

Intravascular laser irradiation of blood in the treatment of fibromyalgia: integrative literature review

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ABSTRACT

Background: Low-Intensity Laser Therapy (LLLT), applied to trigger points, can be used as adjuvant therapy in the treatment of Fibromyalgia. However, in Brazil, the application of intravascular technique applied transdermally on the radial artery has been widespread as a promising modality of treatment. But as far as we know, its effects are still not fully understood in the treatment of this pathology. **Objective:** To investigate the scientific evidence for the use of intravascular laser blood irradiation (ILIB) in the treatment of fibromyalgia. **Method:** this is an integrative literature review (PROSPERO registration CRD42021236744) to identify clinical studies that demonstrate the effect of ILIB on fibromyalgia, without time or language restrictions. Searches were performed and published in 4 databases (PubMed, PeDRO, EMBASE, and Scielo), by 2 independent reviewers, using the descriptors “fibromyalgia” associated with “laser” or “low-level light therapy” or “laser irradiation” or “photobiomodulation” or “phototherapy” or “blood irradiation” or “modified ILIB” or “intra-dermal ILIB”. **Results:** 3,050 articles were identified. Of these, only 62 met the eligibility criteria, and 32 were duplicates. Thus, 30 studies were rich, but none of them correspond to a clinical study using ILIB in fibromyalgia. However, two secondary sources and four secondary cases were found, with low methodological rigor, but which presented positive positive results, as well as antioxidant and circulatory systemic effects. No substantiated evidence of completion of IB clinical trials in fibromyalgia was identified for their clinical substantiation.

Keywords: Fibromyalgia; Laser therapy; Low-Intensity Light therapy; Phototherapy; Blood.

BACKGROUND

Fibromyalgia (FM) is a central sensitization syndrome, whose etiology is not yet fully understood, characterized by chronic and generalized musculoskeletal pain, due to abnormal pain processing⁽¹⁾. Pain, of variable location and intensity, is usually associated with the presence of other comorbidities, such as fatigue, sleep disorders, gastrointestinal symptoms, genitourinary symptoms, and neurocognitive and psychoactive disorders (such as depression and anxiety); that result in decreased functionality and quality of life^(1,2).

Guidelines from different countries^(1,3-4) recommend that the diagnosis of fibromyalgia should be based on the criteria⁽⁵⁾ of the American College of Rheumatology (ACR), updated in 2016. These include generalized pain in at least 4 of 5 regions, present for at least 3 months, quantified by the generalized pain index (WPI-Widesprain pain index) ≥ 7 and symptom severity scale (SSS-Symptom severity scale) ≥ 5 or WPI between 4 to 6 and SSS ≥ 9 , adding the scale of symptoms of fibromyalgia (FS–Fibromyalgia severity), which is the sum of the two, as a complete component of the diagnostic criteria

The main goal of treatment is to decrease symptoms, and increase physical functionality and level of physical activity. Therefore, active and multidisciplinary non-pharmacological therapies are considered the most effective method, and therefore, should be the first line of treatment in this pathology^(4,6-7). While for others, the combination of pharmacological

therapy with alternative therapies may bring more promising results, especially for those patients whose abilities are limited to initiate non-pharmacological therapy⁽⁸⁾. Although, due to practice patterns, drugs are often used first⁽⁷⁾.

Non-pharmacological therapies include self-management education⁽⁹⁾, exercise⁽¹⁰⁾, acupuncture⁽¹¹⁾, and physical therapy⁽¹²⁻¹⁴⁾. Among the physical therapy modalities, we highlight the use of Low-Intensity Laser Therapy (LLLT) or photobiomodulation therapy⁽¹⁵⁾, which can be applied alone or associated with functional exercises⁽¹⁶⁾. This form of therapy, classically applied to the sensitive points of fibromyalgia or tender points, has been justified by its ability to stimulate cellular functions, based on the oxidation of cytochrome c oxidase, inducing cellular oxygen metabolism and ATP (adenosine triphosphate) production, in addition to increasing muscle blood flow and oxygen delivery⁽¹⁷⁻¹⁹⁾. Additionally, LLLT is capable of creating photochemical reactions that alter peripheral and central neuronal activity, reducing pain in FM⁽²⁰⁾.

Therefore, the application could be performed, by a non-traditional method, on large blood vessels^(15,21); invasively, using special disposable sterile photonic catheters positioned inside the arteries or veins (ILBI-Intravenous laser blood illumination or ILIB-intravascular laser irradiation of blood) or transdermally or transcutaneously (NLBI- non-invasive laser blood illumination). This method of intravenous laser therapy was introduced by Russian scientists⁽²²⁻²⁴⁾ in 1981.

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In recent reviews^(15,17) that evaluated the use of LLLT in different fibromyalgia outcomes, most of the included clinical studies used the traditional method of application, that is, on tender points. However, in Brazil, since mid-2010, the ILIB technique has spread clinically as promising and effective in the treatment of FM, being applied in a modified form, with the advantage of being painless and not being considered invasive. This method, called mILIB (modified Intravascular Laser Irradiation of Blood) or modified technique of Intravascular irradiation of Blood with Laser, consists of the direct and continuous application of LLLT, by a probe/diode with wavelength, mostly, in the red spectrum (660nm), continuous, with power between 60-100mW for 30 minutes; through a bracelet/bracelet positioned 2 cm from the styloid process of the radius, under the radial artery⁽²⁵⁻²⁷⁾. This form of application is capable of irradiating the blood from the vessel that will be distributed throughout the body, promoting a systemic improvement in the patient⁽²⁸⁾.

However, as far as we know, its effects are still not fully understood and the existing literature regarding the use of ILIB in FM is in the form of a narrative review⁽²⁹⁾, due to the scarcity of previous clinical studies that could support its use as adjuvant therapy in fibromyalgia patients; or, in the form of an integrative review, evaluating its outcomes in other chronic diseases and not specifically as a therapy for fibromyalgia⁽³⁰⁾. Thus, the objective of this integrative review is to analyze whether Intravascular Blood Irradiation with Laser can improve the clinical picture in individuals with fibromyalgia. If its effectiveness is proven, this technique can be used clinically in the treatment of fibromyalgia and is supported by scientific evidence.

METHODS

An integrative review was carried out to identify evidence of the use of Intravascular Laser Irradiation of Blood (ILIB) as adjuvant therapy in the treatment of people with fibromyalgia and to provide evidence for the parameterization/dosing of this resource.

The PubMed/Medline, SciELO, PeDRO, and EMBASE databases were searched from without restriction of start date (01/01/1000) until the first week of February 2022 (02/01/2022). To identify more publications, a search was performed in clinical trial registries (Clinical Trials and REBEC) and systematic reviews (PROSPERO) in search of unpublished or ongoing studies. The search was performed by two independent researchers by title/abstract review applying the eligibility criteria. Articles that met the criteria were acquired in full to identify data related to the object of study and discussed in a consensual meeting between

the two researchers. A third investigator was contacted in case of disagreement.

The strategy and search terms were based (Table 1) on the PICOS (Participants, Intervention, Comparison, Outcomes, and Study) design. The literature search was performed using the keywords “fibromyalgia” associated (“and”) to “laser” or “low-level light therapy” or “laser irradiation” or “photobiomodulation” or “phototherapy” or “blood irradiation” or “modified ILIB ” or “ILIB therapy”. The protocol was registered (CRD42021236744) in the PROSPERO international prospective registry of systematic reviews

Table 1. Study design based on the PICOS strategy

	Definition	Main search strategy
Participants	adults with fibromyalgia	Fibromyalgia
Intervention	Intravascular Irradiation of Blood with Laser – ILIB	Laser (laser/ low level light therapy/ laser irradiation/ photobiomodulation/ phototherapy/ blood irradiation/ modified ILIB/ intradermal laser irradiation on blood)
Comparisons	Conventional treatments	Not applicable Not applicable
Outcomes	Any clinical outcome such as pain, quality of life, blood markers, among others.	
Study Design	Randomized or non-randomized controlled clinical trials, clinical trials, case series and case studies	clinical trials

Clinical studies (randomized or not) were included that a) used LLLT (Low-Intensity Laser Therapy) applied under blood vessels - ILIB, through a catheter or transdermally with a probe or bracelet, in people with fibromyalgia. Studies published without restrictions on language or year of publication were eligible for inclusion. Review studies, experimental animal studies, case studies and editorials, study protocols, or clinical studies that used LTBI Intensity) not applied under blood vessels or studies that used class IV laser (considered to have destructive and non-therapeutic potential).



RESULTS

Table 2 shows the results of the descriptors used in the research. A total of 3,050 articles were initially identified, distributed in the following databases: Pubmed 986 articles, PeDRO 20 articles, Embase 2037 articles and Scielo with 7 articles.

Table 2. Identification of the number of articles indexed in the researched databases related to the descriptors used.

Descriptors	Pub Med	PeDR O	Embase	Scielo
Fibromyalgia and laser therapy	59	16	150	2
Fibromyalgia and low level light therapy	23	-	24	-
Fibromyalgia and laser irradiation	19	1	3	-
Fibromyalgia and photobiomodulation	6	-	11	-
Fibromyalgia and phototherapy	37	3	58	2
Intravascular laser	802	-	1.439	2
ILIB therapy	35	-	362	1
ILIB modified	5	-	20	0
Total articles searched				3050

After reviewing the title/abstract by manual screening, 94 studies met the eligibility criteria, 27 of which were duplicates, and 5 were not found in full. Thus, the 30 eligible articles were acquired in full to identify data related to the object of study, 22 of which were TLBI studies in tender points, 6 were reviews and 2 were high-power laser studies. Therefore, no clinical studies were found that used TLBI, applied specifically to blood vessels (ILIB), in individuals diagnosed with fibromyalgia (Figure 2).

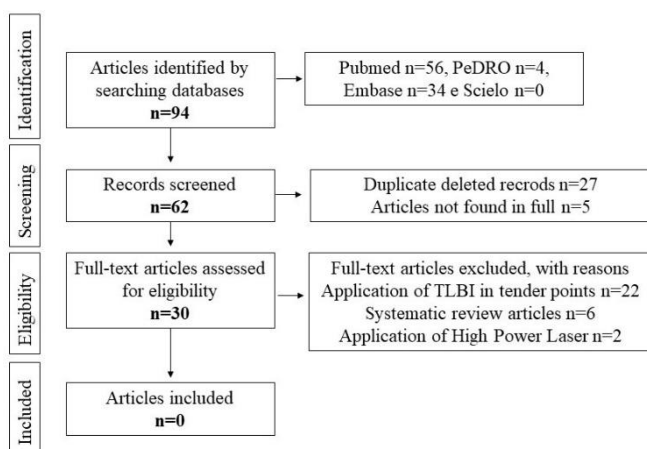


Figure 2. Flowchart of the study search and selection process.

DISCUSSION

This review was conducted with the aim of evaluating the effects of Intravascular Blood Irradiation with Laser (ILIB) as an adjuvant resource in the treatment of patients with fibromyalgia, since its use is already widely used in clinical practice in our country and has been disseminated from effectively and promisingly, in media vehicles by different health services. But as far as we know, its effects are still not fully understood and this is the first integrative review that sought to assess the effects of this resource on FM.

After the methodology used in our studies, using 4 different scientific bases and very comprehensive search terms; surprisingly, we did not find any clinical studies using ILIB in fibromyalgia. Some issues may have limited the findings, such as the lack of registration of the appropriate descriptor of this resource in the databases and the lack of availability in full of articles published in Russian. However, we cannot fail to report that our searches found an opinion review⁽²⁹⁾ that presented the effects of this resource in this pathology and an integrative review⁽³⁰⁾ that evaluated the effects of ILIB in chronic diseases, reported below.

The opinion study⁽²⁹⁾, published in 2015, defended the use of ILIB, through a catheter positioned in a large vein of the elbow or forearm, in the red (632.8nm helium-neon laser) and/or green (532nm) light length, with a power of 1 to 3mW, applied for 20 to 30 minutes. The justification for its use is due to its analgesic, spasmolytic and sedative effects resulting from mitochondrial stimulation, and hypothalamic and limbic activity. But especially, due to energetic stimulation of blood cell lines and acceleration in the conversion of ADP to ATP, proving systemic effects. However, the justifications are general and are not based on clinical studies performed on fibromyalgia patients.

In 2020, Brazilian researchers sought to answer whether the ILIB could be used in chronic systemic diseases, conducting an integrative literature review³⁰ using the terms “humans”, “patients”, “disease”, and “chronic disease” as descriptors of the participants or conditions. associated (and/or) to the intervention terms (“low-level light therapy”, “laser therapy” or lasers) or others (“blood”, “treatment outcome”, “arteries”, and “veins”). So, despite using a very comprehensive search strategy; after applying the eligibility criteria, this review included only 13 clinical studies, randomized or not, using the ILIB in different chronic diseases, such as type II diabetes mellitus, juvenile arthritis, rheumatoid arthritis, heart disease, spinal cord injury, chronic pancreatitis and of the liver. In other words, no studies



were found on the treatment of fibromyalgia, because this was not a descriptor that was used.

However, we researchers, dissatisfied with the findings of the published review (Tomé et al., 2020), and motivated by the large-scale clinical use of ILIB in fibromyalgia in our country; we performed this review study and employed a pathology-specific search strategy as described above. But we were surprised by the lack of clinical studies and sought, in the secondary sources of the articles we had selected, the possibility of case report studies that could have been carried out. Thus, we found four studies⁽³¹⁻³⁴⁾, with low methodological rigor, of ILIB in fibromyalgia.

The first study⁽³¹⁾ found was published by a German scientist in 2008 and is a case report, with a retrospective and prospective phase. In the retrospective phase, a total of 246 individuals diagnosed with fibromyalgia received drug treatment (99%) and physical therapy (86%). When necessary, they also received psychotherapy (22%) or classical acupuncture (20%). In the prospective phase, 72 patients received laser acupuncture, either as a percutaneous therapy at specific acupuncture points (10 applications) or combined with three applications of intravascular blood irradiation. Red (632.8nm) and green (532nm) lasers were used, with treatment duration limited to 5 weeks, resulting in improvement in pain, depression and quality of life. Other characteristics of dosimetry were not described in the publication.

Another study⁽³²⁾, published in 2018 by Taiwanese scientists, carried out with 15 individuals diagnosed with fibromyalgia, showed positive effects on pain, sleep, mood disorders and quality of life. They used a continuous red helium-neon laser (632.8nm) with an output power of 2.5mW, positioned with an intravenous catheter through a surgical incision in the elbow (phlebotomy). Patients received 10 applications, lasting 60 minutes.

In 2018, a group of Brazilian researchers⁽³³⁾ reported the clinical case of a woman who was undergoing cancer treatment for invasive lung carcinoma, using a specific hormone (Tamoxifen-TMX); which was treated concomitantly by photobiomodulation locally in the craniofacial and systemic regions (transdermally, laser irradiation of blood) for symptomatic control of fibromyalgia.

This patient received the modified form (mLIB) of intravascular blood irradiation with a red laser (660nm), power of 100mW, through a bracelet/bracelet on the radial artery, for 15 minutes after application of LLLT in different facial muscles. The results showed that after 10 applications, there was a significant reduction in pain, noticeable after 3 applications. The authors

concluded that this therapy may be promising for pain control.

Finally, another group of Brazilian researchers⁽³⁴⁾ published in 2021, the findings of the application of malibu, in a 47-year-old woman, diagnosed with fibromyalgia at 20 years of age, being treated with antidepressants. The patient reported that she attempted suicide due to her intense pain in teeth, face, neck, hips, knees, and hands. Then, treatment with LTBI was proposed at the pain trigger points (temporomandibular joint, neck, and hand) associated with mLIB through a bracelet in the radial artery, with a portable laser of two wavelengths (660nm in the red spectrum and 808 in the infrared spectrum), with an intensity of 600mW/cm², fluence of 200J/cm², the light beam of 3mm², for 30 minutes. Only two applications were performed, with an interval of 5 days between them. And at the end of the two applications, the patient reported improvement in the condition, without the presence of pain, which remained after 2 months of application and without the need for analgesics, anti-inflammatory drugs, or muscle relaxants.

However, despite these positive results, we still do not have enough solid scientific evidence to support its clinical use in FM. As found by Tomé et al. (2020)⁽³⁰⁾ the understanding of the effects of this therapy is still scarce, with the need for more well-designed clinical studies to understand it. However, a randomized controlled clinical study⁽³⁵⁾ to evaluate the effects of ILIB with an intravenous catheter (continuous red helium-neon laser with 632.8nm, for 20 minutes, totaling 12 applications) in the shoulder myofascial pain syndrome, which also occurs with a similar clinical picture of chronic pain as FM, demonstrated positive effects of pain severity, on the impact that this pain had on the participant's ability and quality of life.

Therefore, in line with the classic literature^(25,36,37), intravenous laser therapy or photohemodynamics with systemic action differs from the application of classical laser therapy, applied to the site of symptomatology in the pathology, with a limited range of action. This systemic effect resulting from the irradiation of blood cells is justified due to: 1) antioxidant action by the potentiation of enzymes, such as SOD (metalloenzyme superoxide dismutase), catalase-peroxidase and ceruloplasmin, which fight free radicals; 2) inhibition of the inflammatory process due to blockade of prostaglandin production by arachidonic acid cyclooxygenase; 3) improvement in blood fluidity due to the increase in prostacyclin (PGI₂) and, consequently, in the cardiac pump; and, 4) improvement of the hemorheological property of the red blood cell, favoring its softness, facilitating its function for gas



exchange. These last two factors may represent a differentiated action of ILIB in FM, since these patients seem to have greater aortic rigidity with less distensibility, compared to healthy individuals⁽³⁸⁾. Despite this evidence, there is still much to be researched so that the effects of ILIB are clarified.

CONCLUSION

The present review did not identify clinical studies with the use of ILIB in patients with fibromyalgia. Therefore, the evidence is still insufficient to support its use in the clinic, as is already the case in our country, requiring well-designed studies to prove it. On the other hand, it was possible to identify four case reports, which may suggest its use as adjuvant therapy in this pathology, with possible systemic antioxidant, anti-inflammatory, and circulatory effects, which should be elucidated in the future by the scientific community.

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