

Osteoarthritis and Cartilage



Review

Effectiveness of low-level laser therapy in patients with knee osteoarthritis: a systematic review and meta-analysis

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ARTICLE INFO

Article history:

Received 5 January 2015

Accepted 2 April 2015

Keywords:

Knee osteoarthritis
Low-level laser therapy
Pain
WOMAC

SUMMARY

Objective: To investigate the efficacy of low-level laser therapy (LLLT) treatment of knee osteoarthritis (KOA) by a systematic literature search with meta-analyses on selected studies.

Design: MEDLINE, EMBASE, ISI Web of Science and Cochrane Library were systematically searched from January 2000 to November 2014. Included studies were randomized controlled trials (RCTs) written in English that compared LLLT (at least eight treatment sessions) with sham laser in KOA patients. The efficacy effective size was estimated by the standardized mean difference (SMD). Standard fixed or random-effects meta-analysis was used, and inconsistency was evaluated by the I-squared index (I²).

Results: Of 612 studies, nine RCTs (seven double-blind, two single-blind, totaling 518 patients) met the criteria for inclusion. Based on seven studies, the SMD in visual analog scale (VAS) pain score right after therapy (RAT) (within 2 weeks after the therapy) was not significantly different between LLLT and control (SMD = -0.28 [95% CI = -0.66, 0.10], I² = 66%). No significant difference was identified in studies conforming to the World Association of Laser Therapy (WALT) recommendations (four studies) or on the basis of OA severity. There was no significant difference in the delayed response (12 weeks after end of therapy) between LLLT and control in VAS pain (five studies). Similarly, there was no evidence of LLLT effectiveness based on Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain, stiffness or function outcomes (five and three studies had outcome data right after and 12 weeks after therapy respectively).

Conclusion: Our findings indicate that the best available current evidence does not support the effectiveness of LLLT as a therapy for patients with KOA.

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Introduction

There are still no disease-modifying treatments for knee osteoarthritis (KOA). The currently available options include palliative pharmacological and non-pharmacological modalities. The core goal of these treatments is to relieve joint pain, improve joint function and gain a better quality of life. Though nonsteroidal anti-

inflammatory drugs (NSAIDs) are widely used to treat these patients, their high incidence of side effects, especially of the upper gastrointestinal tract, has limited their use¹. Thus, many physical therapy agents such as ultrasound², electrical stimulation³, strengthening exercise⁴ and thermal therapy⁵ have been introduced.

Because of its non-invasiveness and advantage of inciting nearly no adverse side effects, low-level laser therapy (LLLT) has

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been widely used to relieve pain in different musculoskeletal disorders^{6,7}. It has been considered a promising therapeutic intervention, mainly because of its stimulatory effects on tissue metabolism and ability to modulate the inflammatory process after injury. Some reported effects include improved cellular oxygenation, release of neurotransmitter associated with pain modulation and release of anti-inflammatory, endogenous mediators⁸. Nonetheless, reported clinical therapeutic outcomes are conflicting. Studies are similarly conflicting regarding its usage in patients with KOA^{9,10}.

Recently there has been an increased number of randomized controlled trials (RCTs) assessing the effectiveness of LLLT in patients with KOA; they have not yet been integrated into a systematic review or meta-analysis. Therefore, the aim of this study was to evaluate, through a systematic review and meta-analysis, the effectiveness of LLLT on symptoms and function in patients with KOA.

Method

Search strategy and study selection

The following bibliographic databases were searched up to 11th November 2014: Medline via PubMed from 2000, EMBASE via OVID from 2000, Web of Science from 2000 as well as the Cochrane Central Register of Controlled Trials. The search strategy was: (Osteoarthritis OR osteoarthros*) AND (knee) AND (low-level laser therapy OR low intensity laser therapy OR low energy laser therapy OR LLLT OR LILT OR LEIT OR infrared laser OR IR laser OR diode laser).

Two reviewers independently identified titles and abstracts relevant to applying LLLT to patients suffering from KOA. Full texts of the published articles, unpublished articles as well as unpublished data of completely finished and analyzed studies were included. The reference list of the full-text articles was also reviewed. To be included in this analysis, studies had to meet the following criteria: (1) be RCTs; (2) involve patients with KOA (as assessed with radiography or according to the American College of Rheumatology guidelines); (3) compare LLLT and placebo laser; (4) report pain and/or function outcomes of patients; (5) attain a PEDro score¹¹ of >5 ; and (6) be written in English. Trials with an unbalanced additional modality (e.g., education or exercise) between groups were excluded.

Quality assessment

Two independent reviewers assessed study quality or risk of bias in each study using the PEDro scale¹¹. The 11-point PEDro scale has been accepted as a reliable¹² and valid¹³ assessment tool and is the one most often employed for physical treatments. Briefly, a study with a score of ≥ 7 is considered to be of high methodological quality, while a study with a score of ≤ 5 is considered to be of low methodological quality. The methodological assessment was conducted by two independent reviewers and results compared. Discrepancies between the two independent reviewers were resolved by consensus after discussion, and a third reviewer was consulted if necessary.

Data extraction

Study data were extracted by two reviewers and checked for accuracy by a third reviewer including the intervention description, inclusion/exclusion criteria, baseline data, values for all outcomes at baseline, post-intervention and later follow-up (12 weeks). The

primary outcomes of interest were the visual analog scale (VAS) pain scores (right after the intervention meaning within 2 weeks after the final therapy session), expressed in millimeters, and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores (pain, stiffness, function and total; right after the intervention). The secondary outcomes of interest were range of motion (ROM) right after therapy (RAT), and VAS pain and WOMAC scores (pain, stiffness and function) at or near 12 weeks after therapy. If the data were not presented in the study as mean and standard deviation, or were presented in a form that prevented calculation of mean and standard deviation, the original authors were contacted.

Statistical analysis

We performed the meta-analysis in conformance with the Cochrane Collaboration and the Quality of Reporting of Meta-analysis guidelines. Because all the primary and secondary outcomes were continuous outcome data, means and standard deviations were used to calculate a standard mean difference (SMD) and 95% confidence interval (CI) in the meta-analysis. We checked all results for clinical and statistical heterogeneity. Clinical heterogeneity, determined by Chi-squared test, was evaluated based on the study baseline, interventions, definition of outcome measures, concomitant treatment and follow-up. A P value <0.05 was considered significantly different. I^2 values were used for the evaluation of statistical heterogeneity (I^2 -of 50% or more indicating presence of heterogeneity)^{14,15}. We used a standard random-effects meta-analysis for the main analyses. Results right after therapy refer to the comparison of LLLT and placebo after the series of therapy sessions ranging from 8 to 20 over 2–6 weeks. Results after 12 weeks of therapy refer to the evaluation of a delayed or maintained response approximately 12 weeks after the last treatment session. A fixed-effects model was applied for the purpose of sensitivity analysis. Data were presented as a forest plot. We analyzed the effect of LLLT in subgroups distinguished by adherence to World Association of Laser Therapy (WALT) guidelines^{16,17} and KOA severity¹⁸. Analyses were conducted using Review Manager Version 5.3 for MAC (The Nordic Cochrane Centre, The Cochrane Collaboration).

Results

Study selection and characteristics

Figure 1 illustrates the selection process for including studies in this meta-analysis. In total, 612 potential studies were found. Based on the title and abstract content, 595 of these studies were excluded. The full texts of the remaining 17 studies were read, and a further eight studies were excluded, resulting in nine studies^{19–27} retained in the qualitative and quantitative synthesis of this review. A total of 518 patients were included: 264 patients in the LLLT group and 254 patients in the placebo group. In keeping with the WALT recommendations^{16,17}, each of these studies provided at least eight therapy sessions (range 8–20) over the course of 2–6 weeks. The characteristics of the included studies are listed in Tables I and II. Each of these studies included a placebo laser arm consisting of sham laser. The methodological quality assessment (Supplemental Table 1) showed that all these nine studies were of high quality (PEDro score of ≥ 7). All outcomes with appropriately reported data were extracted and included in the meta-analysis. Outcome measures were grouped according to their construct and design (Tables III and IV).

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