



Review

Low-level laser therapy in osteoarthritic pain: A narrative review with an approach to integrated clinical use

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ARTICLE INFO

Handling Editor: Professor H Madry

Keywords:

Low-level laser therapy
Osteoarthritic pain
Non-pharmacological pain management
Photobiomodulation

ABSTRACT

Objective: The authors examine how Low-level laser therapy (LLLT) can be used in osteoarthritis (OA) management. LLLT has not, as yet, been widely integrated into OA management, either as a stand-alone modality or in conjunction with standard treatments.

Methods: A narrative review of meta-analyses and trials using LLLT in OA treatment was undertaken to establish how it may be used optimally in OA management. Pubmed, Google Scholar and Cochrane databases were interrogated to identify analyses and trials.

Results: Meta-analysis and trial results are variable, but improvements of up to 14.23 mm are noted in VAS scores following use in knee osteoarthritis (Standardised Mean Difference (SMD) 95 % CI: 7.31:21.14), 13.7 mm in spinal disease (SMD 95 % CI: 9.72; 17.42) and 19.86 mm (SMD 95 % CI: 10.04:29.68) in cervical disease. Positive effects on function were documented, as was a reduction in use of analgesic medication. Integration of LLLT into OA management programmes produced additional improvements. The side-effect profile is excellent. Issues of trial size, comparability, dosing, and assessment of response, mean that further studies are required.

Conclusions: We conclude that LLLT is useful in the management of OA pain, with benefits for stiffness and function. Use as an integral part of an OA management and rehabilitation plan appears to give additional benefits. LLLT has an excellent side effect profile and may reduce need for analgesic medication, making it a potentially valuable adjunct in OA pain management, especially at a time when adverse effects of pharmacological treatment are of increasing concern.

1. Introduction

Low-level laser therapy (LLLT) has been extensively investigated as a non-pharmacological treatment modality for osteoarthritic pain, as well as for many other conditions. Clinical trials and subsequent meta-analyses in osteoarthritis (OA) have been broadly positive but, as will be seen, issues remain about the research and its application in clinical practice. LLLT is the subject of renewed interest at present, largely because of the increasing awareness of adverse side effects associated with standard pharmacological management of chronic OA related pain.

Non-surgical management of OA related chronic pain remains an ongoing challenge in healthcare. OA affects over 500 million people worldwide, 73 % of these being over 55 years of age and 60 % being female [1]. The commonest joint affected is the knee, with a prevalence of 365 million, followed by the hip and hand [2]. An analysis of these data estimates that 344 million people have moderate or severe

osteoarthritis and would benefit from a rehabilitation programme [3]. OA and OA related pain are frequently complicated by both psychosocial issues and co-morbidities, particularly in the elderly [4,5] and these factors may reduce the ability or willingness of patients to engage with definitive exercise rehabilitation and, therefore, compromise the patient's return to optimal function and the normal activities of daily living.

Standard management has utilised physical rehabilitation programmes, where feasible, but non-surgical treatment has primarily been pharmacological. Side-effects of non-steroidal anti-inflammatory drugs are common and potentially serious, especially in the elderly [6]. Use of opioids, leading to overuse and dependence, has become a major issue in the United States [7] and the situation in Europe, while not as severe, is described as an "emerging opioid crisis", most notably in Ireland and the United Kingdom [8]. With these major considerations, increasing attention is being given to non-pharmacological modalities of pain

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management, including LLLT. For example, the US Centers for Disease Control and Prevention has issued guidance on opioid use which places increased emphasis on recommending non-pharmacological modalities including LLLT [9]. Similarly, the American College of Physicians has recommended LLLT in their guidelines [10]. These recommendations are based on the many trials and meta-analyses carried out over the last 30 years or so, as interest in this modality grew. Nonetheless, some uncertainties and controversies remain about LLLT and its use. We aim to address these, using the available scientific literature, in order to facilitate definitive and evidence based use of LLLT in the treatment of OA related pain.

2. Rationale for review, mode of action of low-level laser therapy

The mechanism of action of LLLT at cellular level has been the subject of much investigation but some details remain to be elucidated. It is clear from the evidence, however, that the primary action is photobiomodulation at the mitochondrial level, with cytochrome *c* oxidase acting as a chromophore and resulting in the increased production of adenosine triphosphate [11]. This in turn leads to an increase in nucleic acid synthesis and, at the cellular level, tissue repair and regeneration. *In vitro* work, using endometrial cells, supports this hypothesis [12]. Other actions are less well understood and potentially controversial, but there are convincing data to show that LLLT results in an increase in nitric oxide, a powerful vasodilator, increasing blood flow and augmenting healing [13]. There is also a well described anti-inflammatory effect [14] and, following use of LLLT, a decrease in prostaglandin E2 concentrations has been documented [15]. This anti-inflammatory action suggests a potential role for LLLT in conditions involving inflammation and pain, including OA. While clarification continues, the accepted evidence of the mode of action strongly suggests that the therapeutic effect of LLLT is reparative, regenerative, anti-inflammatory, and analgesic.

3. Methods

Pubmed, Google scholar and the Cochrane databases of systematic reviews were interrogated for meta-analyses, systematic reviews and reviews over the last ten years, with emphasis on the more recent. Search parameters were “low-level laser therapy” plus one of the following: knee osteoarthritis, hip osteoarthritis, low back pain (LBP), head and neck pain. In addition, Pubmed and the Cochrane Central Register of Controlled Trials were used when there were few systematic reviews (e.g. hand pain) and also to identify more recent studies, in order to get as broad a view as possible. Analyses which had result parameters that were consistent and which generated discussion in the scientific literature were particularly selected in order to examine any controversies as thoroughly as possible. A total of 14 meta-analyses and 6 controlled trials were selected.

4. Results

4.1. Knee osteoarthritis

LLLT has been used in the management of osteoarthritis (OA) for many years, and has generated a large number of clinical trials and subsequent analyses examining its clinical use. Most of this work relates to knee OA (KOA), with few studies of hip OA. The results of this research are varied, and even controversial from the start, with many authors finding LLLT effective, while others are more measured in their findings. For example, a recent systematic review and meta-analysis examined both LLLT and high-intensity laser therapy (HILT), (the latter not in the scope of this review), for KOA [16]. The authors concluded that LLLT is beneficial as an adjunct to rehabilitation exercise in the management of KOA, based on the evidence of seven studies that evaluated LLLT. A more recent review, in this journal, examining many

non-pharmacological, non-surgical interventions in KOA [17] was somewhat more cautious, grading the evidence as level C (uncertainty), but still recommending LLLT, both as a complement to exercise, and as a standalone intervention [17]. Other meta-analyses have generated extensive discussion in the scientific literature. Huang et al. in one early and frequently cited meta-analysis of LLLT in KOA [18], noted variation in the results of clinical trials, probably because of the non-standardisation of treatment. These heterogeneous results among study outcomes were attributed to differences in dosing, treatment schedules, energy density, output, and wavelength. While highlighting these limitations in their analysis, the authors concluded that use of LLLT for KOA was not superior to placebo. In particular, they state that the Standardised Mean Difference (SMD) for the Visual Analog Scale (VAS) for pain was not significantly different from control groups, SMD -0.28 [95%CI: 0.1; 0.66]. The validity of their analysis was strongly challenged by Stausholm et al. who highlighted methodological shortcomings in Huang's analysis, and refer to other meta-analyses showing positive results of LLLT in KOA [19]. Analysing the same trials as Huang, using a different statistical approach, Stausholm found that LLLT performed significantly better than placebo for pain relief by 7.22 mm VAS with SMD 0.34 [95%CI: 1.15; 13.3] overall. A subsequent much larger meta-analysis by the same authors, included 22 trials and 1063 patients [20], concluded that LLLT significantly reduced pain, VAS 14.23 [95 % CI: 7.31; 21.14] in KOA which continued during follow up. Disability was also found to be reduced in KOA compared to placebo at the end of treatment, standard mean difference (SMD) 0.59 [95 % CI: 0.33; 0.86] and also at follow-up visits.

The inconsistencies in trial and meta-analysis findings may be attributed to varying trial parameters: dosage, wavelengths, frequency and duration of therapy as mentioned by the above authors. A Cochrane review has emphasised the importance of consistency in reporting of LLLT treatment parameters [21]. More recent work tends to examine individual treatment parameters in more detail. In particular wavelength has been examined because of the issues of varying penetration into tissues of different wavelengths. Fan et al. in a recent meta-analysis found that compared with sham LLLT, wavelengths of 904–905 nm and 785–850 nm significantly reduced knee pain, SMD 1.42 [95 % CI: 0.31; 2.53] and SMD 0.82 [95 % CI: 0.11; 1.50] respectively [22]. Importantly, this meta-analysis did not include studies that paired LLLT with exercise.

The combination of LLLT and exercise therapy has been increasingly examined, but again comparability of both LLLT parameters and exercise programmes together complicates analysis as outlined by Fan et al. [22]. Exercise programmes are strongly supported, by Ferreira et al. as a positive intervention for KOA [17], and the benefit of LLLT is likely to both facilitate exercise and improve the clinical response. A recent review advocates a multidisciplinary approach to pain management in KOA [23] and a recent trial by Stausholm et al. demonstrates that, as well as pain reduction, there was reduced pain medication use and better performance in the sit-to stand test in a group treated with LLLT combined with exercise, compared with a group receiving sham LLLT and exercise [24].

In addition, two recent randomised controlled trials are worthy of mention. Jankaew et al. demonstrated an improvement of +2.16 % ($p < 0.001$) in the strength of knee extensors in a group treated with LLLT (808 nm wavelength), significantly different from results in those treated with either 606 nm LLLT or sham LLLT. They also noted improvements in chair to stand test with 606 nm LLLT (+2.22 times, $p < 0.006$) compared to other groups and recommend LLLT for use concomitantly with rehabilitation programmes for KOA [25]. Robbins et al. further showed that combining LLLT and stretching exercises improves pain during rest, stiffness, range of motion and activities of daily living in KOA [26].

4.2. Spinal osteoarthritis

The aetiology of LBP is complex and includes of course osteoarthritis as well as injuries causing muscle and ligament damage, disc herniation

and degenerative disc disease. It is imperative to establish as accurate a diagnosis as possible, to rule out more sinister causes such as malignancy or cauda equina syndrome, especially in more acute presentations. Assessment of the response of LBP to treatment may be challenging, not just because of the complex aetiology, but also because of psychosocial and lifestyle issues [27]. The assessments of LLLT for LBP have been largely positive. Unsurprisingly, given the complexity of the issue, one meta-analysis calls for larger and more rigorous clinical trials, noting marked heterogeneity among trials, but reporting a moderate benefit of LLLT for LBP [28]. Huang et al. in their meta-analysis support the view that LLLT is effective in reducing non-specific LBP, finding that the weighted mean difference in the VAS pain scores was significantly lower in the LLLT treated group compared to placebo; weighted mean difference -13.7 [95 % CI: 17.42; -9.72] [28]. They did not, however, find a significant effect on function [29].

In addition, a more recent trial noted LLLT to be effective for chronic LBP, with almost 75 % of LLLT treated subjects achieving a ≥ 30 % reduction in LBP scores at two months, and maintaining this improvement at 12 month follow-up. [30]. In this study, Oswestry disability index scores were also favourable. These were 15.8 (Standard Deviation 14.0) at two months and 15.7 (SD 16.1) at twelve months, significantly lower than baseline $p < 0.050$. They also suggest LLLT as a safer alternative to opioids and NSAIDs, while noting that the US Food and Drug Administration has approved LLLT for LBP [30]. Further systematic reviews also agree that LLLT, especially when combined with an exercise programme, benefits LBP both chronic and acute [31,32]. It is also worthy of note that for discogenic LBP, a recent meta-analysis concludes that LLLT is significantly better than placebo and, when used in conjunction with standard physical treatment, achieves better results than standard treatment alone [33].

In the case of cervical osteoarthritis, which is a major contributor to head and neck pain, fewer trials are available. An early meta-analysis noted excellent results with LLLT for neck pain, with patients in eleven trials reporting a reduction in VAS pain score of 19.86 mm (10.04–29.68) [34]. Seven of these trials looked at follow-up and found a persistent VAS pain score reduction of 22.07 mm (17.42–26.72) at 22 weeks [34]. While acknowledging this as a well-designed review, Verhagen et al. considered the positive findings “too optimistic” [35] an opinion refuted by the authors, finding a significant ($p < 0.0001$) mean difference of pain relief (VAS score) of 17 mm and 16 mm at the end of treatment and at 26 weeks respectively, even when the concerns raised were addressed [36]. Other meta-analyses in this area, although not confined specifically to cervical OA, noted very encouraging results with LLLT, when used as part of a multimodal physiotherapy programme, but recommended that further trials would be advisable [37,38]. It is noteworthy that these calls for further and larger trials are consistent throughout the literature on LLLT, even when positive results are reported, presumably for the reasons of comparability and validity already discussed.

4.3. Other conditions

The use of LLLT for other osteoarthritis related conditions is less well studied, but the mechanism producing an effect for knee osteoarthritis has been extrapolated to e.g. hand and foot pain. One early joint specific study in osteoarthritis concluded that LLLT is useful in managing chronic joint pain, including hand osteoarthritis [39]. One trial reported a significant improvement in VAS pain scores, ring size and range of motion ($p < 0.001$ in all cases), effects which persisted at eight week follow-up [40]. Given the paucity of non-pharmacological interventions available for osteoarthritic hand pain, this is encouraging, and further work would be highly desirable. Some trials in this area, while reporting positive findings, have been small observational, uncontrolled studies, emphasising this need for more robust clinical trial data [41].

5. Discussion

5.1. Response to LLLT, dosing and dose delivery

As noted, pain is complex and frequently complicated by psychosocial issues and co-morbidities [4]. Because of this multifaceted nature of pain, the results of any individual treatment is difficult to assess and quantify [27] which contributes to the variabilities and uncertainties in some results. With LLLT there has been, as seen above, many randomised controlled trials with results that, while broadly positive, have been mixed (Table 1.). Meta-analyses have confirmed the positive findings of the trials, but have consistently concluded that further, larger and more rigorous trials would be advisable [28,37]. Many individual trials have been relatively small, and used different treatment parameters making comparability difficult. For example, the uncertainty about which wavelengths to use, and the use of different wavelengths in trials, have made comparison and meta-analysis more difficult. Wavelengths in the range 600 nm–905 nm, with an output of $< 0.5W$, are typically used in LLLT [42], and there is evidence that a wavelength of 808 nm may be superior to 660 nm for some indications, e.g. knee osteoarthritis [25]. For example, a recent clinical trial [43] concluding that LLLT was not superior to placebo has been criticised on the grounds that the dose used was not adequate for the purpose of the trial [44] and that dosing guidelines were not followed [45]. In addition to these issues, details of the time length of individual treatment doses and the frequency of LLLT dosing is often unclear. Such dosing differences as well as differing treatment regimens have made meta-analyses of trials difficult, hence the calls for more trials, even when results of individual trials are, overall, encouraging. It is, for these reasons, very important to use recognised dosing guidelines for LLLT such as those issued by the World Association for Photobiomodulation Therapy [46].

Further issues about the practicalities of delivery of LLLT are worthy of consideration. As a clinic based service, the use of LLLT is influenced by the expense of the equipment to the care provider and, both the availability and expense of clinic visits to the patient. This may make adherence to dosing regimens difficult. The development of smaller equipment, suitable for home use has made LLLT more accessible enabling both the frequency and length of treatments to become more flexible. It will be necessary for providers to address this issue as such devices vary in specification. Any proposed selection of home based devices should ensure they meet appropriate quality standards (e.g. are CE marked) and use wavelengths in line with recommendations [42]. Devices using dual wavelengths of e.g. 650 nm and 808 nm may be useful and appropriate for home therapy [42]. Consultation with the provider would be important to ensure correct clinical use. Home LLLT as a maintenance treatment following clinic assessment and treatment may be an appropriate consideration for some conditions following initial diagnosis and management. Home maintenance LLLT following treatment with the clinic based HILT is also something to be assessed in the future, as HILT (not in the scope of this review) is showing good results especially in KOA [16].

Despite the remaining issues about LLLT, described above, there is a good evidence base supporting its use in the management of osteoarthritic symptoms of pain and stiffness and for a beneficial effect on function. Authors agree that the mechanisms of action at cellular level, support its use as anti-inflammatory, reparative and analgesic [11,13]. The side effect profile is excellent, non-controversial and there are very few contra-indications [47]. In addition, the noted potential of LLLT to facilitate the reduction of analgesic medication is potentially of significant benefit and is worthy of further study [22,24]. It is noteworthy that the American College of Physicians, while noting the issues relating to evidence, and on the basis of its good risk-benefit profile, issued a strong recommendation for use of LLLT in chronic low back pain [10]. Similarly, the US Centers for Disease Control, in their 2022 practice guideline, recommend maximising the use of non-pharmacologic therapies for

Table 1
Relevant meta-analyses and randomised controlled trials with comparable metrics. Metrics taken from published papers.

Author (year)	Reference No.	Study design	No. of studies in meta-analysis/ patients in RCT	OA type	Intervention	Pain outcome	Disability outcome
Huang (2015)	[18]	Meta-analysis	9 RCTs	KOA	LLLT vs sham laser	NSD ^a , SMD 0.28 [95%CI: -0.1; 0.66]	Not examined
Stausholm (2017)	[19]	Meta-analysis	9 RCTs	KOA	LLLT vs sham laser	Positive, 7.22 mm VAS, SMD 0.34 [95 % CI: 1.15; 13.3]	Not examined
Stausholm (2020)	[20]	Meta-analysis	22 RCTs	KOA	LLLT vs sham laser	Positive, 14.23 mm VAS, [95 % CI: 7.31; 21.14]	No conclusion
Fan (2024)	[22]	Meta-analysis	13 RCTs	KOA	LLLT vs sham laser	Positive, SMD 1.42 [95 % CI: 0.31; 2.53] at 904–905 mm Positive, SMD 0.82 [95 % CI: 0.11; 1.5] at 785–850 mm	No improvement shown
Jankaew (2023)	[25]	RCT	47 participants	KOA	LLLT 660 nm LLLT 808 nm Sham laser	Measured muscle strength and functional outcomes	Knee strength +2.16 %, p < 0.001, (808 nm) Chair to stand +2.22 times, p < 0.006, (660 nm)
Robbins (2022) ^b	[26]	RCT	215 participants	KOA	LLLT + stretching Placebo + stretching Stretching alone LLLT alone Control	Knee pain and disability improved. p < 0.001, (LLLT + stretching group)	Improved p = 0.000237
Huang (2015)	[29]	Meta-analysis	7 RCTs	Spinal	LLLT vs placebo	Positive, WMD 13.7 [95 % CI: 9.72; 17.42]	No significant improvement
Berry (2020)	[30]	RCT	23 participants (studied at 12 month post treatment follow up)	Spinal	12 month follow up of treatment	Positive, ≥30 % pain reduction (mean VAS reduction 22.4 mm)	Positive, mean reduction in oswestry disability index 5.1 (p < 0.5)
Chow (2009)	[34]	Meta-analysis	16 RCTs	Spinal	LLLT vs placebo or active control	Positive 19.86 mm VAS, [95 % CI: 10.04; 29.68] persisting up to 22 weeks 2010 revision 17.00 mm VAS	Not examined
(2010)	[36]						

^a No significant difference. SMD=Standardised Mean Difference, WMD=Weighted mean difference.

^b RCT included exercise programme and LLLT.

chronic pain and cite a comparativeness review supporting the use of LLLT for chronic LBP and chronic neck pain in particular [9,48].

6. Conclusions

The clinical evidence as well as the evidence of the mechanisms of action of LLLT support its use as a pain management option, because of its analgesic, anti-inflammatory and reparative effects. We suggest in addition that, based on the evidence outlined, LLLT may be beneficially integrated into comprehensive pain management programmes as a useful adjunct, especially for the more complex issues outlined. This evidence, as discussed above, supports the view that LLLT combined with exercise based interventions achieves optimal results [25,26,33]. It is crucial, however, that appropriate dosing guidelines are used [45,46].

Follow-up with home use LLLT devices is likely to be increasingly considered as these devices become more readily available. Such treatment, if suitable, can be self-administered (following the initial clinical assessment), using a more flexible dosing regimen. It also, importantly, allows patients to take more control of their pain management in a manner that, unlike self-medication with analgesics, has not been shown to be harmful. LLLT, as a maintenance pain control following clinic based HILT, could also be considered in the future.

Comprehensive pain management programmes, incorporating elements of self-management are recognised as important in dealing with chronic pain [49] and LLLT can form a useful part of this. It may also allow fuller engagement with the exercise elements of a pain management programme and, thus, facilitate an earlier return to normal activities and hobbies, which has a direct impact on patient wellbeing. It is of particular interest that such integrated LLLT use has been noted to reduce reliance on pain killing medication [23,24]. At a time when use of opioids and NSAIDs, including self-medication, is a cause for concern internationally, a non-pharmacological, and non-toxic adjunct such as LLLT, for which there is an adequate evidence base, can be considered as a potentially useful, integral part of mainstream pain management.

Contributions

The research papers were analysed and the results were critically examined by both authors. GDC had a primary role in preparing the manuscript, which was edited by SNH. All authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Funding

There was no external funding source for this work.

Declaration of competing interest

GDC is an independent medical advisor and has no conflict of interest.

SNH is a Chartered Physiotherapist whose practice includes use of laser based instruments.

Acknowledgement

We are grateful to Dr N Quinn, Department of Mathematics and Statistics, Munster Technological University for valuable statistical advice.

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