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ALTERNATIVE TREATMENTS FOR PAIN MEDICINE (M JONES, SECTION EDITOR)

A Review of Laser Therapy and Low-Intensity Ultrasound for Chronic Pain States

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Abstract

Purpose of Review Chronic pain management therapies have expanded quickly over the past decade. In particular, the use of laser therapy and ultrasound in the management of chronic pain has risen in recent years. Understanding the uses of these types of therapies can better equip chronic pain specialists for managing complicated chronic pain syndromes. The purpose of this review was to summarize the current literature regarding laser radiation and ultrasound therapy used for managing chronic pain syndromes.

Recent Findings In summary, there is stronger evidence supporting the usage of laser therapy for managing chronic pain states compared to low-intensity ultrasound therapies. As a monotherapy, laser therapy has proven to be beneficial in managing chronic pain in patients with a variety of pain syndromes. On the other hand, LIUS has less clear benefits as a monotherapy with an uncertain, optimal delivery method established.

Summary Both laser therapy and low-intensity ultrasound have proven beneficial in managing various pain syndromes and can be effective interventions, in particular, when utilized in combination therapy.

Keywords Laser therapy · Low-intensity ultrasound · Chronic pain management

Introduction

The chronic pain disease burden is significant — using the World Health Organization's (WHO) World Mental Health Survey in 10 developed countries, Tsang et al. found that about 37% of age-standardized adults in these countries have chronic pain conditions [1]. Adults with chronic pain have multiple sources including the lower back (28.1%), knee (19.5%), severe headache or migraine (16.1%), and neck (15.1%) [2]. Disability from all causes of pain was estimated at $300 billion annually in 2009, which included healthcare expenses and lost productivity related to chronic pain syndromes [2–4]. Taken together, these data show that chronic pain represents a large source of healthcare utilization and effective treatments for addressing chronic pain syndromes can provide several benefits.

Current treatment options for chronic pain states range widely including oral analgesics, topical analgesics, and interventional therapies. According to the WHO guidelines ladder for the use of oral analgesics in managing chronic pain, initial treatment steps include non-opioid analgesics such as NSAIDs or acetaminophen, followed by weak opioids such as codeine or dihydrocodeine for moderate pain [5–8]. The next step in this ladder includes stronger opioids such as hydrocodone, oxycodone, or hydromorphone. Each step can also include adjuvant therapies with proven benefits such as gabapentin, pregabalin, TCAs, and SNRIs [5]. Topical analgesics for transdermal administration such as fentanyl or buprenorphine patches may also be used for localized pain [5–10].

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The WHO ladder, however, does not include interventional therapies such as implantable drug delivery systems, nerve block surgery, laser therapy, or ultrasound. Many studies have proposed including these interventions in the WHO classification ladder [6–8]. Since the WHO ladder was published in 1986, many studies have investigated the efficacy of these new interventions for relieving pain and have suggested that they have proven benefits in combination with oral analgesics. In particular, laser therapies and ultrasound have been studied as interventions for treating chronic, refractory pain syndromes and have been compared against each other and placebos for relieving pain for a variety of pain states [9–12]. Both modalities are non-invasive and conservative therapies that can supplement oral analgesics. Therefore, the purpose of this article was to review the current literature regarding laser therapy and low-intensity ultrasound and to consolidate information about these two therapies when used in the management of chronic pain.

Laser Therapies

Implementation Modality and Mechanism of Action

Laser therapies follow two delivery systems: (1) low-intensity laser therapy (LILT) or low-level laser therapy (LLLT) and (2) high-intensity laser therapy (HILT). Various parameters for LILT and HILT must be optimized including wavelength, power density, and pulse structure. Since it was first studied in mouse models in the 1960s, LILT has been used for three main purposes: (1) promoting wound healing, (2) treating pain syndromes, and (3) reducing inflammation [13]. LILT is also known as photobiomodulation or cold laser therapy [14]. LILT exposes tissues to low-energy or near-infrared light which, compared to HILT wavelengths, has lower power density and does not heat tissues. LILT and HILT are proposed to act differently at the individual cellular level. One hypothesis is that LILT photobiomodulation dissociates the inhibitory nitric oxide from cytochrome C, which increases electron transport and ATP production. Another hypothesis is that LILT activates numerous light-sensitive Ca channels which cause Ca influx into the cell. This results in downstream signaling cascades through reactive oxygen species and cAMP, leading to increased production of transcription factors such as ATF/CREB, HIF1, NFKB, and REF-1 [15–17, 71, 72]. Another characteristic feature of LILT is fibroblastic proliferation [14]. On the other hand, HILT releases high peak power and short-term delivery of high energy to the target tissue. HILT offers deeper penetration into target tissues and the pain-relieving effects of HILT are achieved through increased release of B-endorphins in the central nervous system and decreased release of substance P in the peripheral nervous system, which leads to less pain sensitization [13, 18, 19]. The following paragraphs will summarize recent studies investigating the efficacy of both LILT and HILT for managing various chronic pain processes.

LILT exhibits a biphasic response that is explained by the Arndt-Schulz law — at very low levels, there is no tissue response. As more energy is applied, biomodulation increases but a threshold exists above which biostimulation disappears and is replaced by bioinhibition [20]. The optimal dosages vary depending on the disease process [21]. HILT, on the other hand, utilizes stronger thermal and mechanical effects as well as induces an electromagnetic field and photoelectric and electrochemical changes in exposed tissues [22]. Given HILT's increased penetration, the laser can be used to reach deeper structures.

Usage in Diseased States

In recent years, LILT has been explored as a treatment option for fibromyalgia, plantar fasciitis, Achilles tendinopathy, myofascial neck pain, and Bouchard's and Heberden's osteoarthritis [23–29]. In regards to fibromyalgia, Yeh et al.'s 2019 systematic review and meta-analysis of 9 RCTs found that LILT improved patient Fibromyalgia Impact Questionnaire (FIQ) scores, pain severity, number of tender points, stiffness, depression, and anxiety compared to placebo laser [23]. Similar improvements were seen in LILT's ability to relieve chronic foot and ankle joint pain, although range of motion (ROM) remained unimproved [29]. Similarly, LILT for myofascial neck pain was found to improve pain at rest and movement compared to placebo but ROM was not investigated [28]. Few studies have investigated or reported changes in ROM after LILT therapy and this limitation remains an area of continued exploration for LILT therapy.

Other tested benefits of LILT include improvement in non-specific knee, lower back pain, masseter, and temporalis muscle pain in women with temporomandibular disorder [31–33]. A recent systematic review and meta-analysis demonstrated LILT effectively relieves pain for patients with non-specific chronic low back pain [34]. Another meta-analysis involving over 1000 participants between 15 studies reported an immediate and short-term significant pain reduction for non-specific low back pain for up to 3 months [32]. The pain reduction was greatest in individuals with baseline pain for less than 30 months and with the use of higher laser dosages. The study also quotes a 3-J/point threshold for the laser's benefit. Dosages for LILT are measured by the World Association of Laser Therapy (WALT) in joules (J) per point for arthritis and tendinopathy. In this particular study, there also appeared no upper dose at which the laser was non-effective or caused adverse effects. Other studies corroborate these results demonstrating an improvement in non-specific chronic low back pain but no improvement in ROM, with only short-term improvement for posture stability [34, 35].

HILT effectiveness has been studied in knee arthritis [36]. HILT significantly decreased pain measured by VAS and dolorimetry after 7 days of treatment with HILT versus sham laser [36]. The laser therapy demonstrated a greater decrease in pain at rest, pain upon palpation, and pain during movement as compared to the baseline even at the 3-month follow-up [36]. This contrasts with HILT's effect on lumbar pain which proved ineffective in comparison to transcutaneous nerve stimulation and ultrasound therapy [35]. HILT was similarly not effective when studied in the improvement of postural stability in non-specific low back pain [37]. LILT and HILT characteristics are captured in Table 1.

Combination Therapy

LILT is often used in combination with other therapies including prolotherapy injections or exercise [38–40]. The synergy of the modalities has been shown to reduce joint pain and stimulate greater fibroblastic regeneration. Spinal manipulation in combination with laser therapy and exercise has also been shown to significantly improve non-specific low back pain [41]. Nambi et al.'s RCT from 2018 found that the mixed modality LILT plus exercise therapy demonstrated an improvement in pain and range of motion for up to 12-month follow-up for chronic non-specific lower back pain [41]. A large systematic review from 2017 found that LILT combined with prolotherapy injections was associated with increased musculoskeletal functioning, joint mobility, and quality of life for patients with chronic osteoarthritis [42].

Limitations and Barriers

There continue to exist barriers against the implementation of LILT including the large variability of laser application. Although previous studies have reported better LILT therapeutic effects with higher energy density, number of sessions, and frequency of application, many factors of laser therapy remain uncertain [21, 43]. There are numerous laser types all usable at different wavelengths. Appropriate laser dosages for particular pathologies remain unknown. Continued exploration of LILT and HILT is needed to streamline their possible clinical implementation with a focus on conducting more double-blind RCTs to properly assess effectiveness.

Low-Intensity Ultrasound

Implementation Modality and Mechanism of Action

Low-intensity ultrasound (LIUS) uses pulsed or continuous mechanical waves to elicit regenerative and anti-inflammatory effects on biological tissues like bone, cartilage, or tendon. LIUS generates ultrasound that increases muscle temperature, increases blood flow and connective tissue extensibility, alters nerve conduction velocity, and reduces the likelihood of unfavorable tissue damage [55, 56]. According to recent literature studies on LICUS, the treatment is helpful in reducing pain and increasing function in musculoskeletal ailments. Diagnostic ultrasounds are usually below 0.1 W/cm^2, while LIUS ranges between 0.125 and 3 W/cm^2, and high-intensity ultrasound (HIUS) ranges from 100 to 10,000 W/cm^2 or higher [44]. Different therapeutic effects can be achieved based on not only differing ultrasound power density but also different forms of wave production and delivery. LIUS as a modality can be used in either a pulsed or continuous form, both of which have minimal thermal effects and mainly transmit acoustic energy to tissues [45]. LIPUS (Low-intensity pulsed ultrasound) has been found to have several biological effects on tissues which include inhibition of inflammation and soft-tissue regeneration [46, 47]. LICUS (low-intensity continuous ultrasound) also has a similar biological effect but enables a longer treatment duration (up to 4 h) by preventing the formation of standing waves that could lead to tissue damage [48]. Studies investigating the efficacy of both modes of LIUS delivery have yielded inconsistent results about each [49, 50].

Table 1 Indications, evidence, and characteristics for laser therapies

	Indications	Power	Heating or non-heating	Effective in combination therapy?
Low-intensity laser therapy (LILT)	Strong evidence for foot and ankle pain, fibromyalgia, non-specific knee, lower back pain, TMJ pain	< 0.5 W	Non-heating	Yes
High-intensity laser therapy (HILT)	Most robust evidence in knee arthritis, less clear evidence in lumbar or non-specific low back pain	> 0.5 W	Heating	Yes

Table 2 Indications, evidence, and characteristics for ultrasound therapies

	Indications	Frequency	Average power intensities	Heating or non-heating	Effective in combination therapy?
Low-intensity pulsed ultrasound (LIPUS)	Best-studied in knee arthritis, less clear in other pain states	1–3 MHz	30 mW/cm^2	Non-heating	Yes
Low-intensity continuous ultrasound (LICUS)	Best-studied in knee arthritis, less clear in other pain states	1–3 MHz	> 50 mW/cm^2	Heating	Yes

Usage in Diseased States

LICUS has been utilized in the treatment of chronic myofascial pain [57–60], back pain [61, 62], tendinopathy [63, 64], and joint arthritis pain [65–67]. LIPUS has been studied as a treatment modality for chronic conditions including lateral epicondylitis [68] and patellar tendinopathy [70] with limited efficacy. Improved outcomes have been reported with LIPUS as a treatment modality for chronic prostatitis and pelvic pain syndrome [69]. Current systematic reviews and meta-analyses of studies regarding the efficacy of LIUS in treating chronic pain syndromes, of the neck and lower back in particular, conclude that the true effects of therapeutic US in pain management are uncertain for various reasons including a small number of high-quality randomized trials and the available trials being very small [54, 55]. Ebadi et al.'s meta-analysis in 2020 found that among 10 RCTs of over 1000 patients receiving LIUS for chronic non-specific lower back pain, there was little to no evidence for differences in short-term pain improvement for LIUS versus placebo [54]. While there is some evidence to support combination LIUS plus exercise therapy as beneficial in the short term compared to placebo, long-term effects of LIUS on pain improvement are less clear [54, 55]. Current evidence does not support using LIUS as an effective standalone therapy for managing chronic lower back pain [52–55]. LIUS characteristics are captured in Table 2.

Literature regarding LIUS for treating knee arthritis is robust, with studies reporting improvement in pain without significant adverse effects [22, 51–53]. However, LIPUS versus LICUS delivery methods for treating knee arthritis pain still remains controversial [52]. In addition, LIUS monotherapy may not have a significant impact on symptom or functional improvement but has been proposed to be effective when combined with other modalities including exercise and oral analgesics. When compared to other physical therapy such as exercise, it becomes even less clear if LIUS has any superior benefits [54].

Conclusion

In summary, there is stronger evidence supporting the usage of laser therapy for managing chronic pain states compared to low-intensity ultrasound therapies. As a monotherapy, laser therapy has proven to be beneficial in managing chronic pain in patients with a variety of pain syndromes. On the other hand, LIUS has less clear benefits as a monotherapy with an uncertain, optimal delivery method established. Both LT and LIUS can be effective when combined with other treatment modalities.

Compliance with Ethical Standards

Conflicts of Interest None.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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