not reported/unavailable and were calculated or assumed by reviewers.

*High intensity laser therapy*. Also included manual scanning of fields (2×1400 J). Total dose/session 3000 J.
†Laser device allowed simultaneous stimulation of two points.
‡Total treatment duration 20 mins including eight points and manual scanning of standardised field (time differential not reported but assume <150 s per discrete point). Total dose/session 60 J.
§†Laser/sham mode set by operating a number on dial. Probe had decoy light/sound device inbuilt. Individualised treatment (average 8–9 points/session) including local and distal GV, BL and GB points and ah shi points.
¶Multi-head device stimulating 10 points simultaneously.
**Multi-channel device. Simultaneous stimulation of four points (bilateral BL40 and two ah shi points in lumbar region).**
††‘Laser needle’ fibre-optic cable device. Simultaneous stimulation of eight points (individualised treatment including BL23, BL40, BL60, KI3, GB and ah shi points). Same author previously described³⁴ laser output tip diameters 2.0 and 0.8 mm (=power density 1 W/cm² and 5 W/cm², respectively.
‡‡‘2 cm grid in painful area’ (number of points and irradiation time per point unreported). Spot size given as 0.0015 cm² but 1.1 cm² with irradiation time 100 s according to Cochrane review.¹¹
§§Unclear if manual scanning used.
¶¶Individualised treatment: local (BL26, ah shi points, GV2) and distal (GV14, BL11, LR3, BL60, LI4, ST36, SP6, PC6, HT7).
NR, not reported.
<30 months or if a laser dose of at least 3 J/point is used (see online supplementary data file appendix H). The overall quality of evidence for this outcome was reduced due to limitations in the domain involving risk of bias. For the outcome of global assessment at immediate follow-up, the evidence of benefit of laser
therapy was further reduced to low quality due to uncertainty in details of duration and specificity of LBP in trials and laser intervention parameters in a trial reporting this outcome.

DISCUSSION

This meta-analysis summarised RCTs that compared the effect of low-level laser with sham controls for the treatment of CNLBP. While combining data from all trials, the authors found that low-level laser therapy was more effective than sham controls for pain relief in the short term. However, the quality of the evidence was low due to methodological issues such as insufficient blinding and imprecise reporting of intervention details.

Figure 3: Forest plots: subgroup analysis of pain at immediate follow-up. LA, laser acupuncture.
clinically heterogeneous studies demonstrated a small benefit, subgroup analyses showed larger positive effects of laser on pain, global assessment and disability present up to 12 weeks after treatment, particularly in trials with higher laser dose interventions. The effect size of the pain reduction (over sham) of 1.4 cm in these subgroups approached the minimally important change (MIC) for pain proposed by Ostelo\textsuperscript{36} of 1.5 cm. Disability (ODI) reduction was significant in the short term but less than the MIC of 10%\textsuperscript{36}. In this review, the mean pain reduction in the placebo laser groups averaged approximately 2.0 cm. The total average pain reduction between baseline and short-term follow-up, representing both non-specific
and specific effects of the laser intervention, was about 60%. Our results are consistent with previous findings suggesting benefits of low-level laser in a range of painful musculoskeletal conditions including chronic neck pain. In the trials we examined there appeared to be a dose threshold of 3 J/point for benefit of laser. This is higher than the minimal dose suggested by reviews by Baxter (0.5 J/point for myofascial pain) and Chow (0.8 J/point for chronic neck pain), but closer to the dose recommended by WALT (4 J/point for lumbar spine arthritis). This could be explained by the deeper location of structures in the low back area, requiring a higher laser irradiation dose for penetration. There was no upper dose at which laser appeared not to be effective or caused adverse effects.

Our review also found a relationship between duration of pain and laser effectiveness. This finding is plausible but needs to be explored in further research. Two previous studies examining physical treatment for back pain and acupuncture for chronic pain conditions showed a generally worse outcome for subjects with longer pain duration, but no interaction effect with type of treatment. Acute pain is more likely to resolve spontaneously than chronic pain and, once central sensitisation occurs, a condition may become unresponsive to LLLT.

Most (eight out of 10) non-acupuncture laser therapy trials were positive, that is, they showed a difference between laser and sham groups in primary outcomes; negative trials in this group treated participants with a longer duration of pain with a lower dose. Most non-acupuncture laser trials in this review treated relatively few points in the area of pain, although some also irradiated wider areas using a manual scanning technique. Skin surface application of laser results in photon scattering in the underlying volume of tissue, resulting in more widespread biological effects regardless of the intent of the therapist to stimulate acupuncture points, ah shi points or local anatomical structures. Acupuncturists and other laser therapists both irradiate tender points in the region of pain; the absence of positive acupuncture trials in this review could be related to small laser dosage and other factors unrelated to the approach to treatment. We were not able to determine why two higher dose LA trials were negative in this review.

Heterogeneity of studies and insufficient data were quoted as reasons for the previous inability to establish firm conclusions on the effect of LLLT for LBP. A strength of our review was the larger number of trials and inclusion of more recent eligible publications since the last such review, as well as exclusion of acute back pain and trials without sham laser controls, thus reducing heterogeneity and allowing the study of specific laser effects. Subgroup analysis was important in explaining the heterogeneity.

A major limitation of this review was related to bias from possible unmasking. Low risk of bias in all blinding domains according to the Cochrane tool was present in only about 60% of trials. In positive trials, the success of blinding was not tested and there were other possible deficiencies in blinding. Subject awareness of thermal sensation in trials with higher power devices is possible, which may potentially have unmasked the patients to treatment allocation. These issues arguably reduce the ability of this review to draw firm conclusions. Inadequate reporting of the characteristics of participants and laser parameters also produced uncertainty.

It is critical that rigorous blinding is instituted in any further clinical trials investigating laser therapy for the treatment of pain. The appropriate laser dose range for specific body regions (as recommended by WALT) should be followed, and full and explicit description of the laser parameters, treatment regimen, and baseline characteristics of the participants is important. Future studies may also establish the role of other components of the intervention such as the number and/or location of points, frequency/duration of treatment, and the effect of longer-term follow-up on outcomes. Our meta-analysis suggests that LLLT, when used by itself or in combination with other modalities, may achieve a useful reduction in pain for up to 3 months in CNLBP with few adverse effects. However, we would recommend a degree of caution before widespread implementation, until our results can be confirmed by further rigorously blinded trials using adequate laser doses.

**Summary points**

- This updated systematic review examined the effectiveness of low-level laser therapy compared to sham laser in the treatment of chronic non-specific low back pain.
- There was substantial clinical heterogeneity present between the 15 included trials, related to differences in both participant characteristics and laser interventions.
- Meta-analysis showed a clinically important pain reduction in laser versus sham lasting up to 12 weeks post-completion of treatment (WMD $-1.40$ cm, 95% CI $-1.91$ to $-0.88$ cm).
- Pain reduction occurred in subgroups with non-acupuncture laser interventions, laser dosage $\geq 3$ J per point, and in participants with a shorter duration of baseline pain (30 months).
- Further trials using strict masking and adequate laser doses are needed to ensure that the apparent benefits of laser are not due to bias related to unblinding of participants.
Acknowledgements  The authors would like to thank external reviewers Roberta Chow and Philip Gabel for assessing our own trial, and Yoshi Inoue for helping with the Japanese translation.

Contributors  GG was the doctoral candidate and lead author and was responsible for the conceptualisation of the protocol and conduct of the review. MY and JE made substantial contributions to the design of the work, drafted and critically revised the manuscript for important intellectual content, and agree to be accountable for the content of the work. All authors approved the final version of the manuscript.

Competing interests  None declared.

Provenance and peer review  Not commissioned; externally peer reviewed.

Data sharing statement  Data sharing on this research article is available on request from the corresponding author.

Open Access  This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

REFERENCES


