

PERSPECTIVES

Review of Literature on Low-level Laser Therapy Benefits for Nonpharmacological Pain Control in Chronic Pain and Osteoarthritis

Robert Dima, BMSc; Vinicius Tieppo Francio, DC, MS, MD, PhD(c); Chris Towery, PA-C, MD, PhD(c); Saied Davani, RPh, MD, PhD(c)

ABSTRACT

Introduction • Low-level laser therapy (LLLT) is a form of light therapy that triggers biochemical changes within cells. Photons are absorbed by cellular photoreceptors, triggering chemical alterations and potential biochemical benefits to the human body. LLLT has been used in pain management for years and is also known as cold laser therapy, which uses low-frequency continuous laser of typically 600 to 1000 nm wavelength for pain reduction and healing stimulation. Many studies have demonstrated analgesic and anti-inflammatory effects provided by photobiomodulation in both experimental and clinical trials.

Objective • The purpose of this research article was to present a summary of the possible pain management benefits of LLLT.

Results • In cold laser therapy, coherent light of wavelength 600 to 1000 nm is applied to an area of concern with hope for photo-stimulating the tissues in a way that promotes and accelerates healing. This is evidenced by the similarity

in absorption spectra between oxidized cytochrome c oxidase and action spectra from biological responses to light. LLLT, using the properties of coherent light, has been seen to produce pain relief and fibroblastic regeneration in clinical trials and laboratory experiments. LLLT has also been seen to significantly reduce pain in the acute setting; it is proposed that LLLT is able to reduce pain by lowering the level of biochemical markers and oxidative stress, and the formation of edema and hemorrhage. Many studies have demonstrated analgesic and anti-inflammatory effects provided by photobiomodulation in both experimental and clinical trials.

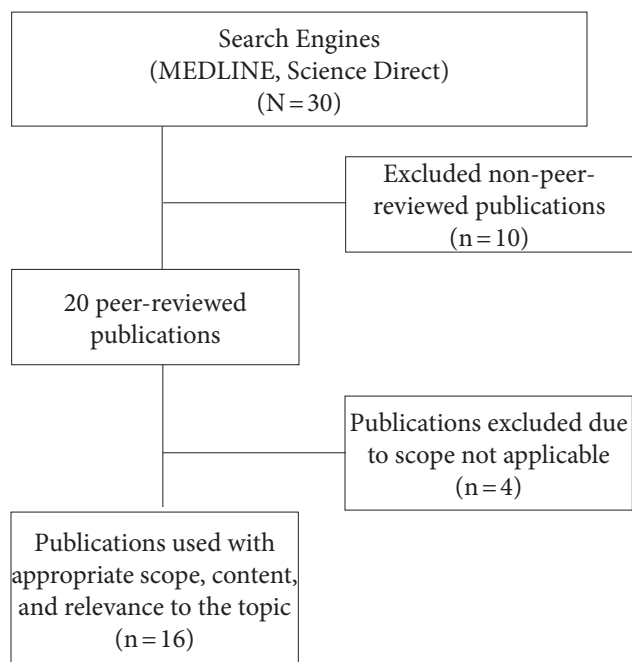
Conclusion • Based on current research, the utilization of LLLT for pain management and osteoarthritic conditions may be a complementary strategy used in clinical practice to provide symptom management for patients suffering from osteoarthritis and chronic pain. (*Altern Ther Health Med.* 2018;24(5):8-10.)

Robert Dima, BMSc; is an undergraduate student in the Medical Radiation Sciences program at McMaster University/ Mohawk College in Hamilton Ontario, Canada; Vinicius Tieppo Francio, DC, MS, MD, PhD(c); Chris Towery, PA-C, MD, PhD(c), and Saied Davani, RPh, MD, PhD(c), are doctoral candidates at University of Science, Arts and Technology-USAT College of Medicine in Olveston, Montserrat.

Corresponding authors: Robert Dima, BMSc
E-mail address: dimars@mcmaster.ca

Nearly 50 million American adults have significant chronic pain, most often due to musculoskeletal injuries and osteoarthritis (OA). Currently, treatment for chronic pain due to OA includes NSAIDs and over-the-counter analgesics; however, due to the comprehensive pathophysiology of OA and the wide manifestation of symptoms in the population (most commonly chronic pain), the most widely used intervention for chronic pain due to OA is opioid therapy.¹ It is estimated that approximately 3% to 4% of the adult US population is prescribed long-term opioid therapy. Evidence supports short-term efficacy of opioids in randomized clinical trials lasting primarily 12 weeks or less; however, few studies have been conducted to rigorously assess the long-term benefits of opioids for chronic pain.² Furthermore, opioid pain medication use presents serious risks, such as opioid induced overdose death. It is estimated that for the

Figure 1. Research Selection



past 15 years, more than 165 000 persons died of overdose related to opioid pain medication in the United States, and it is estimated that in 2013 alone, 1.9 million persons abused or were dependent on prescription opioid pain medication.³

Low-level laser therapy (LLLT) is a form of light therapy that acts on mitochondrial photoreceptors, triggering cell proliferation and fibroblastic regeneration. Light therapy is a broad spectrum term that may encompass coherent and noncoherent light and continuous versus pulsed laser applications. For the purposes of this article, we focus on LLLT, which describes coherent continuous laser of 600 to 1000 nm wavelength. LLLT has been used in pain management for years and is also known as cold laser therapy.⁴ It has seen applications in pain reduction and healing stimulation. Many studies have demonstrated analgesic and anti-inflammatory effects provided by photobiomodulation in both experimental and clinical trials.^{5,6}

Therefore, the purpose of this research article is to present a summary of the possible pain management benefits of LLLT.

METHODS

This research article is a brief summary of LLLT as an alternative pain management treatment method. The search strategy utilized was categorized as a review of the literature including MEDLINE, and Science Direct search with peer-reviewed published research from 1996 to 2016. The search was limited to studies published in English, Spanish, Portuguese and German language with the Medical Subject Headings (MeSH) headings *low-level laser therapy*, *photobiomodulation*, and *chronic pain*. Studies with other scopes with the above headings were excluded (Figure 1).

The search strategy for this review was as follows: Step 1: The reference lists of articles identified by the search engines were searched and triaged into usable relevant publications. Step 2: The relevant research articles were then reviewed by the author(s) and summarized into a relevant table of research. Peer-reviewed articles were included or excluded based on scope, language, relevancy and content pertinent to the publication. Step 3: The author(s) reviewed the articles and summarized the information into the present article, relevant to the topic of OA, chronic pain management, and LLLT.

DISCUSSION OF RESULTS

Chronic pain due to musculoskeletal disorders is known to be one of leading causes of disability in the United States.¹ This condition has increased in prevalence in the last 25 years and is expected to continue rising, further burdening the health care system and decreasing patients quality of life.⁷ To understand the rationale behind treatment methods for pain syndromes due to musculoskeletal injury, it is vital to have an understanding of the pathophysiology of the condition. Musculoskeletal dysfunction is characterized by a loss or failure of the functional/biochemical integrity of a joint.⁸ OA is one of the most well-known joint dysfunctions, and a key pathological feature is the degeneration of articular cartilage within the joint. Decreased articular cartilage, subchondral bone sclerosis, osteophyte development, and chronic low-grade synovial inflammation are all involved in the pathogenesis of OA, and they result in the main symptoms of OA: joint stiffness, joint pain, and dysfunction.⁹ The biochemical properties of OA relate to an abnormal remodeling of the joint, spurred by inflammatory mediators. Cytokines, such as interleukin 1; tumor necrosis factor; interleukin 8; bioactive lipids such as prostaglandin E₂; and well-known proinflammatory chemicals, such as nitric oxide, are seen in high concentration in the osteoarthritic joint; these elevated proinflammatory markers are likely attributed to the synovitis associated with OA, and they contribute to the holistic degeneration of the joint.¹⁰

One therapy that has shown promise in clinical and laboratory studies is LLLT or cold laser therapy. The applications of cold laser therapy in deeper wound healing has been of interest in the scientific community, with literature exploring its potential in Achilles tendinopathy, myofascial neck, and Bouchard's and Heberden's OA.¹⁰ In cold laser therapy, coherent light of wavelength 600 to 1000 nm is applied to an area of concern with hope for photo-stimulating the tissues in a way that promotes and accelerates healing. This is evidenced by the similarity in absorption spectra between oxidized cytochrome c oxidase (CCO) and action spectra from biological responses to light.¹¹ Light is thought to interact with the copper and iron chromophores of cytochrome c to increase oxidation velocity and consequently accelerate cellular metabolism and the production of adenosine triphosphate (ATP). The nitric oxide (NO) hypothesis describes observed increased levels of nitric oxide within

light-exposed tissue. The NO release due to LLLT exposure has been theorized to be due to photo-dissociation of NO from CCO; normally, NO and CCO association (facilitated by mitochondrial NO synthase production of NO) downregulates oxygen metabolism and the production of ATP; by this method, light-induced dissociation both increases the rate of ATP production and allows more free NO available as a vasodilator.^{4,12} Increased ATP production is also known to cause increased concentrations of reactive oxygen species (ROS). These ROS activate transcription factors leading to the upregulation of genes related to cellular proliferation and the production of cytokines and growth factors.^{4,12}

These theories can help to explain the findings of increased levels of ATP synthesis, oxygen uptake, and RNA and protein synthesis seen in individual mitochondria, and the effect of fibroblastic proliferation and wound healing observed on a more macroscopic level.¹² Vasodilation; upregulation of genes related to cellular proliferation; and increased availability of oxygen, cytokines, and growth factors all contribute to the improved healing and strengthening of compromised ligaments and soft tissues. In clinical studies, LLLT has shown promise in managing Achilles tendonitis,¹³ neck pain,¹⁴ extremity OA,¹⁰ and other chronic musculoskeletal chronic pain disorders.¹⁵

Barriers to the implementation of LLLT in treating chronic pain in OA involve the high variation in methods of application. Laser type, ideal dose, and specific wavelength may make health care intimidated to take up laser therapy. Further research is needed to determine ideal dose targets for clinical applications. As per our review, there does not appear to be any distinct wavelength at which healing is optimal, as long as practitioners adhere to the flexible range of 600 to 1000 nm.

CONCLUSION

Based on the findings, we propose a complementary nonpharmacological approach to manage chronic pain, preferably working in collaboration with other traditional conservative strategies. LLLT, using the properties of coherent light, has been seen to produce pain relief and fibroblastic regeneration in clinical trials and laboratory experiments, respectively. LLLT has also been seen to significantly reduce pain in the acute setting; it is proposed that LLLT is able to reduce pain by reducing the level of biochemical markers, oxidative stress, and the formation of edema and hemorrhage. Many studies have demonstrated analgesic and anti-inflammatory effects provided by photobiomodulation in both experimental and clinical trials.^{5,6} Therefore, based on current research, the utilization of LLLT for pain management and osteoarthritic conditions may be a complementary strategy used in clinical practice to provide symptom management for patients suffering from OA and chronic pain.

REFERENCES

1. Neogi T, Zhang Y. Epidemiology of osteoarthritis. *Rheum Dis Clin*. 2013;39(1):1-19.
2. Nahin RL. Estimates of pain prevalence and severity in adults: United States, 2012. *J Pain*. 2015;16(8):769-780.
3. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA*. 2016;315(15):1624-1645.
4. Chung H, Dai T, Sharma S, Huang YY, Carroll J, Hamblin M. The nuts and bolts of low-level laser (light) therapy. *Ann Biomed Engineer*. 2012;40(2):516-533.
5. Ferreira DM, ZaÁngaro RA, Villaverde AB, et al. Analgesic effect of He-Ne (632.8 nm) low-level laser therapy on acute inflammatory pain. *Photomed Laser Surg*. 2005; 23(2):177-181.
6. De Moraes NC, Barbosa AM, Vale ML, et al. Anti-inflammatory effect of low-level laser and light-emitting diode in zymosan-induced arthritis. *Photomed Laser Surg*. 2010;28(2):227-232.
7. Wheaton M, Jensen N. The ligament injury connection to osteoarthritis (extended version). *J Prolother*. 2011;3(4):1.
8. Kean WE, Kean R, Buchanan WW. Osteoarthritis: Symptoms, signs and source of pain. *Inflamm Pharmacol*. 2004;12(1):3-31.
9. Arden N, Blanco F, Cooper C, et al. *Atlas of Osteoarthritis*. New York, NY: Springer Healthcare; 2014.
10. Baltzer AWA, Ostapczuk MS, Stosch D. Positive effects of low level laser therapy (LLL) on Bouchard's and Heberden's osteoarthritis. *Laser Surg Med*. 2016;48(5):498-504.
11. Karu TI. Multiple roles of cytochrome c oxidase in mammalian cells under action of red and IR-A radiation. *IUBMB Life*. 2010;62(8):607-610.
12. Hamblin MR, Demidova TN. Mechanisms of low level light therapy. *Proceeding*. 2006;6140:614001.
13. Bjordal JM, Couppé C, Chow RT, Tunér J, Ljunggren EA. A systematic review of low level laser therapy with location-specific doses for pain from chronic joint disorders. *Austral J Physiother*. 2003;49(2):107-116.
14. Gur A, Sarac AJ, Cevik R, Altindag O, Sarac S. Efficacy of 904 nm gallium arsenide low level laser therapy in the management of chronic myofascial pain in the neck: A double-blind and randomize-controlled trial. *Laser Surg Med*. 2004;35(3):229-235.
15. Bjordal JM, Lopes-Martins RAB, Iversen VV. A randomised, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E2 concentrations. *Brit J Sport Med*. 2006;40(1):76-80.