Low-Level Laser Light Therapy Dosage Variables vs Treatment Efficacy of Neuromusculoskeletal Conditions: A Scoping Review

David N. Taylor, DC, [a] Tyler Winfield, DC, [b] and Shari Wynd, DC, PhD [c]

Abstract

Objective: The purpose of this scoping review was to identify and synthesize literature on dosage variables on the efficacy of low-level laser therapy (LLLT) for neuromusculoskeletal conditions.

Methods: A scoping literature review was conducted by searching the following databases: the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature, Medline, the Physiotherapy Evidence Database, the Index to Chiropractic Literature, manufacturer websites, and online guidelines. The search was modeled after STARLITE criteria. The reporting used Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews (PRISMA-ScR). Articles were included if LLLT was used in any treatment group for a neuromusculoskeletal complaint with dosage and effectiveness reported. This was tabulated by source, dosage variables, conditions, outcome measures, and conclusions. Data were charted in Excel format. Frequency counts were performed on ordinal data. Descriptive statistics were computed for the continuous data.

Results: A total of 86 articles were included in the review. They revealed a broad range of musculoskeletal conditions and diverse dosage parameters. Seven individual parameters were found that would alter the dosage. Although duration of application is an independent clinical factor, the negative-outcome studies were inconsistent in duration. There was lack of statistical difference between the studies with improved vs unimproved outcomes. No statistical differences were noted between the dosage parameters and efficacy.

Conclusion: Although many articles were found on LLLT for neuromusculoskeletal conditions, the studies had amorphous parameters. A heterogeneity of reported doses precluded the synthesis of sufficient evidence to correlate dosage variables with improved or unimproved outcomes. Therefore, based on the current literature, dosage variables for the efficacy of LLLT for neuromusculoskeletal conditions are uncertain at this time. (J Chiropr Med 2020;19;119-127)

Key Indexing Terms: *Low-Level Light Therapy; Musculoskeletal Diseases*

Introduction

Low-level laser therapy (LLLT) or *cold laser* is a term used to describe laser—which is coherent, monochromatic, polarized, red, and infrared light—applied at an intensity that stimulates biological processes. This contrasts with the high-level lasers that are used for cutting in surgery and in industry. Laser therapy (aka *photobiomodulation*) began in the 1960s with the invention of the ruby laser.[1] The therapy subsequently expanded to include new diodes, different wavelengths and intensities, combinations with other therapies, different reported parameters and technologies, and increased applications. This included reports of positive physiological and clinical effects of LLLT in the treatment of many conditions, such as analgesic, anti-inflammatory, and healing effects.[2-4] There is strong evidence that LLLT affects the mitochondria of the cells, resulting in increased adenosine triphosphate production, change of reactive oxygen species, and induction of transcription factors which would stimulate healing.[1,5-7]

The effectiveness of LLLT depends on many treatment parameters.[8-11] These include wavelength, depth of penetration, size of dose, time of application, level of power density, pulse repetition rate, and treatment protocol.[1,2] The therapy is commonly applied at a wavelength range of 600 to 1000 nm,[1,12] output power range from 1 to 50 000 mW,[13] and energy density range of 1 to 9 J/cm.[12] There can be single-, double-, or triple-wavelength lights, or it can be combined with electrical therapy. The fluency of the laser light

[a] Clinical Sciences Department, Texas Chiropractic College, Pasadena, Texas.
[b] Allen, Texas.
[c] Basic Science Department, Texas Chiropractic College, Pasadena, Texas.
Corresponding author: David N. Taylor, DC, DABCN, FIICN, Texas Chiropractic College, 323 Iwama, 5912 Spencer Highway, Pasadena, TX 77505.
(e-mail: *Dtaylor@txchiro.edu*).
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(fluidity of the light emitted) may be continuous, pulsed,[14] or super-pulsed.[15,16] Application of the therapy varies from focused target application to large-area application, with circular motions, overlapping linear grid patterns, or a point technique. Application may be with or without pressure. These different parameters all affect the delivered dosage. Pulsed and super-pulsed frequency may vary from 5 to 3000 or 5000 Hz.[17,18] There is no agreement on whether a continuous wave or pulsed light is best, or which factors govern the choice of pulse parameters.[19] Pulse lasers may be either gated or super-pulsed. Super-pulsed lasers generate pulses in the microsecond or nanosecond duration range, while pulsed lasers are in the millisecond range. Unlike continuous-wave lasers, pulsed and super-pulsed lasers dissipate the thermal effect.

Health care practitioners need information to guide an appropriate purchase and conduct consistent and appropriate application of LLLT. Inappropriate dose parameters are likely to affect outcomes.[12] It is imperative that the practitioner understand the diverse set of parameters to achieve therapeutic efficacy[12] or else risk denying the value of a potential treatment to the patient.

This scoping review examined the optimal doses of LLLT photomodulation for neuromusculoskeletal conditions.[20,21] The purpose of this descriptive literature review was to synthesize the knowledge base of dosage variables and their relationship to outcomes for neuromusculoskeletal conditions and to incorporate the extent of the reported dosage as a factor in the consistent effectiveness of LLLT for neuromusculoskeletal conditions.

Methods

Search

A scoping literature-review method was used to search, tabulate, and organize the dosage variables and outcomes to answer the research question of the dosage effect on outcome. A scoping review was used because of the broad question of dosage variables, the consequence on efficacy in several neuromusculoskeletal conditions, and the need to assess the extent of the knowledge base. As a scoping review, it did not require an evaluation of study quality or bias. The review was not registered because it was a scoping rather than a systematic review. The search was modeled after the STARLITE search criteria.[22] (See Supplementary Data for the search criteria.)

The initial search was conducted by the primary author. The following databases were searched: the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medline, the Physiotherapy Evidence Database (PEDro), and the Index to Chiropractic Literature (ICL). A hand search was conducted of references from reviewed articles, manufacturer websites, and online guidelines such as the National Guideline Clearinghouse. Search terms were "low level laser therapy or photo-biomodulation, or light therapy" AND "dosage." ICL and CINAHL gave limited results, so the search was adjusted to the term "low level laser treatment." The initial Medline search yielded 1341 titles. Reporting was modeled after the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[23,24] That scheme is rigorous, but this study was not intended to be a systematic review or meta-analysis; this was a scoping review, and only 19 of 27 criteria on a PRISMA checklist were appropriate. The reporting was subsequently updated with the Extension for Scoping Reviews (PRISMA-ScR) reporting criteria.[20] No critical appraisal either of individual sources of evidence or within the sources of evidence was conducted, nor was risk of bias evaluated. Summary measures and additional analysis were not applicable. This updated extension consisted of 22 criteria.

The STARLITE method provided a clear way to aid the search. The initial search included clinical studies, outcome studies, and randomized controlled trials. It included scientific peer-reviewed journals, online guidelines, and manufacturer websites. Improved technology and increased applications since 2000 resulted in literature expansion, with recent literature demonstrating a reversal of earlier conclusions. Parameters were not well reported in the earlier studies. The clinical value of LLLT became more recognized for numerous conditions after the turn of the century. Therefore, the search was limited from the year 2000 to December 9, 2017. The search included qualitative studies of musculoskeletal conditions that reported outcomes and dosage. We excluded laboratory studies, studies with participants under 20 years old, and any literature that failed to specify the dosage. We extracted all variables from the literature source and charted the dosage variables, conditions, outcome measures, and conclusions in a tabular form modeled after common systematic reviews (see the Supplementary Data).

Data Analysis and Statistical Methods

We created a Microsoft Excel workbook and entered the data from the charted articles. We initially identified the outcome measures by reviewing the abstracts or the full texts for each article. Additional parameters regarding the LLLT treatment were also identified. We performed frequency counts on ordinal data and computed descriptive statistics for the continuous data. Articles were sorted by outcome (positive clinical outcomes vs no change in clinical outcomes). Using the SPSS data-analysis package (IBM SPSS Statistics, Armonk, New York), we compared the identified parameters using a nonparametric (Mann-Whitney *U*) test. Significant differences between the groups with and without improved clinical outcomes were identified by $P < .05$.

Results

The search identified 1341 Medline titles, 41 CINAHL titles, 14 ICL titles, 279 PEDro titles, 13 Cochrane titles, and 38 titles from hand search. The National Guideline Clearinghouse had no resources related to effective dosage parameters. The total refined search of all databases resulted in 468 titles. The titles were reviewed, duplicates eliminated, and further exclusions created for dental, veterinary, and transcranial studies. Two authors reviewed the abstracts of the remaining 242 titles from all databases. There were an additional 64 papers excluded as irrelevant (transcranial, oral, animal, laboratory, nonmusculoskeletal, or nonclinical studies). After application of all inclusions, exclusions, and duplicates, 86 articles were included. (For the literature-search algorithm, see the Supplementary Data.)

Full texts were then reviewed for the character of the study and reporting of doses. The following exclusions were made: studies with no outcomes, initial prospective studies, animal studies, letters to the editor, withdrawn papers, items from before the year 2000, systematic reviews without parameters, and articles with insufficient reporting of parameters. After 2 authors reached consensus, the data synthesis from Excel was coalesced to compare the variables to outcomes and assess their influence on efficacy. Of the studies reviewed, 64% were double-blind randomized controlled trials and 14.6% were single-blind randomized controlled trials (Table 1). Systematic reviews frequently lacked information on dosage and mainly looked at outcomes with various conditions. Many of these had to be excluded.

Table 1. *Study Types Reviewed*

Study Type	Number of Studies Included
Observational Studies	2
Case Studies	2
Cohort Studies	1
Unblinded randomized controlled trials	11
Double-blind randomized controlled trials	57
Single-blind randomized controlled trials	13
Meta-analyses	1
Clinical guidelines	1
Systematic reviews	1

Most studies were randomized controlled trials, and the majority of those were blinded.

We identified the following variables:

1. Power (peak and average)
2. Wavelength
3. Body area, manner of application, and size of area
4. Type of laser (pulsed, super-pulsed, or continuous)
5. Time of application
6. Pulse frequency (where applicable)
7. Number of treatments

Data-Analysis Summary

Two of the authors compared the following variables in the outcome studies: peak and average power, wavelength, body area and thickness of the tissue, type (fluency) of the laser and pulse frequency, duration of application, and number of treatments.

Peak and Average Power. The variance in power had no influence on the efficacy of the treatment, and total power was rarely reported. When average power was synthesized, there was no difference in outcome. The average (mean) power applied in the studies was 115.95 mW in the improved-outcome studies and 163.32 mW in the unimproved-outcome studies. There was a significant range of 112 to 214 mW in the unimproved-outcome studies and 94 to 137 mW in the improved-outcome studies. A 2-tailed *t* test assuming unequal variances revealed that there was no statistical difference in the average power between improved- and unimproved-outcome studies (Table 2).

Wavelength. Many of the studies reviewed had higher wavelengths, and a true comparison to outcomes could not be determined. This review revealed a mean wavelength of 810 nm for positive outcomes vs 846 nm for unimproved outcomes—a 36-nm difference ($P < .04$). This was a small statistical difference. Although the unimproved-outcome studies used higher wavelengths than the improved-outcome ones, there was a broader range of wavelengths (<900 nm) in the improved-outcome studies (Table 2).

Body Area/Thickness of the Tissue. There has been insufficient reporting of the thickness of the tissue, and a lack of differentiation in application of different wavelengths to different body areas to determine the penetration difference vs wavelength or outcome. The studies were grouped by body regions treated. These body regions were then classified by thick or thin tissue area to be penetrated. A 2-tailed *t* test was performed and compared with the wavelength, revealing that there was no significant difference between wavelengths applied to either thick or thin tissues in the studies with improved outcomes. In addition, there were no statistical differences between the wavelengths of LLLT applied to thin body parts in either the improved-outcome or the unimproved-outcome studies.

Fluency of the Laser and Pulse Frequency. When the type of laser fluency rendered was compared, there was no indication of an influence on the outcome of the laser therapy. A

Table 2. *Dosage Variables vs Outcomes*

Variable	Positive Outcomes (n)	Negative Outcomes (n)	Standard Error of the Mean	
			Positive Outcomes	Negative Outcomes
Average power (mW)	116	163	21.35	51.14
Wavelength (nm)	810	846	12.90	14.39
Duration of application (min)	5.6	6.0	0.71	1.69
Number of treatments	11.7	13.4	0.85	13.38
Pulse frequency (Hz)	2588	1753	732	652

There were no significant differences in outcomes for any variable except pulse frequency. Outcomes were usually measured as changes in level of pain.

2-tailed t test was conducted ($t = 2.17$ [$P < .43$]), indicating that any differences were likely due to chance. Pulsed versus continuous laser light had no statistical difference, with an overlap of the error of the means.

Duration of Application. The studies reviewed lacked a consistent pattern of duration that would influence the clinical outcomes. The unimproved-outcome studies were inconsistent in duration, with a range from 0.26 up to 13 minutes. They showed a mean application duration of 5.36 minutes, compared with 6.36 minutes for the improved-outcome studies. However, a t test showed that there was no statistical difference between the durations between the 2 groups. Wavelengths of 800 to 899 nm were commonly applied for 6 minutes, and 900 to 999 nm for 5 minutes. A 2-tailed t test comparing the wavelength to the duration of application again showed no statistical difference (Table 2).

Number of Treatments. The mean number of treatments per patient was 11.67 for the improved-outcome studies and 13.38 for the unimproved-outcome studies. The negative t test indicated that there was no statistical difference in the outcome related to the number of treatments rendered (Table 2).

Pulse Frequency. The mean pulse frequency was 1753 Hz in the unimproved-outcome studies, compared with 2588 Hz in the improved-outcome studies. The standard error of the mean indicated that there was no statistical difference in mean pulse frequency in the outcomes of the studies. There was a tendency to have higher frequencies in the improved—as compared to the unimproved—outcome studies (Table 2).

Discussion

This scoping review investigated the availability of literature-based evidence for different dosages on the outcomes of LLLT when applied to neuromusculoskeletal conditions. To assess the relationship to effectiveness, only studies that reported dosage were included. There was a heterogeneity of dosages found. One systematic review and meta-analysis on neck pain conducted by a multidisciplinary team defines 4 major dosage variables of clinical significance: power (average and peak power), pulse duration, pulse frequency, and fluency (pulsed or continuous), with priority given to total power per session and per treatment program, energy density, and fluency .[25] Another systematic review for treatment of osteoarthritis reports that a lower dosage of LLLT is "as effective as higher dosage for reducing pain and improving knee range of motion."[26] Other systematic reviews reach conflicting conclusions for various conditions. Some report efficacy relative to placebo, and others report no difference,[27-29] sometimes for the same condition.[2,30] The dosage reporting is inconsistent in the studies. Some report total power, whereas others report energy per point or total energy. Despite the inconsistency in dosage reporting, only 4 out of 71 meta-analyses and systematic reviews (and 11 out of 86 studies accepted for data analysis) report a lack of effectiveness for LLLT.

Although there is little statistical difference in outcomes, the dosage is often nonspecific and rarely reported in detail. Specific dosages (measured in joules) are not calculated for the participants. Dosage is a measure of the energy entering the body and is equal to average power (watts) over treatment time (seconds). The power emitted from the laser probe is determined by the output of the machine and is measured in watts. The longer the treatment time, the larger the dosage of joules administered to the patient (s = J/W). When the fluency is pulsed or super-pulsed, the treatment time of the actual light application is contingent upon the pulse frequency and pulse duration. The dosage is also expected to be highly influenced by the wavelength and site of application (thickness of tissue). It has been suggested that some previous trials of LLLT with inconclusive findings may have delivered dosages below that which is expected to achieve a biological response[3,27] or not within the World Association for Laser Therapy (WALT) recommended dosages.[31-33] Clinical applications are inconsistent, possibly owing to clinicians' lack of appreciation of how dosage is affected by physical and anatomic penetration characteristics[3] and a lack of appropriate compensatory

factors. Studies with improved outcomes on pain were frequently within specific WALT-b dosage guidelines, but recurrences were common after 3 months.[33] In addition, there was heterogeneity in the number of treatments per case in the published studies, which affected the outcomes reported.[3]

Variables Evaluated

Peak/Average Power. The average reported power ranged from 5 to 50 000 mW, with no statistical difference between the improved- and unimproved-outcome studies. A 2007 systematic review on dosages for osteoarthritis of the knee[34] finds an optimal energy dosage of 1 to 4 J/point and power of 12 to 60 mW for a gallium arsenide 904-nm pulsed laser. In a lower-wavelength laser (gallium aluminum arsenide, 820-830 nm), the optimal dose is higher (total power intensity of 30-210 mW/cm^2) at 6 to 24 J.[34] This refines the 2003 broader range of energy for chronic joint pain.[3] Another study successfully used 3 J/point and a total power of 27 J on an osteoarthritic knee, which was within the same parameters of energy as in the above studies,[35] whereas Burger et al report that 6 J/cm^2 was not more effective than placebo.[36]

Energy dosages of 3 and 6 J have been reported to be clinically effective for carpal tunnel syndrome pain, with no differences found for other symptoms, functional status, and grip.[37] Other studies have found dosages of 14 to 18 J significant for an LLLT group for hand grip strength and pinch strength.[38,39] We note that energy dosages are often listed as the amount per point. Not all studies reviewed reported the number of points treated, which would influence the total dosage.

Wavelength. In studies of LLLT-treated neck pain, many trials show the therapy response to be dose-dependent contingent on wavelength.[2,30] For a specific wavelength, the optimal doses for average power and time would determine the patient response. Wavelengths of 820 to 830 nm and mean doses of 0.8 to 9 J for 15 to 180 seconds are reported as optimal. This changes for a wavelength of 904 nm, with mean doses of 0.8 to 4.2 J and 100 to 600 seconds reported as optimal for response. Dosages outside this range do not show a response.[2]

This scoping review revealed a statistically significant difference ($P = .04$), with the unimproved-outcome studies using significantly higher wavelengths than the improved-outcome ones. This is contrary to what is commonly reported, as higher wavelengths are thought to penetrate deeper than lower wavelengths.[2] This may be a result of the fact that there were a limited number of studies performed below the 760-nm wavelength; as a result, the spread of the wavelengths of improved and unimproved outcome were not very different. Bjordal et al find that wavelengths of 632 to 660 nm, or infrared lasers with wavelengths of 810 to 830 nm, show anti-inflammatory effects with an average energy dose density of 7.5 J/cm^2 and a power density of 5 to 171 mW/cm^2. Infrared 904-nm lasers, having strong pulses peaking above 1 W, demonstrate effectiveness with lower doses at 0.7 and 2.8 J.[32]

Body Area and Thickness of the Tissue. One must consider the thickness of the tissue to apply the appropriate dosage for depth of penetration. Our data failed to demonstrate an outcome difference due to expected penetration differences of tissue thickness with the different wavelengths. The appropriate energy for penetration of the part thickness needs to take into account the variables of wavelength, duration of treatment, and number of points treated. These need to be standardized for ranges of different wavelengths and applied to different body parts and conditions. More research is needed to evaluate the dosage differences per body part and patient size.

Fluency. Although there is still much debate about the optimal efficacy of pulsed, super-pulsed, or continuous waves, we do know that pulsed waves can be provided at a much higher peak power (1-50 W) and an average power of 60 mW. This reportedly allows deeper penetration of the therapy without thermal damage and provides for a shorter treatment time.[19] As a result of the pulses, the usual measures to calculate time of application are not applicable. Time of application is calculated by total energy (J) divided by average output power (W) and applied to the square area of application.[40] When pulsed or super-pulsed lasers are used, the laser light is not constantly applied to the body. As a result, pulse duration and frequency need to be considered—power density (mW/cm^2) = pulsed peak power × pulse duration × pulse frequency/ area. There is also some thought that the frequency of the pulses may be in synchronization with the potassium and calcium ion channels in the mitochondria.[19,41,42] Pulsed laser is better than continuous waves (at 10, 25, and 50 Hz) in promoting healing. Higher pulsed frequencies seem to be more analgesic in effect.[19,43,44] This scoping review revealed that there were both improved and unimproved outcomes for pain and disability with all fluencies.

Different fluency effects were noted: physiological effects were present when pulsed light (peak power density of 750 mW/cm^2) was administered for 120 seconds. This produced no neurologic or tissue damage, whereas an equal power density delivered by continuous wave (for the same number of seconds) caused marked neurological deficits.[19,45]

Duration. Although the scoping review showed a broad range of durations of treatment without a correspondence to the outcome, time remains the major independent adjustable variable for clinicians to use, given machines' fixed average/peak power. The systematic reviews by Page et al include studies that range in treatment time from 9 to 16 minutes.[19,28] The World Association for Laser Therapy has published dosage guidelines which recommend fixed dosages for different conditions, based on Laser Class 3B

wavelengths of 780 to 860 nm (5-500 mW) and 904 nm (>5 mW).[33] Bjordal reports in the WALT guidelines recommended times of 30 seconds to 10 minutes for 904-nm and 20 seconds to 5 minutes for lasers from 780 to 860 nm.[32,33,46] This broad range of recommendations lacks direction, but it is pointed out that this is just a starting point for white patients and that dosages may be adjusted up to ±50% until the clinician notes reduction of pain or swelling.[33] Pulsed mode has a reduced time of application, but energy levels are still obtained in deeper tissue. This confounded our findings on treatment duration vs outcomes. The current scoping review revealed a lack of statistical difference in the application times between the improved- and unimproved-outcome studies, and a large associated variance. We were unable to confirm the WALT recommended application times as optimal.

Number of Treatments. The studies in the scoping review did not show any statistical difference in outcomes with different numbers of treatments. The studies all use outcome measures but standardize the number of treatments. The heterogeneity of the number of treatments and cases across the published studies affect the outcomes reported here and in the systematic reviews.[3] The number of treatments applied in clinical practice can potentially affect the dosage and must be individualized to the patient response.

Pulsed Frequency. The higher frequency in the improved-outcome group is in all probability due to pain being the frequent primary outcome. A higher pulsed frequency is bioinhibitive,[32] which benefits pain outcomes measured.[19] Many studies fail to demonstrate a relationship of pulse frequency to the outcomes,[19] and others fail to report the frequencies. This disallowed an evaluation of the effect of pulse frequency on the outcome. One study surprisingly shows a diverse range of 10 to 8 000 Hz as being most effective at pain attenuation.[43]

Clinical Outcomes

Studies confirmed the value of LLT for several conditions. It was as effective as many other interventions for treatment of neck pain, including pharmacologic treatment (celecoxib, meloxicam, diclofenac, and dexamethasone).[2] Pain relief was the result of reduction of inflammation and inflammatory markers at the joint (prostaglandin E, interleukin-1β, tumor necrosis factor α), inhibition of transmission of pain at the neuromuscular junction, disruption of fast axonal flow, or inhibition of neural enzymes[2] and neural conduction blocks.[47] Studies revealed that phototherapy parameters were effective for reducing levels of pain and inflammation at wavelengths of 670 to 830 nm, dosages of 1 to 20 J/cm^2, output powers of 10 to 100 mW, and irradiation durations of 10 seconds to 2.7 minutes.[48,49] The inflammatory reduction may explain the findings that LLLT diminished delayed onset of postexercise muscle soreness and improved recovery when provided prior to exercise.[50] Alghadir et al have found evidence that short-term LLLT improves pain, physical function, and activities in individuals with knee osteoarthritis, possibly via reduced inflammation, but notes the need to compare variables to confirm the results.[51]

Low-level laser therapy has been investigated in several care guidelines written for different conditions. Owing to conflicting evidence at the time of their publication, the European guidelines for the management of chronic nonspecific low back pain do not recommend the use of any physical-therapy modalities, including LLLT. Although some studies included in the review for the guidelines showed improvement in health status, there was not a statistically consistent difference in pain or disability in the laser groups. The guidelines also recognize the lack of consistent dosage parameters, resulting in a heterogenous group in the studies.[52] This concurs with the findings in 2009 of the United Kingdom's National Institute for Health and Care Excellence on the same condition.[53] The American College of Physicians rating of laser therapy for low back pain was unable to estimate efficacy in 2007, concluding that there was insufficient evidence to support the use of LLLT for treatment of low back pain.[54] Ten years later an updated version of this clinical guideline reversed conclusions and recommended LLLT as 1 of the first lines of nonpharmacologic care for acute, subacute, and chronic nonradicular low back pain before pharmacological intervention.[13] This guideline agreed with another 2017 systematic review published the US Agency of Healthcare Research and Quality, which classified LLLT as an "intervention that improved pain and function for at least one month," most notably for low back and neck pain.[55]

Changing recommendations are noted by the evolution of the knowledge base through updated systematic reviews. In 2013, the New York Workers' Compensation Board ruled that LLLT lacked evidence for being beneficial in changing outcomes for carpal tunnel syndrome (CTS).[56] In 2016, Zhi-Jun conducted a meta-analysis on LLLT in CTS and concluded that objective measures were improved in CTS.[57] A meta-analysis by Chow et al concludes that LLLT decreases acute pain immediately and chronic pain up to 22 weeks after care completion.[2] A meta-analysis by Clijsen et al found that LLLT was an effective modality for treating musculoskeletal pain.[4] A systematic review by Bjordal et al concludes that LLLT is effective in treating chronic joint pain.[3] Brosseau et al find that LLLT is advantageous in a systematic review for rheumatoid arthritis; the Cochrane meta-analysis study concludes that LLLT can help with pain management, but the study lacks data on how the variables affect the outcomes.[58] A meta-analysis by Lian et al finds increased grip strength in wrist enthesopathies with LLLT.[59] In 2017 the United States Agency for Healthcare Quality and Research concluded that LLLT was beneficial for neck pain, back pain, and osteoarthritic pain for both pain and function.[55] The contradictions of

outcomes in the literature may be attributed to the Arndt-Shultz principle or conflicts of the multiple dosage parameters. The Arndt-Shultz principle describes effects related to dosage, from no effect to biostimulatory, bioinhibitive, or destructive effect.[40] It is apparent that the current literature supersedes the previous literature. The clinical value of LLLT is recognized, but the most effective parameters of treatment dosage still need research.

The recommended dosages published in the WALT guidelines are a good beginning point. Practitioners need to recognize the possibility of insufficient or excessive dosage due to application technique. It is recommended that clinicians calculate the optimal time of application, consider the thickness of the tissue, and apply appropriate application technique to customize treatment dosage for individual patients.

Limitations and Future Studies

This scoping review contained a range of literature, including some lower-quality studies. We chose to perform no evaluation of the quality of the studies included in this review. Therefore, certain validity assumptions were made regarding the methods and outcomes of these studies.

Additional studies with dosage randomization for similar conditions need to be performed to provide clinicians better definitions of appropriate time, wavelength, and power densities. Time is the primary independent variable to affect the dosage. Studies are needed to compare the optimal use of continuous, pulsed, and super-pulsed wave administration. More definitive dosage information is needed to improve patient outcomes.

Conclusion

A heterogeneity of reported doses precluded an ability to synthesize sufficient literature-based evidence to correlate dosage variables with improved or unimproved outcomes. There is still much to be learned about appropriate therapeutic dosages to promote a consistent physiological response to obtain either an anti-inflammatory effect, a biostimulatory effect, or a bioinhibitory pain-management effect.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.jcm.2020.06.002.

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Contributorship Information

Concept development (provided idea for the research): D.N.T.
Design (planned the methods to generate the results): D.N.T.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): D.N.T.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): D.N.T., T.W.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): D.N.T., S.W.
Literature search (performed the literature search): D.N.T.
Writing (responsible for writing a substantive part of the manuscript): D.N.T.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): D.N.T.

Practical Applications

- The articles revealed a broad range of musculoskeletal conditions and used diverse dosage parameters.
- Seven individual parameters were found that would alter dosage.
- Although duration of application is an independent clinical factor, the unimproved-outcome studies were inconsistent in duration.
- There was lack of statistical difference between the studies with improved vs unimproved outcomes.

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