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Technology Assessment Update - Low Level Laser Therapy for Musculoskeletal Disorders

Low level laser therapy (LLLT) is a noninvasive treatment that involves the application of light from a low-intensity laser at a specific wavelength. L&I reviewed the technology for various musculoskeletal (MSK) conditions in 2004 and made a non-coverage decision.

The efficacy and the mechanism(s) of action of LLLT have not been established, although there have been many trials on LLLT conducted and published since the last review. In addition, there is no standardized protocol (e.g., dose, number of treatments, duration of treatment) for performing LLLT in treating MSK conditions. The purpose of this document is to review the new evidence and assess the effectiveness and harm of LLLT for treating MSK conditions. We focused on randomized controlled trials (RCTs) by reviewing relevant systematic reviews and meta-analyses. Six systematic reviews were found and reviewed.

A. Evidence reviewed

We searched Cochrane Database of Systematic Reviews and found three relevant systematic reviews on LLLT for MSK disorders. One of them (Brosseau et al. 2007) was withdrawn due to incompleteness in evidence collection and errors in data extraction. We reviewed the other two (Rankin et al. 2017; Yousefi-Nooraie et al. 2008) in detail.

We searched Hayes' database and assessed three systematic reviews on LLLT for MSK disorders, including carpal tunnel syndrome (Hayes, Inc. 2016, updated 2017), joint pain (Hayes, Inc. 2008, update 2012) and soft tissue pain (Hayes, Inc. 2008, updated 2012).

A recent systematic review on LLLT for pain in patients with MSK disorders (Clijisen et al. 2017) found in PubMed was also reviewed.

B. Quality assessment of the systematic reviews

The quality (Good, Fair or Poor) of the systematic reviews was assessed using the [quality assessment tool](#) developed by the NIH National Heart, Lung and Blood Institute. All the systematic reviews assessed have either good or fair quality.

C. Summary of the evidence

1. LLLT on pain in patients with MSK disorders or soft tissue pain

1.1. (Clijisen et al. 2017) – Good quality

The meta-analysis includes 18 RCTs comparing the effect of LLLT on pain in patients with different MSK disorders. From the 21 head-to-head comparisons, 17 favored LLLT while four comparisons (extracted from three studies) reported no beneficial effects of LLLT on pain. The overall weighted raw mean difference (*D*) in pain between LLLT and the control groups was -0.85 [95% CI: -1.22 to -0.48] ($P < 0.001$). Heterogeneity of the studies was high ($I^2 = 85.6\%$) and statistically significant (Cochran's $Q = 139.2$; $df = 20$; $P < 0.001$).

The authors concluded that “LLLT appears to be an effective treatment modality to achieve pain relief in adult patients with MSK disorders”. Though this is a meta-analysis of good quality, there are several limitations with the results. 1). the heterogeneity of the studies included was quite high ($I^2 = 85.6\%$); 2). The overall weighted raw mean difference in pain was difficult to interpret, because it was derived from 18 studies with 7 different comparators for 13 different pain conditions; 3). The overall weighted raw mean difference was small and may not be meaningful clinically.

1.2. (Hayes, Inc. 2008, Updated in 2012) – Fair quality

Evidence evaluated in this report covers the years 2005 to February 2008, and was updated in 2012. The previous version of this report covered literature published between 1980 and July 2005. Only randomized placebo-controlled trials and meta-analyses of randomized placebo-controlled trials were considered for inclusion. Eighteen trials of LLLT for different indications were selected for detailed analysis, including: Achilles tendinopathy (2 trials); ankle sprain (1 trial); carpal tunnel syndrome (3 trials); lateral epicondylitis (5 trials); low back pain (2 trials); and neck and/or shoulder girdle pain (5 trials).

Authors' conclusion: the available RCTs of LLLT reported a mix of negative (no effect) and positive results for a variety of soft tissue pain conditions, which can be summarized by indication as follows: (1) Achilles tendinopathy, very positive in younger, athletic patients but otherwise negative; (2) ankle sprain, negative; (3) carpal tunnel syndrome, conflicting but on balance negative; (4) lateral epicondylitis, conflicting but best study strongly positive; (5) low back pain, small positive effect according to sparse evidence; and (6) neck/shoulder girdle pain, on balance positive with an apparent correspondence between positive results and number of spots treated. The trials addressing each indication had several limitations. Possible combinations of treatment parameters far exceed those tested in the trials that were selected, and data relevant to specific combinations of dose, wavelength, and spot number/size were sparse. LLLT appears to be safe, but no long-term assessment has been made. The authors concluded that low-quality, inconsistent evidence showing potentially improved outcomes for treatment of pain and

disability due to Achilles tendinopathy, lateral epicondylitis, low back pain, and myofascial pain syndrome or similar symptomatology in the neck and shoulder girdle region, but substantial uncertainty remains regarding the extent of treatment benefit in comparison with other treatment modalities, long-term health benefits, safety, and patient selection criteria. There is limited evidence of no benefit or no benefit beyond end of treatment for treatment of pain and disability due to ankle sprain or carpal tunnel syndrome.

We believe there are several limitations with the conclusions. 1). the quality of RCTs included was not assessed explicitly in the systematic review. The authors seemed to assume the quality of these studies was equally good because they were RCTs; 2). Some conclusions were made based on very limited number of studies. For example, there were two studies reviewed for Achilles tendinopathy, one showed positive results and the other had negative results; 3). No meta-analysis done on multiple studies for specific indications; 4). Short term follow-up for most of the studies; 5). The effect size was small if any, and it is uncertain about clinical significance.

2. LLLT on carpal tunnel syndrome

2.1. (Rankin et al. 2017) – Good quality

The authors identified 22 trials randomizing 1153 participants that were eligible for inclusion; nine trials (525 participants, 256 randomized to LLLT) compared LLLT with placebo, two (150 participants, 75 randomized to LLLT) compared LLLT with ultrasound, one compared LLLT with placebo and LLLT with ultrasound, two compared LLLT with steroid injection, and one trial each compared LLLT with other non-surgical interventions: fascial manipulation, application of a pulsed magnetic field, transcutaneous electrical nerve stimulation (TENS), steroid injection, tendon gliding exercises, and applying a wrist splint combined with non-steroidal anti-inflammatory drugs. Three studies compared LLLT as part of multiple interventions. Risk of bias varied across the studies, but was high or unclear in most assessed domains in most studies. Most studies were small, with few events, and effect estimates were generally imprecise and inconsistent; the combination of these factors led the authors to categorize the quality of evidence for most outcomes as very low or low.

The authors concluded that evidence is of very low quality and they found no data to support any clinical effect of LLLT in treating CTS. Only VAS pain and finger-pinch strength met previously published MCIDs but these are likely to be overestimates of effect given the small studies and significant risk of bias. There is low or very low-quality evidence to suggest that LLLT is less effective than ultrasound in the management of CTS based on short-term, clinically significant improvements in pain and finger-pinch strength. There is insufficient evidence to support LLLT being better or worse than any other type of non-surgical treatment in the management of CTS. Any further research of LLLT should be definitive, blinded, and of high quality.

2.2. (Hayes, Inc. 2017) – Fair quality

A total of 11 RCTs met predefined inclusion criteria and answered 1 or more relevant questions. Of the eligible RCTs, 6 evaluated LLLT compared with sham laser for the treatment of mild to moderate carpal tunnel syndrome (CTS) in adults. Six RCTs also evaluated LLLT compared with an active control, including ultrasound, splinting, or steroid injections either alone or in combination with another conservative treatment. All studies evaluated LLLT for the treatment of mild to moderate CTS in adults.

Results were conflicting regarding the efficacy and comparative effectiveness of LLLT compared with sham laser, ultrasound, or splinting for the treatment of mild to moderate CTS. For all outcomes, there were unexplained inconsistencies across studies when comparing LLLT with sham laser. In 3 RCTs comparing LLLT with ultrasound, inconsistencies in comparative effectiveness exist. In general, patients treated with LLLT reported improved clinical symptoms and nerve conduction compared with baseline, as did patients in control groups. Evaluations of safety were limited and were only reported in 2 RCTs. Long term follow-up was not evaluated in any study. The authors concluded that there was low-quality and inconsistent evidence showing potentially improved outcomes among patients with mild to moderate CTS receiving LLLT either alone or in combination with other conservative treatments. Substantial uncertainty remains regarding the extent of treatment benefit in comparison with other treatment modalities, long-term health benefits, safety, and patient selection criteria. The evidence for LLLT for treatment of severe CTS in adults was lacking.

3. LLLT on non-specific lower back pain

3.1. (Yousefi-Nooraie et al. 2008) – Good quality

Seven heterogeneous English language RCTs with reasonable quality were included. Three small studies (168 people) separately showed statistically significant but clinically unimportant pain relief for LLLT versus sham therapy for sub-acute and chronic low-back pain at short-term and intermediate-term follow-up (up to six months). One study (56 people) showed that LLLT was more effective than sham at reducing disability in the short term. Three studies (102 people) reported that LLLT plus exercise were not better than exercise, with or without sham in the short-term in reducing pain or disability. Two studies (90 people) reported that LLLT was not more effective than exercise, with or without sham in reducing pain or disability in the short term. Two small trials (151 people) independently found that the relapse rate in the LLLT group was significantly lower than in the control group at the six-month follow-up.

No side effects were reported.

The authors concluded that based on the heterogeneity of the populations, interventions and comparison groups, there are insufficient data to draw firm conclusions on the clinical effect of LLLT for low-back pain. There is a need for further methodologically rigorous RCTs to evaluate the effects of LLLT compared to other treatments, different lengths of treatment, wavelengths and dosages.

4. LLLT on joint pain

4.1. (Hayes, Inc. 2008, update 2012) - Fair quality

This updated report covers literature published in the years 2005 to February 2008 (the previous version of this report covered literature published between 1980 and July 2005) including eight studies: six original blinded, placebo-controlled, randomized trials and two meta-analyses of such trials. Four of the original trials and one meta-analysis applied LLLT to knee osteoarthritis. Another original trial applied LLLT to hand osteoarthritis. One meta-analysis of trials of LLLT for rheumatoid arthritis was selected. A single trial of LLLT for patellar chondromalacia was selected. Pain assessment for all indications was typically made according to a visual analog scale (VAS). Numerous tools were used for assessment of function or disability.

The authors concluded that evidence derived from several placebo-controlled, randomized trials suggests that LLLT administered above a certain dosage level can accelerate improvement in patients with osteoarthritis of the knee by bringing immediate relief of pain and disability but that the effect is temporary. Evidence from a single placebo-controlled, randomized trial demonstrated no effect from LLLT on pain or disability in patients with osteoarthritis of the hand. Evidence from a single placebo-controlled, randomized trial indicated modest, temporary pain relief from rheumatoid arthritis of the hand and foot. A single, very small trial failed to demonstrate clinically significant improvement of pain and disability associated with chondromalacia. The trials addressing each indication had a number of methodological limitations, including variation in treatment parameters, small sample size, and lack of comparison with other treatment modalities. The authors further concluded that low-quality, inconsistent evidence showing potentially improved outcomes for treatment of pain and disability due to knee osteoarthritis, but substantial uncertainty remains regarding the extent of treatment benefit in comparison with other treatment modalities, long-term health benefits, safety, and patient selection criteria; there is either limited evidence of no benefit or no evidence of LLLT for treatment of pain and disability due to hand osteoarthritis, osteoarthritis in joints other than the knee or hand, rheumatoid arthritis in the hand and foot; and chondromalacia patellae, respectively; there is no evidence for patient-administered LLLT pertaining to the efficacy and safety of LLLT used outside of healthcare settings.

D. CMS and selected private payer coverage policies on LLLT

Table 1. Other Payer's Policy on LLLT

Payer	Policy	Note
CMS	The use of infrared and/or near-infrared light and/or heat, including monochromatic infrared energy, is non-covered for the treatment, including the symptoms such as pain arising from these conditions, of diabetic and/or non-diabetic peripheral sensory neuropathy, wounds and/or ulcers of the skin and/or subcutaneous tissues	National Coverage Decision (NCD) for Infrared Therapy Devices (270.6). Effective date: 10/24/2006.
Blue Cross	Investigational	2017 Federal employee program
NICE	No policy or guideline was found on LLLT	
Aetna	Experimental and investigational	2017-2018
Cigna	Experimental, investigational or unproven	2017-2018
Humana	Not covered	2018
Regence	Investigational	2017

E. Conclusions

1. There are numerous RCTs conducted and published since last review in 2004 on LLLT for various indications related to MSK conditions. Overall, the quality of the evidence for LLLT was low or very low.
2. Safety data are sparse, especially the long term data. Some adverse events associated with LLT or sham laser reported include mild pain, discomfort and tingling sensation during LLLT treatment. No reported treatment-related mortality was noticed. LLLT appears to be safe.
3. The results on efficacy are highly inconsistent. There seems to be a small statistically significant difference between LLLT and placebo for some indications in short term, but the clinical meaningfulness is uncertain. Long term data are lacking.
4. Laser wavelength, energy density, treatment duration, numbers of sessions and site of application are highly variable. Substantial uncertainty remains regarding the treatment benefit in comparison with other treatment modalities, long-term benefits, safety, and patient selection criteria.
5. None of the major payers covers LLLT for MSK disorders.

F. References

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