High-intensity laser for the treatment of pain: systematic review

Laser de alta intensidade para tratamento da dor: revisão sistemática

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ABSTRACT

BACKGROUND AND OBJECTIVES: Pain is one of the most prevalent causes of disability in the world, and the adverse effects promoted by analgesics can limit therapeutic success. In this context, laser appears as a complementary therapy that can enhance analgesia without increasing the incidence of undesirable adverse events. The aim of this study was to carry out a systematic review on the effectiveness and efficiency of high intensity laser (HIL) in the treatment of pain.

CONTENTS: A systematic search was carried out in Medline, LILACS, Pubmed and PEDro, from July 2020 to August 2022. The keywords pain, chronic pain, high intensity laser and treatment were considered. The quality of selected studies was assessed using the PEDro scale. Included systematic reviews were assessed for methodological quality using the AMSTAR tool. The main measure studied was pain intensity. 227 studies were found and, based on the inclusion and exclusion criteria, 32 articles were read in full, whit one being excluded for not assessing pain. Musculoskeletal disorders corresponded to 70,96% of the assessed diseases and the visual analogue scale (VAS) was the only pain measurement tool used in 100% of the studies. Approximately 57% of the studies were of high methodological quality (PEDro=7). In 53,84% of the trials, HIL was used as a single intervention, and in 46,16% it was associated whit exercises. In 96.15% of clinical trials and 100% of systematic reviews there were positive effects of HIL on pain.

CONCLUSION: HIL is an effective modality for analgesia by promoting significant pain relief, rapid recovery and improvement in patient's quality of life, in a safe way. The diversity in irradiation parameters (dose, duration, interval and number of sessions) used, indicates the need for further randomized studies to establish its long-term efficiency.

Keywords: Pain, High-intensity laser, Therapy.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor é uma das causas mais prevalentes de incapacidade no mundo, e os efeitos adversos promovidos pelos analgésicos podem limitar o sucesso terapêutico. Nesse contexto, surge o laser como terapia complementar que pode potencializar a analgesia, sem aumentar incidência de eventos adversos indesejáveis. O objetivo deste estudo foi realizar uma revisão sistemática sobre a eficácia e a eficiência do laser de alta intensidade (LAI) no tratamento da dor.

CONTEÚDO: Foi realizada uma busca sistemática nas plataformas Medline, LILACS, Pubmed e PEDro, de julho de 2020 a agosto de 2022. As palavras chaves dor, dor crônica, laser de alta intensidade e tratamento foram consideradas. A qualidade dos estudos clínicos selecionados foi avaliada utilizando a escala PEDro. As revisões sistemáticas incluídas foram avaliadas quanto à qualidade metodológica através da ferramenta AMSTAR. A principal medida estudada foi a intensidade de dor. Foram encontrados 227 estudos e com base nos critérios de inclusão e exclusão, 32 artigos foram lidos na íntegra, tendo sido excluído um por não avaliar a dor. As desordens musculoesqueléticas corresponderam a 70,96% das doenças avaliadas e a escala analógica visual (EAV) foi a única ferramenta de mensuração da dor utilizada em 100% dos estudos. Aproximadamente 57% dos estudos tinham alta qualidade metodológica (PEDro=7). Em 53,84% dos ensaios o LAI foi utilizado como intervenção única, e em 46,16% foi associado a exercícios. Em 96,15% dos ensaios clínicos e 100% das revisões sistemáticas, o LAI promoveu alívio da dor.

CONCLUSÃO: O LAI é uma modalidade eficaz para analgesia ao promover significativo alívio da dor, rápida recuperação e melhora na qualidade de vida dos pacientes de forma segura. A diversidade nos parâmetros de irradiação (dose, duração, intervalo e número de sessões) empregados, indica a necessidade de mais estudos randomizados para estabelecer sua eficiência em longo prazo.

Descritores: Dor, Laser de alta intensidade, Tratamento.

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HIGHLIGHTS

- Pain is a common, often debilitating condition that has a significant impact on its sufferers' quality of life.
- Laser is a non-invasive, painless, and safe alternative for pain reduction in acute and chronic pain syndromes.
- More than 50% of the clinical trials in this study have moderate to high quality according to the PEDro scale.

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INTRODUCTION

Pain is an important domain of human experience. No other physical symptom is more pervasive than pain, characteristically accompanied by psychological experiences of intense human suffering and stress[1,2], being "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage"[3].

Through the phenomenon of recognition of painful signals by nervous system, called nociception, the painful information is processed and differentiated into physiological and pathological pain[4]. The first is expressed as an adaptive sensation, as a warning sign for survival, and the second as a bad adaptation of the organism, being harmful and independent of the stimulus that generated it[5-7]. While protective behavior as a response to pain may bring benefits, prolonged painful states persistently stimulate nociceptive afferents, inducing changes that increase the deleterious effects of pain[6].

Data from the Global Burden of Disease points out an increase in the number of patients with chronic pain in the last decade, being one of the most prevalent causes of disability in the world[8]. The pain is considered chronic when it persists for a period longer than three months, it is defined as primary when it is not explained by the presence of another clinical condition, and as secondary when it is initially expressed as a symptom of another disease, but persists even after the treatment and resolution of the latter[9]. It involves social, family, emotional, and cognitive aspects that need to be considered in its therapeutic approach[6].

The search for an antinociceptive treatment is, therefore, an arduous and increasingly necessary endeavor. The currently available therapeutic arsenal includes drugs, adjunctive therapies, and invasive procedures. The adverse effects of many therapies can further reduce quality of life and result in patients abandoning treatment. Adjuvant therapies potentiate analgesia without resulting in an increase in undesirable effects, and they can also bring financial advantages to the health system[10]. In this context, physical exercises, transcutaneous electrical nerve stimulation (TENS), pulsed electromagnetic field (PEMF), ultrasound (US), complementary therapies (meditation, massage, acupuncture, psychotherapy, etc.) and, more recently, laser therapy[11-13] stand out.

Laser is an English acronym that in free translation means "light amplification by stimulated emission of radiation". It is a coherent, convergent and monochromatic beam of electromagnetic radiation, in which the photons propagate practically parallel, concentrating in a well-defined area, so that all particles have the same behavior and propagate in the same direction[14]. It is considered one of the most important inventions of the 20th century and, in medical practice, it has been used as a non-invasive treatment modality, administered for a wide range of disorders, with low incidence of adverse effects when employed by a skilled operator[15].

Lasers considered as therapeutic are low intensity lasers, corresponding to 5-500 mW devices, and high intensity laser (HIL), with more than 500 mW[16]. HIL use a specific waveform, with regular amplitude peaks, which make it possible to reach deep structures, with stable effect and shorter application time. They rapidly induce photothermal effects, such as increased metabolic rate and blood flow, photochemical and photomechanical effects, which stimulate cell metabolism, proliferation and differentiation[17].

HIL has been used in several pain syndromes, acute and chronic, with special emphasis on musculoskeletal disorders, such as low back pain[18-21] and knee osteoarthritis[22-25]. In a systematic review with meta-analysis[26] that evaluated studies involving patients with musculoskeletal pain of various etiologies, the intensity of pain in these patients was reduced after HIL application, in relation to the pre-intervention values and in comparison to the results obtained by control groups.

Thus, there are already reviews[26-30] about HIL application in patients with chronic and acute pain, showing that its application in subsequent sessions, in continuous or pulsed mode, has shown fast effects in relief and reduction of pain intensity and recovery time.

However, because it is a subjective experience, pain cannot be objectively determined by physical instruments that usually measure other vital signs, making it challenging to assess changes in its intensity[31]. The parameters and scales used for this are very variable, in such a way that, for the same therapy, the results of the studies can be different, depending on how pain is measured[32,33].

Taking into account the literature and the importance and complexity of the subject, it is clear the need to organize and compare the methods and results of the main evidence found on the subject. In this line, the present work aims to perform a systematic review on the efficacy and efficiency of high intensity laser in reducing pain.

CONTENTS

The research and writing process of this article was carried out according to the methodology for systematic literature review[34], which allows a synthesis of knowledge to obtain an overview and reliable estimation of the intervention effect. To do so, the following steps were followed: 1. formulation of the research question structured in acronym PICO (Population, Intervention, Control, and Outcome) format; 2. definition of eligibility criteria; 3. literature review; 4. data extraction; 5. methodological quality assessment; 6. methodology documentation; 7. interpretation of results; and 8. synthesis and presentation of results[35]. The guiding research question was, "Is high intensity laser therapy effective and more efficient than conventional therapies for the treatment of pain?"

Following the acronym PICO, the population included in the studies is patients with acute or chronic pain, the intervention to be investigated is the use of HIL, the control groups were placebo, conventional pain management therapies, and exercise, and the outcome investigated is the reduction of pain intensity in patients who received HIL[35].

A systematic search was conducted for articles published in journals indexed in the Medline, LILACS, Pubmed and PEDro databases during the period July 2020 to August 2022. It was

made use of primary descriptor 'High intensity laser' combined with the Boolean operator AND and OR and crossed with the secondary descriptors 'AND chronic pain', 'AND pain', 'AND treatment', 'OR high intensity laser therapy', in English and Portuguese. The reference lists of the selected articles were also a source of manual search.

This research included articles related to the proposed theme, that is, the use of HIL in pain treatment, published between 2010 and 2022. This was done to obtain a more current literature, considering that it is a recent and constantly evolving technology. Articles available in Portuguese or English, in their entirety, whose design was clinical trials, randomized or not, and systematic reviews was selected. Articles addressing the use of HIL for dental treatment, articles describing studies in animals, studies that did not include the measurement of pain intensity, dissertations, theses and case reports, as well as duplicate articles in electronic databases was excluded.

A total of 227 articles were found, of which 88 were located in Medline, two in LILACS, 81 in Pubmed, and 56 in PEDro. A first evaluation was performed based on the titles of the articles, and those that did not meet the inclusion criteria were excluded. Then, the abstracts were read and those that met the inclusion criteria were selected. These were read in full, and from them data collection was performed. The information collected for qualitative analysis was: authors, journal, place of publication, year of publication, objectives, sample, method, and conclusion. All those that did not meet the inclusion criteria were excluded, resulting in 31 articles for analytical reading, being these randomized and non-randomized clinical trials and systematic reviews. Figure 1 shows the flowchart of the study selection process.

To systematize the data, table 1 was prepared, with the characteristics of the randomized and non-randomized clinical trials and systematic reviews: identification of the authors, intervention protocol, duration, pain assessment method, and outcomes, following the PRISMA[36] criteria.

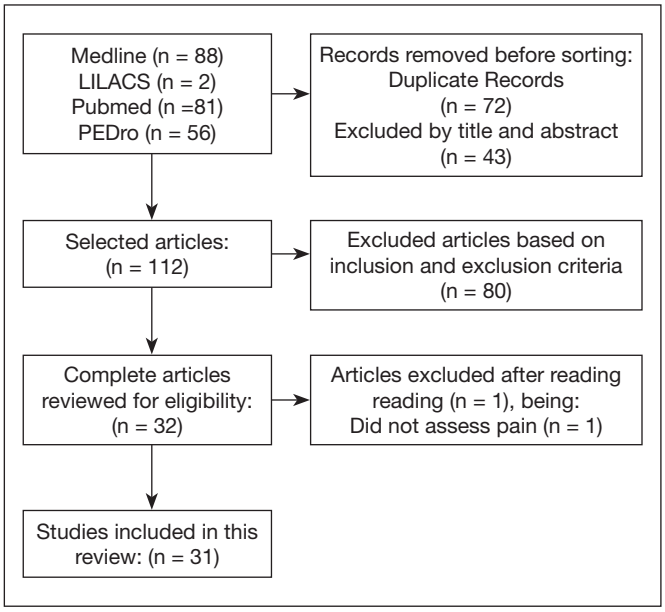

Figure 1. Flowchart of the study selection process

Table 1. Characteristics of the studies according to the PRISMA criteria

Authors	Protocol for intervention	Duration	Pain assessment method	Outcome
Nazari et al.[22] Knee osteoarthritis	n=93 G1= HIL 3x/week + exercise G2 = Conventional Therapy (TENS and US) + exercise G3 = exercise	12 weeks	VAS	HIL + exercise was more effective for pain reduction than conventional therapy + exercise and exercise alone.
Angelova and Ilieva[23] Knee osteoarthritis	n=72 G1= HIL 3 sessions: 300 J/ 2 min 4 sessions 3.000 J/ 10 min G2= placebo laser	12 weeks	VAS and dolorimetry	Pain scores were significantly reduced in G1 after 7 days of treatment and were better when compared to G2.
Kheshie, Alayat and Ali[24] Knee osteoarthritis	n=53 G1=HIL+exercise 1250 J/ 15 min G2=LIL+exercise 1250 J/32min and 33 seconds G3=placebo laser + exercise	6 weeks	VAS	HIL and LIL associated with exercise are more effective than exercise alone in reducing VAS scores. HIL + exercise was more effective than LIL + exercise
Stiglicć-Rogoznica et al.[25] Knee osteoarthritis	n=96 G1= HIL 20 min/day - 10 days	2 weeks	VAS	HIL significantly reduced pain, from 45-70mm to 10-30mm (p>0.001)
Alayat et al.[37] Low back pain	n=72 G1= HIL+exercise 3x/week, 15 min by 4 weeks G2: placebo laser + exercise 3x/ week by 4 weeks G3= HIL	12 weeks	VAS	G1 significantly reduced VAS scores when compared to G2, with the smallest effect experienced by G3 at both 4 and 12 weeks

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Table 1. Characteristics of the studies according to the PRISMA criteria – continuation

Authors	Protocol for intervention	Duration	Pain assessment method	Outcome
Fiore et al.[38] Low back pain	n=30 G1= HIL by 10 min, 15 sessions G2= US 10 min, 15 sessions. Both 3 weeks 5x/week	3 weeks	VAS and OLBPDQ	HIL significantly reduced pain when compared to US.
Boyraz et al.[39] Discopathy	n=65 G1= 10 sessions HIL G2= 10 sessions US G3= isometric exercises	12 weeks	VAS	HIL significantly reduced pain at the 3-month assessment when compared to groups 2 and 3, but there were no significant differences after 10 days of treatment
Chen et al.[40] Low back pain	n=63 G1= HIL+ decompression (1 session 10 min) G2= decompression	6 weeks	VAS	HIL reduced pain (lower back and lower limbs) non-significantly ($p>0.05$) at week 2, and significantly at week 4
Cantero-Téllez et al.[41] thumb OA	n=43 G1: HIL 3x/week- 4 weeks G2: placebo laser	12 weeks	VAS	HIL reduced pain significantly after a period of 4 weeks when compared to G2.
Atan and Bahar-Ozdenir[42] Adhesive Capsulitis	n=36 G1= HIL+ exercise G2= placebo laser+ exercise G3= exercise 5x/week	3 weeks	VAS SPAID	HIL + exercise was more beneficial than placebo laser + exercise, and than exercise alone ($p<0.05$)
Korkmaz et al.[43] Post-stroke shoulder	n=44 G1= HIL, + exercise G2= exercises only	3 weeks	VAS SPAID	HIL associated with exercise was better at relieving pain, reducing dysfunction, and improving quality of life than exercise alone ($p<0.05$)
Aceituno-Gómez et al.[44] Impaction syndrome	n=46 G1- HIL G2= placebo laser G3= exercise 5 sessions/week by 3 weeks	3 weeks	VAS and ECM	HIL + exercise was no more effective than exercise alone in reducing pain and improving function
Ezzati et al.[45] Carpal tunnel	n=98 G1= exercise + LIL (8J/cm2) G2= exercise + LIL (20J/cm2) G3= exercise + HIL (8J/cm2) G4= exercise + HIL (20J/cm2) G5= exercise	3 weeks	VAS	All groups had significant pain reduction. HIL + exercise was superior to all other groups LIL with low fluence (8J/cm2) obtained the most significant pain reduction
Venosa et al.[46] Cervical spondylosis	n=84 G1= HIL + exercise G2= US, TENS and exercise	4 weeks	VAS	Pain reduction was observed in all groups. HIL was more effective than US+TENS+exercise in reducing pain ($p<0.05$)
Thabet and Alshehri[47] Endometriosis	n=40 G1= HIL, 3x/week G2= placebo laser 3x/week	8 weeks	VAS and NRS	HIL significantly reduced pain when compared to the placebo laser
Ordahan, Karahan and Kaydok[48] Faceitis plantaris	n=75 G1= LIL (3 sessions/ week) G2= HIL (3 sessions/ week)	3 weeks	VAS	Both lasers improved pain, but in the HIL group the reductions were significant ($p<0.05$)
El-Shamy e Abdelaal[49] Hemophilic arthropathy	n=30 G1= HIL + physiotherapy G2= placebo laser + physiotherapy Both 3x/week	12 weeks	VAS	HIL was shown to be more effective in improving pain, functional capacity, and gait when compared to the placebo group
Thabet et al.[50] Primary dysmenorrhea	n=52 G1= HIL G2= PEMF Both 3 cycles of 3 sessions	6 months	VAS and NRS	Both therapies promoted pain relief, but HIL was the one that generated the most significant result ($p<0.05$)
Ebid et al.[51] Burned	n=49 G1= HIL 3x/week by 6 weeks G2= placebo laser	18 weeks	VAS	HIL significantly reduced pain and pruritus compared to the placebo group
Alayat et al.[52] Chronic cervical pain	n=60 G1= HIL + exercise G2= placebo laser + exercise	6 weeks	VAS	There was pain reduction in both groups, but significant pain reduction in the HIL group after 6 weeks of treatment

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Table 1. Characteristics of the studies according to the PRISMA criteria – continuation

Authors	Protocol for intervention	Duration	Pain assessment method	Outcome
Ebid and El-Sodany[53] Post-mastectomy	n=61 G1= HIL 3x/week G2= HIL 3x/week	12 weeks	VAS	Pain was significantly reduced in the HIL group when compared to the placebo group.
Kim et al.[54] Frozen shoulder syndrome	n= 63 G1= HIL 3x/week by 3 weeks G2= placebo laser	12 weeks	VAS	HIL group had significantly lower VAS scores at 3 and 8 weeks, but this difference was not maintained at week 12
Dundar et al.[55] Lateral epicondylitis	n=93 15 days in a row: G2= HIL 1 sessions/day G2= placebo laser 1 sessions/day G3= use of counterforce belt	12 weeks	VAS	HIL and counterforce belt reduced pain at 4 and 12 weeks with significance compared to G2.
Dundar et al.[56] Trapezium	n=76 G1= HIL 1x/day by 15 days + exercise G2= placebo laser + exercise	12 weeks	VAS	HIL reduziu os escores da VAS na 4ª e 12ª semanas de forma significante em comparação com o grupo placebo
Nouri et al.[57] Patellofemoral pain	n=40 G1=placebo laser + exercise G2= HIL 5 sessions + exercise	12 weeks	VAS and WOMAC	The reductions in VAS with HIL were more significant than those in the placebo group. The reductions in WOMAC scale were not different between groups (p>0.05)
Yesil et al.[58] Heel pain	n=42 G1=HIL+exercise G2= placebo laser+ exercise	12 weeks	VAS and RMS	Both VAS and RMS were significantly reduced in both groups at weeks 4 and 12 compared to pre-treatment measurements, however there was no difference between groups at any time point.
Song et al.[26] Musculoskeletal pain	n=736(12 studies) GL= HIL GC= placebo, exercise, US, TENS, bandages	2-12 weeks	VAS	In 11 studies HIL significantly reduced pain when compared to the control groups. The quality of the included studies was moderate; however, there was significant heterogeneity.
Ezzati et al.[28] Musculoskeletal pain	n= 19 studies G1= HIL (11 studies) G2= other interventions (8 studies)		VAS	It has been observed that the addition of HIL-related co-interventions can enhance the beneficial effects of laser therapy
Starzec-Prosepio et al.[29] Vulvodynia and chronic muscle pain	n=726(13 studies) GL= HIL GP= placebo laser, LIL, US, PEMF or exercise	Up to 12 weeks	VAS	There was pain reduction in all 13 HIL groups in all 13 studies, with only 1 study showing no statistically significant difference (HIL vs. LIL). However, the findings on LIL in vulvodynia are insufficient to recommend its use in clinical settings
Wyszynska and Bal-Bochenska[30] Knee osteoarthritis	n=395 (6 studies) GL= HIL GC=placebo, other rehabilitation therapies, pharmacotherapies	2-6 weeks	VAS, WOMAC, Fisher's dolorimeter	HIL showed favorable results in pain relief, more than the other interventions, and is efficient in pain reduction and functional improvement in patients with knee OA. However, the quality assessment indicated a high risk of bias in four of the six studies
Alayat et al.[27] Spinal pain	n=750 (10 studies) G1= HIL G2=conventional therapy (exercise, US, traction, drugs)	1-12 weeks	VAS	The combination of HIL and exercise or conservative physical therapy was superior to placebo, exercise, or physical therapy alone. However, the quality of the body of evidence was rated from "very low" to "low".

VAS = visual analog scale; CMS = Constant-Murley Score; RMS = Roles Maudsley Score; SPAID = Shoulder Pain and Disability Index; WOMAC = Western Ontario and McMaster Universities Arthritis Index; NRS = numeric rating scale; OLBPDQ = Oswestry Low Back Pain Disability Questionnaire; US = ultrasound; TENS = Transcutaneous nerve stimulation; PEMF = Pulsed electromagnetic field; HIL = high intensity laser; LIL = low intensity laser.

RESULTS

Of the 31 articles selected, 21 are randomized clinical trials, 5 are non-randomized clinical trials, and 5 are systematic literature reviews. All clinical studies, randomized and non-randomized, compared the efficacy of HIL with another type of therapy or placebo. In 61.53% of the 26 clinical studies a placebo laser was used in control group and physical exercises were associated in 37.50% of them; in the rest other treatment modalities were used (US, LIL, PEMF, spinal decompression, medical therapy and lateral counterforce belt). In 53.84% of the studies HIL was used as the sole intervention, and in 46.16% it was associated with physical exercises, spinal decompression, or conservative physical therapy.

All studies measured pain using the visual analog scale (VAS), and some included the Roles Maudsley Score (RMS), The Western Ontario and McMaster Universities Arthritis Index (WOMAC), the Oswestry Low BackPain Disability Questionnaire (OLBPDQ), the Constant-Murley Score (CMS), the Shoulder Pain and Disability Index (SPADI), dolorimetry (measured with a standard Fisher dolorimeter), the validated Spanish version of the SPADI, the Score Disabilities of the Arm, Shoulder and Hand (DASH) and the Patient-rated Tennis Elbow EAVluation (PRTEE-BR).

The studies were conducted in different countries: Egypt (6), UK (5), Turkey (5), Iran (3), Spain (2), Italy (2), South Korea (2), and the others in Poland, China, Saudi Arabia, Croatia, Canada, and Bulgaria. The samples ranged from 30 to 98 participants for the clinical trials and 6 to 19 articles for the systematic reviews. The oldest were published in 2011 and the most recent in 2022, with 2019 predominating (8 articles).

In 96% of clinical trials and 100% of systematic reviews, HIL showed favorable analgesia outcomes compared to control groups. Whether HIL was used as the sole therapy or in combination with another intervention, its results were more effective.

Characteristics and parameters of the lasers used in the included studies

The treatment protocol and laser parameters varied among the studies and are summarized in tables 1 and 2. The most commonly used device was HIRO 3, appearing in 50% of the clinical studies[24,25,37,46,47,49-56,58]. The main configuration used was Nd:YAG laser (Neodymium laser), pulsed emission, wavelength 1064 nm. One study[41] used laser of two wavelengths (800 + 970 nm). The energy density ranged from 0.51 - 150 J/cm2. In seven studies[22,24,37,41,46,52,53], there were 12 intervention sessions; in six studies[38,42,43,55,56,58], there were 15 sessions; the shortest protocol[45,57] consisted of 5 sessions and the longest[49] consisted of 36 sessions. The treatment period ranged from 3 to 12 weeks and the follow-up from 4 to 6 months.

To obtain the missing data, physical formulae were used to calculate the unreported LASER parameters[29].

$$Dose\ of\ energy(J) = Potency(W) \times Time(s)$$

$$Density\ de\ energia = \frac{Dose\ of\ enervy(J) =}{area(cm^2)}$$

Table 2. High intensity laser technical parameters in selected studies

Authors	Model	Wavelength (nm)	Energy density (J/cm²)	Maximum power (W)	Mode	Frequency (Hz)	Time per spot	Sessions
Cantero-Tellez et al.[41]	KLaser, K1200	800 + 970	15	3	Pulsed	2	15seg	12
Aceituno-Gómez et al.[44]	iLux	1064	50 250	15	Pulsed	50	-	15
Venosa et al.[46]	HIRO3	1064	-	3000	Continuous	10 – 40	120–150 µs	12
Nazari et al.[22]	E20780	1064	60	5	Continuous	30	-	12
Thabet and Alshehri[47]	HIRO3	1064	0.51 0.65	3000	Continuous	10 – 40	14 s	24
Ordahan, Karahan and Kaydok[48]	BLT-6000	1064	6 120 - 150	12	Pulsed	-	Phase 1: 75s Phase 2: 30s	9
El-Shamy and Abdelaa[49]	HIRO3	1064	0.61 0.71 0.81	-	Pulsed	-	14 s	36
Thabet et al.[50]	HIRO3	1064	0.51 - 0.64	3000	Pulsed	10 – 40	14 s	-
Ebid et al.[51]	HIRO3	1064	0.61 0.71 0.81	3000	Pulsed	10 – 40	14 s	18
Alayat et al.[52]	HIRO3	1064	27.3	3000	Pulsed	10 – 40	14 s	12
Angelova and Ilieva[23]	BTT	1064	12 - 120	12	Pulsed	25	120 s	7
Ebid and El Sodany[53]	HIRO 3	1064	0.61 0.71 0.81	3000	Pulsed	10 – 40	14 s	12
Boyraz et al.[39]	GaAlAs	1064	-	3,8	Pulsed	-	-	10
Kim et al.[54]	Hilthera	1064	-	8000	-	20 – 30	5 s	9
Dundar, et al.[55]	HIRO3	1064	1.78	3000	Pulsed	-	6 s	15
Dundar and Turkmen[56]	HIRO 3	1064	0.36 0.41 0.50	3000	Pulsed	10 – 40	6 s	15

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Table 2. High intensity laser technical parameters in selected studies – continuation

Authors	Model	Wavelength (nm)	Energy density (J/cm²)	Maximum power (W)	Mode	Frequency (Hz)	Time per spot	Sessions
Alayat et al.[37]	HIRO 3	1064	0.61 0.71 0.81	3000	Pulsed	10 – 40	14 s	12
Kheshie, Alayat and Ali[24]	HIRO 3	-	0.61 0.71 0.81	-	Pulsed	-	14 s	12
Fiore et al.[38]	HIRO 1	1064	0.76	6	Pulsed	-	-	15
Nouri et al.[57]	BTL-6000	1064	120	12	-	-	120 s	5
Stiglicć-Rogoznica et al.[25]	HIRO 3	1064	-	3000	Pulsed	-	< 120 s	10
Yesil et al.[58]	HIRO 3	1064	0.36 – 1.78	3000	Pulsed	10 – 40	120 – 150 µs	15
Korkmaz et al.[43]	BTL-6000	1064	12 100	12	Phase 1: Pulsed Phase 2: Continuous	25	-	9
Atan and Bahar-Ozdemir[42]	iLux	1064	100	15	Continuous	-	-	15
Ezzati et al.[45]	-	808	High fluency: 8 Low fluency: 20	1.6		10	100 – 250 s	5
Chen et al.[40]	BLT -6000	1064	150	12	-	-	-	10

Qualitative Assessment

The five systematic reviews[26-30] included in this survey assessed the quality of their clinical trials using the PEDro scale[59], GRADE system and the revised CONSORT statement guidelines.

In this integrative review, methodological quality and risk of bias of the twenty-six selected clinical trials were also evaluated by the PEDro scale (Table 3). The score of the clinical trials ranged from 2 to 9 points (≥ 7 = high quality; ≤ 5 = low quality), being: 23.07% low quality, 19.23% moderate quality, and 57.70% high quality. The level of evidence of the five systematic reviews was assessed using the AMSTAR 260 tool (Table 4). Three of the five systematic reviews showed low overall confidence in the assessment of methodological quality and two showed moderate overall confidence.

Table 3. Evaluation of methodological quality by the PEDro scale

Authors	Crit. 1	Crit. 2	Crit. 3	Crit. 4	Crit. 5	Crit. 6	Crit. 7	Crit. 8	Crit. 9	Crit. 10	Crit. 11	Total score
Cantero-Tellez et al.[41]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9/10
Ezzati et al.[45]	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8/10
Aceituno-Gómez et al.[44]	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8/10
Venosa et al.[46]	No	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Nazari et al.[22]	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10
Thabet and Alshehri[47]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9/10
Ordahan, Karahan and Kaydok[48]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	8/10
El-Shamy and Abdelaal[49]	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	6/10
Chen et al.[40]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
Thabet et al.[50]	No	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Ebid et al.[51]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	7/10
Alayat et al.[52]	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Angelova and Ilieva[23]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Ebid and El-Sodany[53]	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	8/10
Boyraz et al.[39]	Yes	Yes	No	Yes	No	No	No	No	No	Yes	No	3/10
Kim et al.[54]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9/10
Dundar et al.[55]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10

Continue...

Table 3. Evaluation of methodological quality by the PEDro scale – continuation

Authors	Crit. 1	Crit. 2	Crit. 3	Crit. 4	Crit. 5	Crit. 6	Crit. 7	Crit. 8	Crit. 9	Crit. 10	Crit. 11	Total score
Dundar et al.[58]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	8/10
Alayat et al.[537]	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	Yes	5/10
Kheshie, Alayat and Ali[24]	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7/10
Fiore et al.[38]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Nouri et al.[57]	Yes	Yes	No	Yes	Yes	No	No	Yes	No	Yes	Yes	6/10
Rofoznica et al[25].	No	No	No	No	No	No	No	Yes	Yes	Yes	No	3/10
Yesil et al.[58]	No	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7/10
Korkmaz et al.[43]	No	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	6/10
Atan and Bahar-Ozdemir[3142]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	8/10

Table 4. Presentation of the systematic reviews methodological quality results analysis with AMSTAR 2 tool

Autor / Ano	Cr1	Cr2	Cr3	Cr4	Cr5	Cr6	Cr7	Cr8	Cr9	Cr10	Cr11	Cr12	Cr13	Cr14	Cr15	Cr16	Confiança geral
Song et al.[26]	Y	PY	Y	PY	Y	N	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Baixa
Alayat et al.[27]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Baixa
Ezzati et al.[28]	Y	PY	Y	PY	Y	Y	Y	PY	Y	Y	-	-	Y	Y	-	Y	Moderada
Starzec-Prosepio et al.[29]	Y	Y	Y	PY	Y	Y	Y	Y	Y	Y	-	-	Y	Y	-	Y	Moderada
Wyszynska & Bal-Bochenska[30]	Y	Y	Y	PY	Y	Y	Y	Y	Y	Y	-	-	N	Y	-	Y	Baixa

Cr – Criterion, Y - Yes, PY - Partially yes, N - No

DISCUSSION

The pain control effect achieved by HIL can be attributed to multiple mechanisms. In central nervous system it increases the secretion of endogenous opioids, such as betaendorphins, while in peripheral system it reduces the secretion of substance P, responsible for hyperalgesia, as well as reduces the release of histamine and bradykinin in injured tissues, increasing the pain threshold[26]. HIL characteristics prevent thermal accumulation and result in increased radiation spread in target tissues with very low histological risk, leading to the possibility of effective treatment on deep tissues and structures[27].

To understand the HIL results, it is also necessary to understand the pain measurement methods used in each study. Because it is a subjective experience, these methods consisted in the application of one-dimensional or multidimensional tests[31]. The one-dimensional tests try to quantify pain considering it as a simple quality, unique and that varies only in intensity[31-33], as in the cases of the numerical rating scale (NRS) (0 = no pain, 10 = worst possible pain), and the visual analog scale (VAS) (marking over a 10 cm line, from no pain = 0 cm, to the worst possible pain = 10 cm). Multidimensional methods quantify the sensory, affective and cognitive-behavioral aspects of pain, as in the case of the McGill Pain Assessment Questionnaire[32]. All studies included in this review used only unidimensional pain measurement instruments, the main one being the VAS.

Musculoskeletal disorders (MSDs) were evaluated in 22 studies, being the area with the highest number of analyses for HIL use in pain management, probably because it is the main cause of chronic pain in adults[48]. Knee osteoarthritis (KOA)[22-25] and low back pain[26-29] were the most studied. All seven papers evaluating KOA found significant reduction in pain intensity in the groups treated with HIL[22-25,38,46]. In a study comparing HIL with LIL[24], after six weeks of therapy, a decrease in pain intensity and reduction of disability were observed in all treatment groups, but HIL associated with exercises obtained better results than LIL with exercises and both modalities were more effective for pain reduction and improvement of functionality than exercises alone. In a systematic review on KOA, five of six studies indicated superiority of HIL, but CONSORT evaluation pointed to high risk of bias in 4 of the 6 studies[30].

Among the studies that evaluated low back pain, two compared HIL to ultrasound therapy (US)[19,20], reporting that both interventions showed pain relief and increased functionality. Although one of them[19] reported that HIL had a greater beneficial effect than US, the other study[20] found no statistical difference between HIL and US after a 3-month follow-up. In a study[21] that compared HIL + spinal decompression with decompression alone in patients with lumbar disc protrusion, it was found that both groups experienced decreased pain in lumbosacral portion and decreased radiation pain in lower limbs, according to VAS. It was found that the combination HIL + traction achieved greater improvement than traction alone after one month of follow-up.

In a systematic review with meta-analysis[27] on HIL effectiveness in the management of spinal disorders, 10 randomized clinical trials were evaluated, four on cervicalgia and six on low back pain. The results showed that HIL with exercise was significantly more effective in reducing pain than placebo with exercise (SMD -1.11; 95% IC -1.42 to -0.80; P <0.00001; I2 0%). HIL alone or

associated with conventional physical therapy exercises provided significantly better results than exercise alone.

A research[28] evaluated the beneficial effects of HIL and co-interventions in the treatment of musculoskeletal pain through a systematic review in which 57.89% of studies tested HIL alone or with exercises and 42.10% tested HIL with other interventions. Approximately 94% of the studies showed positive effects of HIL on pain. In HIL and exercise group the largest effects were on osteopenia and the smallest on lateral epicondylitis. On the other hand, the largest and smallest effects of HIL with co-interventions were in chronic low back pain and low back pain with unilateral leg pain, respectively.

Studies evaluating hand and wrist pain (review of 19 carpal tunnel studies) found significant reduction of pain scores in experimental groups, with the effect lasting until three-month follow-up in the second study[41,45]. In studies on shoulder pain (frozen shoulder, HIL vs placebo[54]; adhesive capsulitis, HIL + exercise vs placebo + exercise[42]; post-stroke hemiplegic shoulder pain, HIL vs rehabilitation therapy[55]) HIL has been shown to be effective in reducing pain ($p<0.05$). One study[54] found improvement at week 3 and 8, but not at week 12; another study (subacromial impingement, HIL + exercise vs exercise alone)[44] demonstrated pain reduction at month 1 and 3, but without significance.

Both in the study of lateral epicondylitis[55] and in the study of plantar pain due to calcaneal spur[58], there was VAS reduction on the 4th and 12th weeks in HIL groups, but without statistical significance in the second research. In plantar fasciitis, HIL produced better analgesia than LIL[49]. Five studies evaluated HIL for back pain: four showed significant improvement in VAS scores[18,19,21,28], and one showed no difference between the groups[20] ($p>0.05$).

In myofascial syndromes, HIL significantly reduced pain scores when compared to placebo group[56]. In a review with 14 studies on vulvodynia, 12 showed favorable results for pain reduction with the use of HIL ($p<0.05$)[29]. HIL also achieved better analgesia in patients with post-burn pain and pruritus (including reduced need for antihistamine)[51]; in primary dysmenorrhea (comparing the use of HIL 15 min/session with PEMF 30 min/session)[50]; in post-mastectomy cancer pain (with results maintained at 4- and 12-week follow-up)[53] and in endometriosis (reduced pain and grade of disease, and improved quality of life)[47].

In general, the studies that demonstrated positive effects of HIL on pain had in common: follow-up for a long period of up to 6 months and physical exercise as co-intervention. The most commonly used device was NdYag, with a wavelength of 1064 nm, pulsed, frequency of 10-40 Hz, maximum power of 3000W, exposure time of 14 seconds, 12 to 15 sessions.

On the other hand, the study that did not show a positive HIL effect used a different device than most protocols, did not specify irradiation location or time, and employed consecutive alternating allocation, which is not a specific method of randomization. Only the first subject was strictly randomized, and the therapist who applied the laser was not blinded to the group[20].

The present study shows as strengths the evaluation of pain reduction through HIL in a significant number of distinct pain disorders, being musculoskeletal and non-musculoskeletal pain disorders (endometriosis, primary dysmenorrhea, post mastectomy pain, and burns), allowing a comprehensive evaluation of its effects. In addition, the quality of more than half of the included studies was rated moderate to high on the PEDro scale, and the five systematic reviews included in this paper support the result that HIL is effective for pain reduction. Therefore, the results of this review can be considered reliable.

As limitations of this study, it is possible to highlight lack of standardization in the technical parameters of the protocols for HIL use. There was significant technical variability in the application of HIL for pain treatment in the disorders evaluated. The choice of more recent studies, published only between 2010 and 2022 and available only in English and Portuguese, also limited this study.

CONCLUSION

HIL has been shown to be an effective modality for pain reduction in various syndromes. There was great heterogeneity among the diseases studied and important variability in treatment protocols. Larger, well-designed, high-quality clinical trials are needed to standardize irradiation parameters and establish the long-term efficiency of HIL.

AUTHORS' CONTRIBUTIONS

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Statistical Analysis, Data Collection, Conceptualization, Research, Methodology, Writing - Preparation of the Original
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Conceptualization, Project Management, Writing - Review and Editing, Supervision, Validation
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Methodology

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