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Medical Policy Manual

Topic: Low-Level Laser Treatment of Neuromuscular Pain Disorders and Other Miscellaneous Conditions

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Low-level laser therapy (LLLT), also called photobiomodulation, refers to the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and Watts from 5 to 500 milliwatts. This is in contrast to surgical lasers that typically use 300 Watts. Low-level laser energy that is applied to acupuncture points on the body may be referred to as "laser acupuncture."

When applied to the skin, low level lasers produce no sensation and do not burn the skin. Because of the low absorption by human skin, it is hypothesized that the laser light can penetrate deeply into the tissues where it has a photobiostimulative effect. The exact mechanism of its effect is unknown; hypotheses have included improved cellular repair and stimulation of the immune, lymphatic, and vascular systems.

LLLT has been proposed as a treatment of carpal tunnel syndrome, painful musculoskeletal disorders such as temporomandibular joint disfunction and low back pain, soft tissue injuries, tendinopathies, and osteoarthritis. LLLT has been used outside the US to treat oral mucositis associated with radiation and chemotherapy, stimulate healing of chronic wounds, treat nerve injuries, and as an adjunct to antituberculosis drug treatment.

Regulatory Status

A number of low level lasers have received US Food and Drug Administration (FDA) 510 (k) clearance, including:

- MicroLight ML830® (MicroLight Corporation of America)
- GRT LITE™ PRO-8A (GRT Solutions, Inc.)
- LightStream™ Low Level Laser (RJ Laser Canada Corp.)
- TouchOne™ (OTC)

MEDICAL POLICY CRITERIA

Low-level laser treatment and laser acupuncture are considered **investigational** for all indications, including but not limited to the following:

1. Acute or chronic headache
2. Acute pain (e.g., postoperative pain, strains and sprains, labor pain)
3. Arthritis
4. Back, neck or shoulder pain
5. Bell's Palsy
6. Carpal tunnel syndrome
7. Fibromyalgia
8. Lateral or medial epicondylitis
9. Medial tibial stress syndrome
10. Meniscal knee pain
11. Oral Mucositis
12. Orofacial pain
13. Orthodontic pain
14. Other pain disorders
15. Temporomandibular joint (TMJ) pain
16. Tendonitis
17. Tinnitus
18. Wound healing

SCIENTIFIC EVIDENCE

The principal outcomes associated with treatment of carpel tunnel syndrome and musculoskeletal conditions are relief of pain, return to work, and improved functional level. Relief of pain is a subjective outcome that is typically associated with a placebo effect. Therefore, data from adequately powered, blinded, randomized controlled trials (RCT) are required to control for the placebo effect, determine its magnitude, and determine whether any treatment effect provides a significant advantage over the placebo.

The technology must also be evaluated in general groups of patients against existing treatments. In patients with mild to moderate symptoms, low-level laser treatment (LLLT) or laser acupuncture may be compared to other forms of conservative therapy such as splinting, rest, non-steroidal anti-inflammatory medications, or steroid injection. In patients who have exhausted conservative therapy, LLLT or laser acupuncture must be compared to surgical treatment, if any.

The focus of this policy is on peer-reviewed publications of sham-controlled randomized trials which follow patients (with the exception of those undergoing preventive treatment for oral mucositis) for at least 2 weeks beyond the end of the treatment period.[1]

Low-level Laser Treatment

Achilles Tendinopathy

Randomized Controlled Trial (RCT)

The available literature on LLLT for Achilles tendinopathy consists of a single randomized controlled trial.[2] However, because durability of treatment effects was not studied for any length of time past treatment, interpretation of these results is limited. Additional trials are needed to identify and establish an estimate of treatment effect and durability.

Conclusion

Current evidence is not available to determine if LLLT improves health outcome for the treatment of Achilles tendinopathy.

Bell's Palsy

Randomized Controlled Trial (RCT)

In 2013, Alayat and colleagues reported on a randomized double blind placebo-controlled trial of laser therapy for the treatment of 48 patients with Bell's palsy.[3] Facial exercises and massage were given to all patients. Patients were randomized to one of 3 groups: high intensity laser therapy, low level laser therapy or exercise only. Each group included 17 patients that were blinded to treatment. Laser treatment was given 3 times per week to eight points of the affected side for 6 weeks. At 3 and 6 weeks after treatment, outcomes were assessed using the facial disability scale (FDI) and the House-Brackmann scale (HBS). The authors reported that significant improvements in recovery were seen in both laser therapy groups over exercise alone with the most improvement seen with high intensity laser.

Conclusion

The current evidence is limited to 1 RCT that includes a small study population, the study does not report long-term health outcomes, and does not establish the clinical utility, or how health outcomes, are improved following LLLT for the treatment of Bell's palsy.

Carpal Tunnel Syndrome (CTS)

The literature on the use of LLLT for CTS consists of a single technology assessment and several randomized controlled trials (both sham and active control).

Systematic Review

The largest body of evidence for LLLT describes its use in the treatment of CTS. This evidence was evaluated in a 2010 BlueCross BlueShield Association (BCBSA) Technology Evaluation Center (TEC) Assessment, which concluded that the existing randomized clinical trials were insufficient to determine the effect of low-level laser therapy on CTS.[1]

For inclusion in the assessment, studies had to meet the following criteria:

- Published in a peer-reviewed journal
- Randomized
- Sham-controlled
- If adjunctive therapies were used, they had to be applied to both groups of patients
- Outcomes had to be measured at least 2 weeks beyond the end of the treatment period

Only 4 studies met the above inclusion criteria, and findings from these studies were inconsistent. No one study was so methodologically sound that its results were considered definitive. Overall, the available studies were small and most did not follow patients for sufficient periods of time beyond the treatment period to determine the durability of any treatment effects.

Randomized Controlled Trials (RCTs)

- A small, double-blinded RCT (19 patients with rheumatoid arthritis and carpal tunnel syndrome) found slight improvement in subjective scales of pain and function (e.g., 27-point improvement vs. 13-point improvement on VAS) compared with sham laser therapy) but no differences between groups in objective functional measures (e.g., grip strength, 0.3 vs. 0.3, respectively), or in measures of nerve conduction (e.g., motor nerve conduction velocity, 55 vs. 55, respectively) 10 weeks following the end of treatment.[4]

- Chang and colleagues reported on an RCT with short follow-up comparing LLLT with sham treatment in 36 patients.[5] After 2 weeks of treatment and 2 weeks after the end of treatment, VASs for pain were lower in the treatment group than in the sham group ($p<0.05$). After 2 weeks of treatment, differences in grip strength, symptoms, and functional assessment were not significant but were significant ($p<0.05$) at the 2-week follow-up. There were no significant between-group differences on nerve conduction studies at either time point.

Conclusion

Although additional randomized controlled trials have since been published, the lack of a placebo treatment group[6,7] or the lack of study of durability of treatment effects (at least 2 weeks following the treatment period)[8-10] limit the interpretation of these findings.

Chronic Neck Pain

Systematic Reviews

- The 2010 BCBSA TEC Assessment also determined that the evidence was insufficient to allow conclusions regarding the effect of LLLT on chronic neck pain.[1] The 6 trials that met the assessment inclusion criteria reported variable results, and no single study was methodologically sound. It was not possible to explain the differences in results due to the numerous differences in patient selection, treatment regimens, and trial co-interventions.

- In a 2013 systematic review and meta-regression, Gross and colleagues evaluated 17 trials on LLLT for neck pain.[11] Ten of these trials were found to demonstrate high risk of bias. Two trials consisting of 109 subjects were considered to be of moderate quality and found LLLT produced better outcomes than placebo for chronic neck pain treatment. Evidence showed improved outcomes with LLLT compared to placebo for acute neck pain, acute radiculopathy and cervical osteoarthritis but was considered to be low quality. There was conflicting evidence on chronic myofascial neck pain.

- In a recent systematic review by Kadhim-Saleh and others, authors analyzed 8 randomized controlled trials (N=443 patients) to determine the efficacy of LLLT in reducing acute and chronic neck pain as measured by the visual analog scale (VAS).[12] Authors concluded the evidence was inconclusive and the benefit seen in the use of LLLT did not constitute the threshold of minimally important clinical difference.

Randomized Controlled Trials (RCTs)

Subsequent to the publication of this technology assessment, an additional randomized controlled trial was published.[13] However, interpretation of results from this trial is limited by lack of study of treatment durability (follow-up for at least 2 weeks beyond end of the treatment period).

Conclusion

The current evidence on the use of LLLT for the treatment of chronic neck pain has methodological limitations and the conclusions of the reports are conflicting; therefore it cannot be determined if LLLT improves health outcomes.

Elbow Pain

Systematic Review

A single systematic review has been identified on the use of LLLT in elbow pain. Published in 2008, the review grouped placebo-controlled randomized clinical trials by application technique and laser wave length and reported on the 7 of 13 included trials with a common, narrowly defined regimen where lasers of 904 nm wavelength with low output (5-50 MW) were used to irradiate the tendon insertion at 2–6 points on the lateral elbow.[14] Positive results in these trials were consistent with outcomes of pain

and function, and significance persisted for at least 3–8 weeks after the end of treatment. However, among the articles included in this review, there were considerable differences in treatment protocol and type of patient treated, indicating that these results may not be generalizable to all patients with elbow pain. The authors noted that the conclusions of their review differed from conclusions of prior reviews of this topic.

Conclusion

The current evidence on LLLT for the treatment of elbow pain is insufficient due to the variability across studies in the patient population and treatment protocols used. Based on this evidence, it cannot be determined if health outcomes are improved on the use of LLLT for the treatment of elbow pain.

Fibromyalgia

Randomized Controlled Trial (RCT)

Available evidence to date on the use of LLLT in fibromyalgia consists of a small (n=20) randomized control trial comparing laser treatment and stretching exercises with stretching alone.[15] However, interpretation of these results is limited as comparison with sham is required to rule out non-specific (e.g., placebo effects) from the estimated impact of the treatment.

Conclusion

The current evidence is limited to 1 RCT with methodological limitations; therefore whether the use of LLLT for the treatment of fibromyalgia improves health outcomes cannot be determined.

Low Back Pain

Systematic Reviews

- An update of the Cochrane Database systematic review of LLLT for nonspecific low back pain was conducted in 2008.[16] The authors stated that "based on the heterogeneity of the populations, interventions, and comparison groups, we conclude that there are insufficient data to draw firm conclusions on the clinical effect of LLLT groups for low-back pain."

- A systematic review by Chou and colleagues assessed benefits and harms of nonpharmacological therapies including LLLT for acute and chronic low back pain.[17] The reviewers did not find good evidence of efficacy for LLLT for either indication.

Randomized Controlled Trials (RCTs)

Since publication of the Cochrane Review, several additional randomized trials have been published:

- In a 2007 study by Djavid et al., 61 patients were randomized to LLLT alone (n=20), LLLT with exercise (n=21), or sham laser treatment with exercise (n=20).[18] Outcomes of pain on VAS, lumbar range of motion (ROM), and disability were measured by blinded assessors after 6 weeks of treatment, after another 6 weeks and 12 weeks without treatment. By intention-to-treat (ITT) analysis, there were no between-group differences for any outcome measure immediately after the 6-week intervention. After 6 weeks without intervention, there was no difference between the LLLT

alone group and the placebo laser therapy plus exercise group; however, in the LLLT plus exercise group, pain had reduced by 1.8 cm (95% confidence interval [CI]: 0.1 to 3.3, p=0.03), lumbar ROM increased by 0.9 cm (95% CI: 0.2 to 1.8, p=<0.01) on the Schober Test and by 15 degrees (95% CI: 5-25, p<0.01) of active flexion, and disability reduced by 9.4 points (p=0.03) on the Oswestry Disability Index more than in the placebo laser therapy plus exercise group. The authors advised that larger trials are needed to detect differences between groups for some outcomes.

- In a large double-blind placebo-controlled study, Konstantinovic et al. randomized 546 patients with acute low back pain to medication, LLLT, medication and LLLT, or placebo.[19] Treatments were given 5 times per week for 15 weeks. However, duration of primary outcomes was not measured, limiting interpretation of these results.

- Ay and colleagues randomized 80 patients with acute and chronic low back pain attributed to lumbar disc herniation (LDH) into 4 groups of 20.[20] All patients received hot-packs and group 1 (acute LDH) received laser therapy; group 2 (chronic LDH) received laser therapy, group 3 (acute LDH) received placebo laser therapy; and group 4 (chronic LDH) received placebo laser therapy for 15 sessions over 3 weeks. However, because durability of treatment effect was not reported, interpretation of results from this study is likewise limited.

- Fiore and colleagues published results from an additional RCT, which compared LLLT with ultrasound.[21] However, lack of comparison with placebo limits interpretation of these findings.

Conclusion

Evidence in the available literature does not lend itself to consensus regarding the use of LLLT in low back pain.

Lymphedema

Randomized Controlled Trial (RCT)

A randomized double-blind sham controlled trial of LLLT in 50 patients with post-mastectomy lymphedema has been identified in the literature.[22] However, because durability of treatment effects was not assessed, interpretation of results from this trial is limited.

Conclusion

There is insufficient evidence in the available literature to determine if the use of LLLT for the treatment of lymphedema improves health outcomes.

Medial Tibial Stress Syndrome

Systematic Review

In a 2013 systematic review by Winters et al., of treatments for medial tibial stress syndrome, LLLT was not found to be effective.[23] All studies included in the systematic review were considered to have methodological bias.

Conclusion

The evidence is insufficient due to the methodological limitations identified in the available literature; therefore it cannot be determined if the use of LLLT for the treatment of medial tibial stress syndrome improves health outcomes.

Meniscal Knee Pain

Randomized Controlled Trial (RCT)

In a 2013 study, Malliaropoulos et al, reported on a randomized, double-blind, placebo-controlled study of LLLT in 64 patients with unilateral medial knee pain for more than 6 weeks that was related to meniscal pathology (i.e., grade 3 tiny attenuation or intrasubstance tears on MRI). Pain improved significantly with LLLT than placebo ($p<0.0001$). However, 4 patients (12.5 %) did not have improvement with LLLT. Pain returned in 3 patients at 6 months and in 5 patients after 1 year. Repeat MRIs were not performed.

Conclusion

The current evidence is limited to 1 RCT that includes a small study population, the study does not report long-term health outcomes, and does not establish the clinical utility, or how health outcomes, are improved following LLLT for the treatment of meniscal knee pain.

Oral Mucositis

Treatment of malignant diseases with cytotoxic chemotherapy or radiotherapy is associated with severe ulceration of the oral mucosa. LLLT has been proposed as a sole or adjunctive preventive treatment in oral mucositis. The principle outcomes associated with the study of oral mucositis include: resolution of the infection (including rate of healing systemic infection and time in hospital), treatment of pain, and quality of life outcomes.

Systematic Reviews

- Following evaluation of the evidence for LLLT in the treatment of oral mucositis, a 2010 Cochrane review concluded. "There is weak and unreliable evidence that LLLT reduces the severity of mucositis."[24] The review called for additional sham-controlled clinical trials to evaluate the effectiveness of this treatment.

- The Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) published a systematic review of laser and other light therapy for the management of oral mucositis in 2012.[25] A total of 24 trials were included for the review. Based on their review of the evidence, the MASCC/ISOO made a new recommendation for LLLT for the prevention of oral mucositis in adult patients receiving hematopoietic stem-cell transplantation (HSCT) conditioned with high-dose chemotherapy. This recommendation was based on what was considered to be one well-designed placebo-controlled randomized trial (described in more detail below),[26] together with a series of studies classified at a lower level of evidence. Evidence was insufficient to provide a guideline for laser as a treatment of oral mucositis in HSCT patients. The MASCC/ISOO made a new "suggestion" for low-level laser for the prevention of oral mucositis in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer. This guideline was

based on 3 studies that showed positive results but were considered to have major flaws. Evidence was considered encouraging but insufficient to recommend LLLT in other populations. The authors emphasized that due to the variety of laser devices and the variation in individual protocols, results of each study apply exclusively to the cancer population studied and the specific wavelength and settings used.

- In 2013, Figueiredo and colleagues reported on a systematic review and meta-analysis of laser therapy (LT) for oral mucositis (OM).[27] In the systematic review of 12 studies and meta-analysis of 7 studies, laser therapy was found to be more effective in preventing grade >3 oral mucositis than patients who did not receive laser treatment (OR: 9,5281, CI 95% 1,447-52,0354, p=0,0093). The authors noted larger studies were needed for better evaluation of the prophylatic effect of OM grade > 3 by LT..

Randomized Controlled Trials (RCTs)

- Gouvêa de Lima and colleagues reported on a randomized sham-controlled trial evaluating the use of LLLT versus sham laser therapy as a preventive therapy for oral mucositis in a cohort of 75 head and neck cancer patients undergoing concurrent radiotherapy.[28] The number of patients diagnosed with Grade 3 or 4 mucositis, was compared at 2, 4, and 6 weeks after commencement of radiotherapy and found no difference between treatment groups ($p \geq .08$). Assessment of proportion of patients in severe pain (score >7 on the visual analog scale; a secondary outcome) did not differ as well. However, significantly fewer patients experienced interruptions in treatment due to mucositis (0 patients in the group receiving LLLT versus 6 in the sham treatment group, $p < .02$), leading the researchers to conclude:

  "In the present study, LLL therapy was not effective in reducing Grade 3 or 4 oral mucositis, although a marginal benefit could not be excluded in terms of reducing RT [radiotherapy] interruptions which might translate into improved CRT [chemoradiotherapy] efficacy. For LLL therapy, the most efficient schedule of LLL application (dose and timing) and a standardization of LLL parameters (wavelength and power) must be established."

- The pivotal study for the MASCC/ISOO recommendation was a randomized double-blind sham-controlled trial with 70 patients who were undergoing HSCT.[26] Patients were randomized to 650 nm laser, 780 nm laser, or placebo (randomization method not described). Patients in the 650 nm laser group were more likely to have received a TBI-containing regimen compared to the other 2 groups, otherwise, the groups were comparable. LLLT began on the first day of conditioning and continued for 3 days post-transplant. Of the 70 patients, 47 (67%) had complete or nearly complete mucositis measurements over time; the average number of visits per patient was similar for the 3 groups. The difference between groups in mean oral mucositis scores was greatest at day 11 (placebo 24.3, 650 nm 16.7, 780 nm 20.6), and this difference between the 650 nm group and placebo approached statistical significance (p=0.06). Thus, there was no significant difference in mean oral mucositis scores between the 650 nm and placebo group at the other time points. Patient-specific oral mucositis scores were significantly different between the 2 groups only when adjusted for total body irradiation (TBI) exposure. Of the 70 patients in the study, 17 (24%) were assessed for oral pain. With group sizes of 5 and 6, the 650-nm group had significantly lower patient-specific average pain scores (15.6) compared to placebo (47.2). No adverse events from LLLT were noted. This study, which formed the basis for the MASCC/ISOO recommendation, suffers from limitations that include not achieving statistical

significance for the primary outcome measure and a very small percentage of patients with pain assessments.

- Gautam et al. reported 2 double-blinded randomized sham-controlled trials in 2012.[29,30] One of the studies reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 121 oral cancer patients.[30] The second publication reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 221 head and neck cancer patients.[29] There is an apparent overlap in patients in these 2 reports, with the head and neck cancer report including the 121 patients with a primary tumor site in the oral cavity. Patients in these studies received LLLT prior to radiation therapy at 66 Gy delivered daily in 33 fractions, 5 days per week and concurrent with cisplatin. LLLT was delivered at a wavelength of 632.8 nm, power density of 24 mW/cm2 and a dosage of 3 - 3.5 J. In the report on oral cancer, LLLT prior to radiation treatment led to significant reductions in the incidence of severe oral mucositis (29% vs. 89%) and its associated pain (18% vs. 71% with a VAS >7) opioid analgesic use (7% vs. 21%) and total parenteral nutrition (30% vs. 39%, all respectively) during the last weeks of chemoradiotherapy. LLLT also reduced the duration of severe oral mucositis (4.07 vs. 13.96 days), severe pain (5.31 vs. 9.89 days), and total parenteral nutrition (14.05 vs. 17.93 days, all respectively). In the 221 patients treated for head and neck cancer, LLLT was reported to lead to significant reductions in the incidence and duration of severe oral mucositis (8.19 vs. 12.86 days) and its associated pain (VAS of approximately 4 vs. 7), total parenteral nutrition (45.0% vs. 65.5%), and opioid analgesic use (9% vs. 26% for step III, all respectively). In 2013 Gautam et al,[31] reported on patient-reported outcomes from the same study of 220 head and neck cancer patients[29] using the Oral Mucositis Weekly Questionnaire-Head and Neck (OMWQ-HN) and the Functional Assessment of Cancer Treatment- Head and Neck (FACT-HN) questionnaire. Patients in this study received LLLT prior to radiation therapy at 66 Gy delivered daily in 33 fractions, 5 days per week and concurrent with cisplatin. LLLT was delivered at a wavelength of 632.8 nm, power density of 24 mW/cm2 and a dosage of 3.0 J. Patients in the LLLT group reported significantly better outcomes than the placebo group with lower scores on both the OMWQ-HN ($p<0.001$) and FACT-HN ($p<0.05$).The authors identified the limitation that the impact of various OM grades with the patient's reported measures of OM and QOL between the laser and placebo group were not compared.

- In 2013 Antunes and colleagues also reported on LLLT to prevent oral mucositis in a double-blinded randomized sham-controlled trial of 94 head and neck squamous cell carcinoma patients.[32] Patients received LLLT prior to radiation therapy at 70.2 Gy delivered daily in 39 fractions, 5 days per week and concurrent with cisplatin. In this study, LLLT was delivered at a higher dose of 660 nm, 100 mW and 1 J– 4 J/cm2. Three patients (6.4%) in the LLLT group developed grade 3-4 oral mucositis as measured by the World Health Organization oral mucositis scale compared to 19 patients (40.5%) in the placebo group (relative risk ratio: 0.158, CI 95% 0.050–0.498). Additionally, 28 patients (59.6%) in the LLLT group did not develop ulcers compared to 10 patients (21.3%) in the placebo group ($p<0.001$). Incidence of severe pain, narcotic analgesic use and gastrostomy was also lower in the LLLT group. Differences in radiation and LLLT dosages and oral hygiene protocols used may influence outcomes in these studies.

- Another randomized sham-controlled trial from 2012 evaluated the effect of LLLT on quality of life in 60 patients undergoing radiotherapy in the region of the major salivary glands.[33] Quality of life (QOL) was measured by the University of Washington QOL questionnaire at baseline and after 15 and 30 treatment sessions. QOL decreased significantly in both groups over the 30

treatment sessions, but there was a smaller decrease in QOL in the LLT group compared to the placebo group. The domains of appearance, activity, recreation, speech, taste, pain, chewing, and saliva were less affected in the LLLT group compared to the placebo group at either the mid-treatment or final assessment. More patients in the sham control group had an interruption of radiotherapy (25 vs. 12), which was due primarily to mucositis.

- Similarly, Oton-Leite and colleagues reported on the use of LLLT versus sham treatment in the prevention of oral mucositis in a group of 60 patients with head and neck cancer receiving radiotherapy.[33] Primary outcomes consisted of severity of oral mucositis, and quality of life (QOL; measured with the University of Washington QOL questionnaire). Patients received a baseline treatment and treatment for 5 consecutive days before each subsequent session of radiotherapy, for up to 7 weeks. Following inception of chemoradiotherapy, patients in the LLLT group experienced less of a decrease in quality of life measure (in other words, greater maintenance of initial quality of life following treatment) as compared with patients in the placebo treatment group. Additionally, significant differences were found in incidence of oral mucositis and frequency of radiotherapy interruption (both in favor of the active therapy group). Nonetheless, although care was taken such that patients did not uncover their treatment allocation, it was not reported whether their treating physicians, or the researchers themselves, were blinded to treatment allocation, suggesting that these results are at risk of bias from open allocation of treatment. Such bias may overestimate the treatment effect of LLLT.

- Carvalho and colleagues published results from a study comparing low (5mW) to high (15mW) power delivery of LLLT in the prevention of oral mucositis.[34] However, lack of comparison with placebo does not allow for the isolation of treatment effect, and limits interpretation of these findings.

Conclusion

Findings from published RCTs on the use of LLLT in oral mucositis differ and are at present insufficient to demonstrate that use of LLLT leads to improved health outcomes beyond placebo alone. Additional randomized controlled trials are required to clearly demonstrate the impact of LLLT on net health outcomes.

Orofacial Pain

Systematic Review

Authors assessed the effectiveness of LLLT as a treatment for orofacial pain in 33 studies[35] represented by 1,522 chronic pain patients meeting inclusion criteria in a systematic review. Trials were included if they were randomized, had a comparison group, had a study population with an orofacial pain condition including dentin hypersensitivity and musculoskeletal pain, and included a measurement of pain relief. In addition, a high quality scoring system was used the literature was analyzed by 2 independent researchers. Of the 23 RCTs reviewed, all but 2 were rated as low quality. The review concluded there was limited evidence that indicated LLLT was more effective than placebo, sham laser, and other active treatments.

Randomized Control Trials (RCTs)

- Manca and others investigated the effects of ultrasound (US) and LLLT on myofascial trigger points (MTP) of the upper trapezius muscle (uTM).[36] In the double-blind, randomized, placebo-controlled study, 60 participants with at least one active MTP in uTM (28 women and 32 men; mean age 24.5 ± 1.44 years) were recruited and randomly assigned to one out of five groups: active US (n = 12), placebo US (n = 12), active LLLT (n = 11), placebo LLLT (n = 11) and no therapy (control, n = 14). After the 2-week intervention, all groups showed pressure pain threshold, numerical rating scale and cervical lateral flexion significant improvements ($p < 0.05$), which were confirmed at the follow-up. The authors concluded that ultrasound and LLLT provided significant improvements in pain and muscle extensibility.

- In a small randomized trial not included in the above systematic review, the effect of LLLT on masticatory performance, pressure pain threshold (PPT), and pain intensity in 21 patients with myofascial pain[37] was evaluated. Patients were either assigned to the laser group (N=12) or the placebo group (N=9). A reduction in the geometric mean diameter of crushed particles and an increase in PPT were seen only in the laser group when comparing the baseline and end-of-treatment values. Both groups showed a decrease in pain intensity at the end of treatment. Authors concluded that LLLT promoted an improvement in MP and PPT of the masticatory muscles. This is a study of limited sample size and the randomization of the patient population is not clear.

Conclusion

Findings from published RCTs on the use of LLLT in orofacial pain are insufficient due to the methodological limitations in the study designs; therefore it is uncertain that use of LLLT leads to improved health outcomes.

Orthodontic Pain

Systematic Review

He et al. investigated the efficacy of LLLT in the management of orthodontic pain in a systematic review of 4 RCTs and 6 additional studies (N=641 patients).[38] Authors concluded because of the methodological shortcomings and risk of bias of included trials, evidence of the benefits of LLLT was limited in delaying pain onset and reducing pain intensity. Authors suggested larger and better-designed RCTs are required to provide recommendations.

Conclusion

The evidence from published studies on the use of LLLT in orothodontic pain is insufficient to demonstrate that use of LLLT leads to improved health outcomes due to methodological limitations.

Osteoarthritic (OA) Knee Pain

Systematic Review

In 2007, Bjordal et al. published a systematic review of placebo-controlled RCTs to determine the short-term efficacy of physical interventions for osteoarthritic knee pain.[39] They concluded that LLLT offered clinically relevant pain-relieving effects on VAS scores compared to placebo control. Follow-up

data up to 12 weeks were sparse, but positive effects seemed to persist for at least 4 weeks after the course of treatment.

Randomized Controlled Trial (RCT)

Hegedus et al. reported a randomized double-blind sham-controlled trial of LLLT in 35 patients with knee OA in 2009.[40] Eight patients from the sham group left the experiment, leaving 18 patients in the active LLLT group and 9 in the sham group. Treatments were delivered twice a week over a period of 4 weeks. Follow-up was performed immediately, 2 weeks, and 2 months after completing the therapy. In the group treated with LLLT, a significant improvement was found in pain (5.75 to 1.18), pressure sensitivity (2.33 to 0.77) and flexion (105.83° to 122.94°) at 2 months. In the placebo group, baseline to post-treatment changes in joint flexion and pain were not significant. It was not reported if these changes were significantly improved in comparison with the sham group. Additionally interpretation of these results is limited by the high loss to follow-up, which may have biased the results towards the treatment group.

Conclusion

Though RCTs are available on the use of LLLT for the treatment of osteoarthritic knee pain, the interpretation of the results is limited due to small patient sizes and limited long-term follow-up of patients. Further, the clinical utility, or how health outcomes are improved following treatment with LLLT is not addressed.

Plantar Fasciitis

The available literature consists of a randomized double-blind sham-controlled trial from Kiritsi and colleagues on LLLT in 30 subjects with plantar fasciitis.[41] However, because durability of treatment effects was not reported, interpretation of results from this study is unclear.

Conclusion

Evidence on the use of LLLT in plantar fasciitis is insufficient to demonstrate that use of LLLT leads to improved health outcomes.

Rheumatoid Arthritis (RA)

Systematic Review

A 2005 Cochrane Review included 5 placebo-controlled randomized trials and found that relative to a separate control group, LLLT reduced pain and morning stiffness, and increased tip-to-palm flexibility.[42] Other outcomes did not differ between groups, including functional assessment, range of motion, and local swelling. For RA, relative to a control group using the opposite hand (1 study), there was no difference observed between the control and treatment hand for morning stiffness duration and no significant improvement in pain relief. The authors noted that "despite some positive findings, this meta-analysis lacked data on how LLLT effectiveness is affected by four important factors: wavelength, treatment duration of LLLT, dosage and site application over nerves instead of joints."

Randomized Controlled Trial

A randomized double-blind placebo-controlled trial comparing outcomes of pain reduction and improvement in hand function in 82 patients with RA treated with low-level laser or placebo laser was reported by Meireles et al.[43] However, co-treatment (such as pain medication) was not controlled during the trial and durability of treatment effects was not measured, limiting interpretation of these findings.

Conclusion

Studies on the use of LLLT for the treatment of rheumatoid arthritis have methodological limitations that preclude the interpretation of the results; therefore valid conclusions cannot be made to determine if the use of LLLT leads to improved health outcomes.

Shoulder Pain

Systematic Review

Favejee and colleagues published results from a systematic review of randomized controlled trials on the use of non-surgical treatment (including LLLT) for frozen shoulder (adhesive capsulitis).[44] Five Cochrane reviews and 18 randomized controlled trials were evaluated. The researchers reported finding a strong association between LLLT and reduced pain and disability. However, commentary on these findings points to the lack of distinction between primary (or idiopathic) capsulitis versus secondary adhesive capsulitis (due to trauma, diabetes, or thyroid dysfunction).[45] Because secondary capsulitis is less responsive to treatment, lack of sub-group analysis of treatment outcomes by patient type may limit the generalizability of these results to a specific patient population.

Randomized Controlled Trials (RCTs)

- Eslamian and others evaluated the effects of LLLT in combination with conventional physiotherapy endeavors in 50 patients.[46] Twenty-five patients were randomly assigned to the control group and received only routine physiotherapy. The additional 25 patients were assigned into the experimental group and received conventional therapy plus LLLT. Authors concluded that LLLT combined with conventional physiotherapy had superiority over routine physiotherapy in decreasing pain and improving the patient's function, but no additional advantages were detected in increasing shoulder joint range of motion in comparison to other physical agents. This study had a limited study population and did not include a sham group for comparison.

- Stergioulas and colleagues conducted a randomized, controlled, double-blind trial comparing an 8-week program of LLLT (n=31) with placebo (n=32) among 74 patients with frozen shoulder.[47] Compared with the sham group, the active laser group had a significant decrease in overall, night, and activity pain scores after 4 weeks and 8 weeks of treatment, and at the end of 8 more weeks of follow-up. At the same time intervals, a significant decrease in shoulder pain, disability index (SPADI) scores, and Croft shoulder disability questionnaire scores was observed, while a significant decrease in disability of arm, shoulder, and hand questionnaire (DASH) scores was observed at 8 weeks of treatment and at 16 weeks' post-randomization; and a significant decrease in health assessment questionnaire scores was observed at 4 weeks and 8 weeks of treatment. Results from this study are not reliable because 11 patients included in the original randomization were excluded from analysis after leaving the study to seek other treatments. It is not known how this loss might have biased the final outcomes of the study.

- Results from additional RCTs remain limited by lack of sham control[46,48-50] and/or lack of study of treatment durability.[51-53]

Conclusion

In sum, conflicting results from available randomized controlled trials limit conclusions about the effectiveness of LLLT in shoulder disorders.

Temporomandibular Joint Disorders (TMD)

Systematic Review

- In a systematic review by Maia and others, authors investigated the effect of LLLT on temporomandibular joint disorders (TMD).[54] Of the 14 studies reviewed, authors concluded the lack of standardization across the studies limited the interpretation of the review's results. Authors suggested further research is necessary in order to obtain a consensus regarding the best application protocol for pain relief in patients with TMD.

- In an additional systematic review on TMD, authors reviewed 14 studies evaluating the efficacy of LLLT for the treatment of TMD.[55] The outcomes of the trials were controversial and not related to any features of the laser beam, to the number of laser applications, or their duration. Authors concluded that based on the results of the review no definitive conclusions could be drawn on the efficacy of LLLT for the treatment of TMD.

- A systematic review by Petrucci and colleagues identified 6 sham-controlled randomized clinical trials for inclusion.[56] Using change in pain (as measured with a visual acuity scale) as the primary treatment outcome, the researchers concluded that LLLT was not more effective than placebo alone.

- He et al. investigated the efficacy of LLLT in the management of orthodontic pain.[38] Four RCTs, two quasi-RCTs, and two controlled clinical trials (CCTs) were selected from 152 relevant studies, including 641 patients. The meta-analysis demonstrated that 24% risk of incidence of pain was reduced by LLLT (RR = 0.76, 95% CI range 0.63-0.92, P = 0.006). In addition, compared to the control group, LLLT brought forward "the most painful day" (MD = -0.42, 95% CI range -0.74- -0.10, P = 0.009). Furthermore, the LLLT group also implied a trend of earlier end of pain compared with the control group (MD = -1.37, 95% CI range -3.37-0.64, P = 0.18) and the pseudo-laser group (MD = -1.04, 95% CI range -4.22-2.15, P = 0.52). Authors concluded due to the methodological shortcomings and risk of bias of included trials, the evidence for LLLT in delaying pain onset and reducing pain intensity was insufficient.

Randomized Controlled Trials (RCTs)

Results from available sham-controlled randomized trials are detailed below:

- Carrasco et al. randomly assigned 60 patients with myofascial pain and one active trigger point in the anterior masseter and anterior temporal muscles to 6 groups.[57] Three groups received laser treatment twice a week for 4 weeks using different energy levels for each group (25 J/cm2, 60 J/cm2, or 105 J/cm2). The other 3 groups received placebo treatment simulating the same parameters as the treated groups. Pain scores were assessed just before, immediately after the 4th and 8th

applications, and at 15 days and 1 month after treatment. An analgesic effect was seen starting from the third evaluation in both the treated and placebo groups, and placebo was as effective as laser ($p<0.05$). Differences in pain VAS between groups treated at different energy levels were not significant.

- Venezian et al. randomized 48 patients with myofascial pain to one of 2 doses of laser (25 J/cm2 or 60 J/cm2) or placebo twice a week for 4 weeks.[58] Surface electromyography (EMG) at the conclusion of testing showed no difference between the groups. Pain with palpation was measured by VAS before, at the conclusion of, and 30 days after laser therapy. VAS scores declined in all groups and were more consistently decreased (more regions of the palpated muscles) after active laser therapy. However, there were no significant differences in VAS between the active and sham-controlled groups.

- Ahrari and others in a randomized, double-blind clinical trial assessed LLLT in 20 patients with myogenic TMD.[59] Patients were randomly divided into laser and placebo groups. There was a significant increase in mouth opening and a significant reduction of pain symptoms in the laser group that was not observed in the placebo group. Between-group comparisons revealed no significant differences in pain intensity and mouth opening measurements at any of the evaluation time points. Using a very limited sample size, authors concluded that LLLT can produce a significant improvement in pain level and mouth opening in patients affected with myogenic TMD.

Additional RCTs lacking study of durability of treatment effects have also been published.[60-66]

Conclusion

The available literature does not support the use of LLLT over placebo for treatment of TMJ pain. These findings should be considered inconclusive as failure to find statistical differences between treatment groups may be related to the small sample size.

Wound Healing

Systematic Review

Evidence on LLLT for wound healing consists of a systematic review from the Agency for Healthcare Research and Quality (AHRQ) in 2004.

The evidence report on vacuum-assisted and low-level laser wound therapies for treatment of chronic non-healing wounds prepared for the AHRQ was based on 11 studies of LLLT.[67] The review concluded:

> "The best available trial [of low level laser wound therapy] did not show a higher probability of complete healing at 6 weeks with the addition of low-level laser compared to sham laser treatment added to standard care. Study weaknesses were unlikely to have concealed existing effects. Future studies may determine whether different dosing parameters or other laser types may lead to different results."

Conclusion

Evidence is limited on the use of LLLT for the treatment of wound healing and therefore valid conclusions cannot be made to determine if the use of LLLT leads to improved health outcomes.

Other Indications

LLLT has been studied in randomized controlled trials for use in indications such as treatment of venous leg ulcers,[68] perineal pain after episiotomy,[69] chronic periodonitis,[70] and improvement of visual acuity in ambylopia.[71] A systematic review of active-control clinical trials (some lacking randomization to treatment) has also been published on the use of LLLT for treatment of hypertrophic scars.[72] However, before this evidence can be used to make determinations about treatment benefit in this indications, all individual studies require replication with one or more subsequent randomized controlled trials to validate any findings of treatment benefit.[68-71] Where present evidence lacks placebo control,[68,70,72] any such replication should include comparison with sham.

Conclusion

Available evidence is therefore considered insufficient to make conclusions about the effectiveness of LLLT in venous leg ulcers, perineal pain after episiotomy, chronic periodonitis, and improvement of visual acuity in ambylopia.

Laser Acupuncture (LA)

The randomized clinical trial data related to laser acupuncture (LA) is limited to 5 short-term studies, each focused on a different pain condition. The conditions included low back pain, chronic tension headache, migraine and tension headaches in children, whiplash injury, and osteoarthritis of the knee.

- Glazov et al. determined if infrared LA may have a specific effect in reducing pain and disability in treatment of chronic low back pain (LBP).[73] The double-blind sham laser controlled trial included 144 adults with chronic non-specific LBP. Participants were followed-up at 1 and 6 weeks, and 6 and 12 months post treatment. The analysis showed no difference between sham and the laser groups at 6 weeks for pain or disability. There was a significant reduction in mean pain and disability in all groups at 6 weeks ($p<0.005$); Numerical Pain Rating Scale (NPRS): sham (-1.5 (95% CI -2.1 to -0.8)), low dose (-1.3 (-2.0 to -0.8)), high dose (-1.1 (-1.7 to -0.5)). ODI: sham (-4.0 (-7.1 to -1.0)), low dose (-4.1, (-6.7 to -1.5)), high dose (-2.6 (-5.7 to 0.5)). All secondary outcomes also showed clinical improvement over time but with no differences between groups. The authors concluded that laser acupuncture using energy density range (0-4 J/cm(2)) for the treatment of chronic non-specific LBP resulted in clinical improvement unrelated to laser stimulation.
- Ebneshahidi and colleagues in a single-blind, randomized, placebo-controlled trial of 50 patients with chronic tension headache reported that laser acupuncture using a LLLT device may provide benefit over placebo.[74] The study was small and the acupuncturists administering the true or sham treatments as well as the assessors were aware of the allocation and thus could have positively influenced the laser acupuncture group. In addition, the baseline measures were different from the subsequent measurements performed in follow-up. The results from this small study need to be validated in a larger, randomized, double-blind clinical trial.
- A second trial of laser acupuncture on 43 children with both migraine and tension headaches provided highly individualized treatment and additional therapies which do not permit conclusions regarding the independent effects of laser treatment.[75]
- Two studies reported no significant difference between patients treated with active vs. sham laser acupuncture for the treatment of whiplash injury[76] and knee osteoarthritis[77].

Conclusion

The available clinical trial data does not permit scientific conclusions concerning the impact of laser acupuncture on health outcomes for any of these conditions.

Clinical Practice Guidelines

Several clinical practice guidelines have been identified which address the use of LLLT as a treatment of various conditions.

American Academy of Orthopaedic Surgeons

The American Academy of Orthopaedic Surgeons 2008 clinical practice guideline on the treatment of carpal tunnel syndrome included laser treatment among treatments that carry no recommendation for or against their use because there is insufficient evidence to recommend their use.[78]

American Pain Society (APS)

The 2007 American Pain Society guideline states that there is insufficient evidence to recommend LLLT for treatment of low back pain and LLLT is not mentioned in the 2009 guideline.[79]

Orthopaedic Section of the American Physical Therapy Association

The 2010 guidelines released by the Orthopaedic Section of the American Physical Therapy Association recommend the use of LLLT for Achilles tendinitis, stating: "Clinicians should consider the use of low-level laser therapy to decrease pain and stiffness in patients with Achilles tendinopathy."[80] This is a grade B recommendation, based upon a "single high-quality randomized controlled trial or a preponderance of level II studies." Two small ($n \leq 40$) non-randomized studies (comparative and observational) are cited in this recommendation, neither of which is included in the discussion above due to high risk of bias in estimation of treatment effects (from lack of treatment randomization and small study size). Although these guidelines state that they are evidence-based, it is unclear how the evidence was appraised in making this recommendation.

American College of Occupational and Environmental Medicine (ACOEM)

- In recommendations regarding treatment of carpal tunnel syndrome (CTS) published in 2011, the ACOEM recommended against the use of LLLT for CTS.[81] This recommendation was based upon Level C evidence (at least intermediate evidence that harms and costs exceed benefits based on limited evidence").
- In a 2009 update to existing guidelines on disorders other than CTS of the hand, wrist, and forearm, the ACOEM recommended against the use of LLLT for treatment of hand or finger osteoarthrosis based upon a Level B recommendation ("moderately not recommended," based upon "intermediate evidence that the intervention is ineffective, or that harms or costs outweigh benefits").[82]

Summary

The available literature has not shown low-level laser therapy (LLLT) to be as effective as established treatments for a variety of indications, including carpal tunnel syndrome, various musculoskeletal

conditions, chemotherapy-induced mucositis, and wound healing. Outcomes of studies comparing LLLT with sham laser therapy for treatment of pain and other conditions are inconsistent and generally involve small numbers of participants. Most studies found no statistically significant difference in symptom relief or functional status between the active LLLT group and the control group. Therefore, low-level laser therapy (LLLT) remains investigational for all indications.

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	None	
HCPCS	S8948	Application of a modality (requiring constant provider attendance) to one or more areas; low level laser, each 15 minutes