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CASES WITH A MESSAGE

Treatment of drug-resistant fibromyalgia symptoms using high-intensity laser therapy: a case-based review

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Abstract Fibromyalgia is a chronic musculoskeletal condition characterized by widespread pain in the body and is associated with tender points at the shoulder, back and hip regions. A wide variety of pharmacologic drugs and dietary supplements have been used with limited success in treating the musculoskeletal pain. Early clinical studies with low level laser therapy (LLLT) alone or in combination with drugs commonly used to treat fibromyalgia suggested that LLLT may be effective in reducing musculoskeletal pain and stiffness, as well as the number of tender locations. However, a sham-controlled study reported that LLLT was not significantly better than the sham treatment and kinesiotape. Preliminary studies with high-intensity laser therapy (HILT) suggest that it may be more effective than LLLT for treating chronic pain syndromes. Therefore, we evaluated low (1 W), intermediate (42 W) and high level (75 W) HILT in a woman with long-standing fibromyalgia syndrome which was resistant to both standard pharmacotherapy and treatment in an interdisciplinary pain management program. The patient received a series of treatments with a HILT device (Phoenix Thera-lase) at a wavelength of 1275 nm administered at both the paraspinous region and tender points in the shoulder and hip regions. Although the 1 W treatment produced minimal symptom relief, both the 42 and the 75 W treatments produced a dramatic reduction in her overall pain, improved quality of sleep, and increased her level of physical activity for 4–10 days after these treatment sessions. This case illustrates the potential beneficial effects of using higher power levels of HILT for patients with fibromyalgia syndrome who have failed to respond to conventional interdisciplinary treatment regimens.

Keywords Fibromyalgia · Chronic pain · High-intensity laser therapy (HILT)

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Introduction

Fibromyalgia syndrome (FMS) is a heterogeneous disease which affects an estimated 12 million Americans (> 2% of the population) and accounts for ~ 6% of patients suffering from chronic pain outside the USA [1–3]. Middle-aged women are ten times more likely to get this disease than men. It is the second most common musculoskeletal condition after osteoarthritis (OA). The common characteristics of fibromyalgia include widespread muscle and joint pain and fatigue which can lead to depression and social isolation. The symptoms commonly associated with fibromyalgia include anxiety and/or depression, decreased pain threshold with point tenderness, incapacitating fatigue, and widespread musculoskeletal pain. Often these patients experience

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pain, achiness and stiffness at the joints in the neck, shoulders, lower back and hips, and numbness and tingling in the fingers and toes. Other less common symptoms of fibromyalgia include abdominal pain, incontinence, irritable bowel syndrome, chronic headaches, dryness of the eyes, nose and throat, hypersensitivity to cold and/or heat, and inability to concentrate (so-called "fibro fog").

A wide variety of pharmacologic agents have been used to treat the symptoms of fibromyalgia, including gabapentinoids or alpha-2 delta ligands (e.g., gabapentin and pregabalin), serotonin–norepinephrine reuptake inhibitors (e.g., duloxetine, milnacipran, venlafaxine), selective serotonin reuptake inhibitors (e.g., fluoxetine, paroxetine, sertraline), tricyclic antidepressants (e.g., amitriptyline, nortriptyline), skeletal muscle relaxants (e.g., cyclobenzaprine), as well as both opioid (narcotic) and non-opioid analgesics (e.g., acetaminophen, non-steroidal anti-inflammatory drugs [NSAIDs]). Amitriptyline, pregabalin and duloxetine are the most commonly used drugs to treat FMS [3]. Although of questionable efficacy, nutritional practices (e.g., vegan diet) and dietary supplements (e.g., S-adenosylmethionine, 5-hydroxy-tryptophan, magnesium glycinate/citrate/malate, D-ribose, Coenzyme-Q10, acetyl-carnitine, Vitamin B complex, melatonin) have also been recommended.

For many patients suffering with fibromyalgia symptoms, pharmacologic and nutritional therapies provide only modest benefits and can be associated with unacceptable side effects. Aerobic and muscle strengthening exercises are considered the foundation of the non-pharmacologic management of FMS [4]. However, the effectiveness of physical therapy (e.g., exercise, movement-based therapies) and cognitive behavioral therapies (e.g., biofeedback, mindfulness, relaxation-based therapies) is unclear as the quality of the supporting scientific evidence is very low [5]. Electrotherapy modalities and photobiomodulation ("laser") therapy have been reported to be effective in treating a variety of myofascial musculoskeletal disorders, including FMS [6–9].

Low-level laser therapy (LLLT) is a non-thermal phototherapy used to facilitate wound healing and reduce acute and chronic pain. In 2002, Gür et al. [8, 9] published two sham-controlled studies describing the use of LLLT alone and in combination with low-dose amitriptyline for treating the symptoms of fibromyalgia. These investigators reported that LLLT was safe and effective in reducing musculoskeletal pain and stiffness, as well as the number of tender points. However, in a more recent placebo (sham)-controlled study involving LLLT [10], it was not found to be significantly better than sham treatments and kinesiotape. Not surprisingly, the recently updated guidelines for treating FMS did not recommend the use of LLLT [11]. In a preliminary sham-controlled study using laser heat therapy at 10 W of power (compared to < 1 W with LLLT), the investigators reported that this laser therapy was beneficial for improving pain management and upper body range of motion in women with FMS [12]. Recently, Choi et al. [13] reported that high-intensity laser therapy (HILT) reduced pain and improved activities of daily living compared to physical therapy alone in patients with chronic back pain. Of interest, Kheshie et al. [14] reported that the use of HILT was significantly more effective than LLLT in treating chronic pain associated with osteoarthritis of the knee. These early findings with HILT (vs. LLLT) were confirmed in a study involving patients with Bell's palsy [15].

Therefore, we postulated that use of HILT at 42 and 75 W of power would produce a more profound and longer-lasting symptom relief than HILT at 1 W in a patient suffering from intractable FMS. This case report review describes the results of using three different power levels of HILT to treat a woman who experienced persistent symptoms of fibromyalgia despite receiving commonly used pharmacologic agents, dietary supplements, and a standard interdisciplinary pain management regimen (which included laser heat therapy).

Case report

A 67-year-old retired female veterinarian with long-standing fibromyalgia (~ 7 years) which was resistant to standard pharmacotherapy (including pregabalin) presented at the McDermott Center for Pain Management at UT Southwestern Medical Center in Dallas, TX in October, 2016. Her baseline pain score was 6–7 on an 11-point visual analog scale (VAS), with 0 = no pain to 10 = intolerable pain. The patient completed the standard questionnaires used for assessing patients with fibromyalgia-like symptoms. Her Widespread Pain Index (WPI) score was 10/18, Symptom Severity (SS) Scores were 6/9 (Part A) and 1/3 (Part B). Her symptom impact questionnaire (SIQ) score was 38.3/100, with difficulty primarily expressed for household chores, lifting and carrying groceries, climbing stairs and prolonged sitting (> 45 min). Her medical problems often prevented her from accomplishing her weekly goals. She also reported symptoms of depression, difficult sleeping, memory and balance problems, and sensitivity to touch, loud noises, bright lights, odors and cold. She also completed a RAND Short Form 36 (SF-36) health survey, with scores of 45/100 on the physical functioning subscale, 0/100 on the role limitations due to physical health and emotional problem subscales, 30/100 on the energy/fatigue subscale, 56/100 on the emotional well-being subscale, 25/100 on the social functioning subscale, 10/100 on the pain subscale, and 25/100 on the general health subscale.

Despite receiving an interdisciplinary pain management program biweekly for 4 weeks, including physical/manual therapy, cognitive behavioral therapy, meditation,

biofeedback and a limited series of laser treatments with a 25 W LightForce (810–980 nm wavelength) laser device (LiteCure LLC, Newark, DE), as well as pharmacotherapy with Cymbalta 80 mg po qd and Tylenol 1–2 g/days, she reported only a very transient (minor) improvement in her fibromyalgia symptoms. Of interest, this was the same laser device used in the earlier study by Panton et al. [12]. She was also continuing to take hydrocodone 5 mg po 4–5 times per month for severe discomfort due to acute 'flare ups' in her fibromyalgia symptoms. The patient consented to receiving a series of laser treatments with the Phoenix Thera-lase device (Phoenix Thera-lase Systems, LLC, Dallas, TX). This FDA-approved laser possesses a power range from 1 to 75 W at a wavelength of 1275 nm. The initial 42 W laser treatment was administered bilaterally at the lower thoracic and lumbar paraspinous region and ten tender points located at her shoulder and hip regions. The designated body areas were treated with a series of 60-s treatments located approximately 4–6″ apart over the symptomatic area with the laser probe held ~ 12″ from the skin surface. The initial treatment with the Phoenix Thera-lase lasted 40 min and produced a beneficial effect on her joint pain (VAS = 1–2), as well as improved range of motion, mood, level of physical activity and quality of sleep lasting for 1 week. During this time, she required no opioid-containing analgesic medication. On an 11-point visual rating scale (VRS) for pain relief, with 0 = no relief to 10 = complete relief, she reported her pain relief as a 7 after the initial treatment. After 1 week, her generalized pain had returned to 50% of the initial level. She stated she would be willing to pay $90 USD out-of-pocket to receive additional HILT treatments with this laser device.

One month later, she returned for a more abbreviated 42 W HILT treatment to the lower thoracic and lumbar paraspinous region only (lasting 30 min) and reported excellent pain relief (VRS = 6) with the beneficial effect lasting ~ 4 days. Approximately 2 weeks later, she was administered a 1 W HILT treatment in the same paraspinous region (lasting 30 min) with the Phoenix Thera-lase and reported minimal pain relief (VRS relief score = 2–3) lasting only 2–3 h post-treatment. When her pain returned to her baseline level (~ 1 week later), she returned for a HILT treatment at 75 W lasting ~ 30 min to the same paraspinous region and reported profound pain relief (VAS pain score = 0–1 and a VRS pain relief of 8–9) and the beneficial effect lasted for > 10 days. At 2 weeks after her 75 W HILT treatment, her fibromyalgia pain symptoms returned to > 50% of her baseline level; however, she was no longer using opioid-containing analgesic medications.

Discussion

The objective of cold laser therapy is to deliver light energy to damaged cells using infrared radiation to stimulate local release of nitric oxide (a vasodilator), to improve cellular energy by stimulating mitochondria to accelerate ATP production, and to increase cell growth and metabolic activity, improving wound healing (via increased blood flow and anti-inflammatory actions) and peripheral nerve function [16]. In addition, laser therapy appears to be capable of 'desensitizing' local nociceptors to decrease pain input into the central nervous system (CNS). Compared to other 'alternative' pain therapies such as acupuncture (8000–3500 BC), chiropractic (1895) and even physical medicine and rehabilitation (1947), laser therapy is a relatively recent development in clinical medicine. While the first cold laser was FDA approved for treating pain in 2001, LLLT has only been widely used in the USA since 2002, and HILT is an even more recent development with the initial peer-reviewed publications on its use for pain management appearing in 2011.

LLLT using Class II and III lasers (producing less than < 1 W of power) is a non-invasive, painless therapy for superficial medical and surgical conditions when used as an adjuvant to both pharmacologic analgesia and physiotherapy (e.g., women with nipple pain associated with prolonged breastfeeding, pain secondary to plantar fasciitis, facilitating wound healing) (Table 1) [17–22]. LLLT devices use red beam or near infrared non-thermal lasers with a wavelength between 600 and 980 nm and from 5 to 500 mW of power. Although LLLT has been reported to have a suppressive effect on cancer cells, [23–26] studies using rodent models suggest that it might modify cancer cell behavior and lead to stimulation of dysplastic cells [27–30]. For example, Rhee et al. [31] reported that LLLT can increase tumor size in rodents when thyroid cancer cells were directly exposed to photodynamic (laser) therapy. Clinical studies with both LLLT and HILT are clearly needed in patients with cancer.

Recently, HILT has been administered using more powerful Class IV lasers which are associated with a tissue-warming effect. These FDA-approved devices have been introduced as non-invasive treatment modalities for both acute and chronic pain allowing for greater energy dispersion to deeper tissues [15]. HILT has also been used to treat acute headache pain, degenerative joint conditions, neuropathic pain syndromes and a wide variety of musculoskeletal disorders [14, 15, 32, 33]. The Phoenix Thera-Lase used in this case study is a powerful laser with up to 75 W of power that also functions at a longer infrared wavelength (1275 nm) than other commercially available LLLT and HILT devices (Table 1). The wavelength is important because higher wavelength have reduced absorption of the laser beam by melanin and hemoglobin (Fig. 1), thereby allowing deeper penetration into the soft tissue. Thus, a more powerful laser which

Table 1 Comparison of low level laser therapy (LLLT) and high-intensity laser therapy (HILT) devices and clinical uses which have been reported in the peer-reviewed literature

	LLLT	HILT
Laser class	I, Im, II, III	IV
Wavelength	600–980 nm	660–1275 nm
Power	< 1 W	1–75 W
Penetration abilities	Low (< 2 cm)	Deep (5–15 cm)
Temperature changes	< 1.0 °C	Low thermal accumulation
Applications for acute and chronic pain	Superficial postoperative pain Osteoarthritis Low back pain Neck pain Plantar fasciitis Dental pain Mucositis-associated pain Acute and chronic pain related to herpes virus Trigeminal neuralgia Wound repair The pain of muscle injury Shoulder pain Carpal tunnel syndrome Fibromyalgia-related pain Headache Opioid dependency	Postoperative pain Osteoarthritis Haemophilic arthropathy Low back pain related to herpes virus Myofascial pain syndrome Shoulder pain Fibromyalgia-related pain Opioid dependency *Note* Several of the applications listed for LLLT have not been studied using HILT devices. However, there is no reason to expect they would not respond as well or better
Commercial cold laser systems (Wattage [W] and wavelength [nm])	Erchonia XLR8 laser® (7.5–20 mW laser diodes at 635 nm) BioLight Aura PTL® (5 mW at 635 nm) Multiradiance LaserStim® (7.5 mW at 660 nm to 25 W at 905 nm) Irradia Mid-Laser® (120 mW at 660 nm to 20 W at 904 nm) Avant (0.66–1.4 W at 808 nm) THOR Laser® (150 mW at 660 nm to 2 W at 810 nm) Ga–Al–As laser® (50 mW at 809 nm)	Nd:YAG laser® (0.25 W at 1064 nm) Phoenix Thera-Lase® (37–75 W at 1275 nm) Light Force/LiteCure® (10–25 W at 810/980 nm) TerraQuant® (15–50 W at 660–905 nm) Cutting Edge® (1.1–3.3 W at 810 nm) BioLase Epic (10 W at 940 nm) Apollo® (0.5–5 W at 810 nm) Pilot Diode Laser® (9 W at 810 nm) Aspen Summit® (7–15 W at 810–980 nm) Nexus® (10 W at 810–980 nm) K-Laser® (15 W at 660–980 nm) Lumix Series® 2–3 (45–250 W at 810–910 nm)

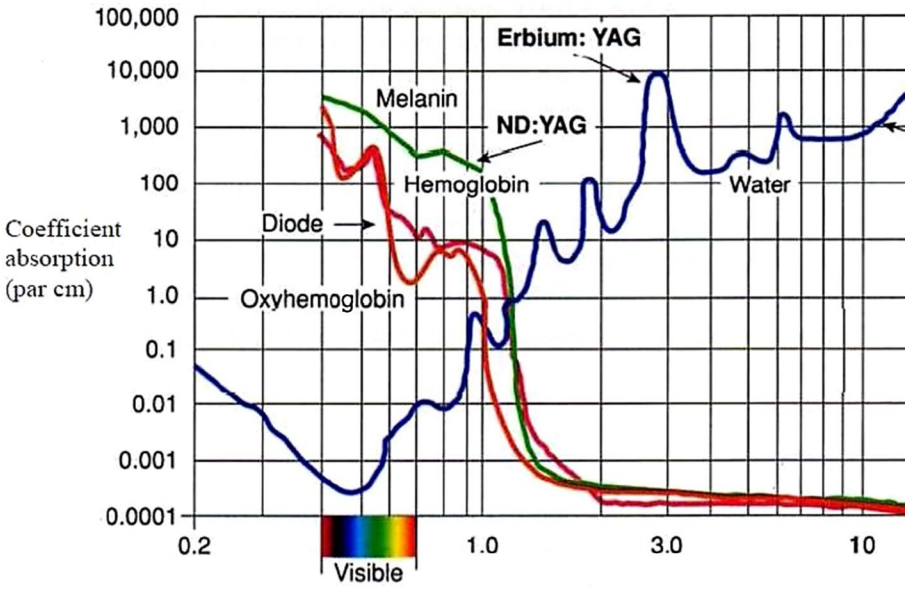

Fig. 1 This graph illustrates the absorption effect of the infrared light by water, hemoglobin, oxyhemoglobin and melanin at different wavelengths (microns). It illustrates one of the important differences between the Phoenix Thera-lase, LightForce/LiteCure, and other commercially available HILT devices (light absorption spectrums are available from online sources)

also functions at a longer wavelength can stimulate larger tissue areas while also penetrating more deeply into the soft tissue [34, 35].

Fibromyalgia is a chronic musculoskeletal condition, characterized by widespread pain in the body, associated with particular tender points at the shoulder, back and hip regions. Given the limited success of pharmacologic drugs and dietary supplements in treating the musculoskeletal pain, patients are increasingly turning to "alternative therapies" for pain relief (e.g., yoga, tai chi, acupuncture, manual therapies [massage, chiropractic/osteopathic manipulation], as well as mindfulness-based stress reduction, hypnosis and biofeedback). Interestingly, the American Pain Society recommends moderately intense aerobic exercise at least two or three times per week, something many of these patients simply cannot physically accomplish. Although HILT is not a cure for FMS, this case study provides evidence of a sustained clinical benefit (up to 10 days after a single treatment) using high-powered HILT treatments in a patient with long-standing classical FMS which failed to respond to currently used treatment regimens (including pharmacologic therapies and less powerful HILT treatments). Although there may be some cumulative beneficial effects associated with multiple treatment sessions, even the most effective treatment we administered at 75 W of power would require that the patient return for additional 'maintenance' treatments. This patient indicated that she would be willing to pay-$90 per treatment session out-of-pocket to continue receiving the 42 and 75 W HILT treatments 2–3 times per month.

If the use of LLLT and HILT can improve pain control and physical activity without untoward side effects, this non-pharmacologic modality could prove to be extremely beneficial in minimizing the negative social impact of debilitating chronic diseases such as fibromyalgia. Although the woman in this Case Report found that the lower power (1 and 25 W) HILT treatments were of limited benefit, the 42 and 75 W treatments were highly effective in reducing her joint pain symptoms, as well as improving her physical activity level, quality of sleep, and sense of well-being (and overall quality of life) for 4–10 days after each of these treatment sessions. Importantly, she was able to discontinue her use of opioid-containing medication after the 42 and 75 W treatments, confirming the findings from a recent case series involving use of 42 W HILT treatments in patients who had become opioid-dependent after surgery [36].

Laser therapy has rarely been considered in the management of patients with fibromyalgia despite the benefits described in two sham-controlled studies by Gür et al. [8, 9]. These investigators demonstrated that LLLT alone and in combination with amitriptyline was safe and effective in the treatment of fibromyalgia symptoms when administered daily for 2 weeks. The findings of Gur and colleagues were confirmed in a more recent study by Ruaro et al. [37]. In the later study, patients receiving three treatments per week for 4 weeks reported that all of their fibromyalgia symptoms showed significant improvements compared to placebo ("sham") treatments. Importantly, these previously published laser studies utilized low power levels (< 1 W) and shorter wavelengths of light (< 900 nm) which can influence the ability of the light beam to penetrate beneath the skin surface (Fig. 1). By administering a more powerful laser beam at a longer wavelength, it is possible to enhance the magnitude and duration of pain relief and symptom improvement [35, 36]. Laser therapy is simple to administer (using a "point-and-shoot" technique) by non-medically trained personnel who are certified in laser safety.

In reviewing the peer-reviewed medical literature, LLLT appears to be an effective approach to improving pain control and accelerate healing when used as an adjuvant to analgesic medications and physiotherapy for superficial medical and surgical conditions [17–22]. However, HILT has been reported to be more effective than LLLT in treating acute headache, degenerative joint conditions, lateral epicondylitis, neuropathic pain syndromes and a wide variety of musculoskeletal disorders [14, 15, 32, 33, 38–40]. This case report further suggests that the use of HILT at 42–75 W of power can produce more profound and long-lasting beneficial effects than a standard treatment protocol for fibromyalgia which incorporates less powerful laser treatments. We are currently performing a sham-controlled, double-blind study utilizing 42 W HILT in patients with treatment-resistant FMS at UT Southwestern Medical Center in Dallas (ClinTrials Reg. NCT02948634). Although additional sham-controlled studies are clearly needed, use of more powerful photobiomodulation laser therapy could potentially improve the lives of millions of patients suffering from the painful symptoms of fibromyalgia while also reducing the risk of opioid dependence.

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Compliance with ethical standards

Conflict of interest Dr. White is a non-paid Consultant to Phoenix Thera-lase and Mr. Hernandez is a paid employee of Phoenix Thera-lase Systems, LLC. Dr. Zafereo has received a study Grant from Phoenix Thera-lase. Dr. Elvir-Lazo has nothing to disclose.

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