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REVIEW ARTICLE

Clinical outcomes of intravenous laser irradiation of blood in reducing inflammatory processes in obesity: a systematic review

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Abstract

Introduction: In the setting of hematologic diseases, Intravenous Laser Irradiation of Blood (ILIB) at a wavelength of 630-640 nm was developed to treat several diseases. Studies have shown that ILIB acts directly on the parameters of all blood cells, the state of the plasma, and all structural components of the vascular wall. Furthermore, by acting on cells of the immune system, hormones, and exchange processes, ILIB can influence all other systems of an organism. **Objective:** This was to conduct a systematic review to present the main clinical outcomes of using ILIB in restoring blood fluidity and reducing inflammatory processes. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was conducted from April to May 2025 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument, and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** Ninety-four articles were found. A total of 25 articles were evaluated and 08 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 35 studies with high risk of bias and 19 studies that did not meet GRADE. Most studies showed homogeneity in their results, with X^2 = 87.2% >50%. It was concluded that ILIB causes systemic effects, with improvements in blood rheological properties and microcirculation, as well as reduction in infarction area, cardiac arrhythmias and sudden death. ILIB can reduce low-density lipoprotein (LDL) and increase high-density lipoprotein (HDL), and is also effective in relieving oxidative stress and mitochondrial dysfunction in patients with comorbidities or injuries. ILIB has shown an important role in reducing and controlling blood pressure in humans. Furthermore, patients with stroke may benefit from ILIB. Pro-inflammatory cytokine levels can be reduced, as well as corrections of immune disorders have been achieved with the use of ILIB compared to drug therapy alone.

Keywords: Obesity. Comorbidities. Hematological diseases. Intravenous Laser Irradiation of Blood. ILIB. Inflammatory processes.

Introduction

In the context of hematologic diseases, Intravenous Laser Irradiation of Blood (ILIB) at wavelengths of 630-640 nm has been developed for the treatment of various diseases since 1988 **[1]**. Accumulating clinical and experimental data has allowed us to elucidate the mechanism of action of this type of treatment, defining the indications and contraindications for its use in clinical practice, and revealing the myriad of effectively treatable diseases **[1]**.

In this context, for over 25 years, studies have shown that ILIB acts directly on the parameters of all blood cells, the state of the plasma, and all structural components of the vascular wall. Furthermore, by acting on cells of the immune system, hormones, and metabolic processes, ILIB can influence all other systems in the body **[2]**.

Therefore, there is exponential growth in the clinical applications of ILIB in various pathological processes, such as pain management, tissue repair, and postendovascular restenosis **[2]**. The literature has also documented mitochondrial morphological changes resulting from ILIB use, as well as the activation of metabolic energy processes **[3-5]**. In this sense, the ILIB process appears to modulate redox signaling in the respiratory chain by stimulating mitochondrial components and the plasma membrane.

In this regard, adenosine triphosphate (ATP) production and a reduction in free radical generation would be increased by improving electron flow through the respiratory chain **[4,5]**. Mitochondria differ from other cellular organelles in that they possess their genome (mtDNA), distinct from nuclear DNA. In mammalian cells, mitochondrial DNA is a circular molecule of approximately 16,500 base pairs that encodes 13 proteins: 22 tRNAs and 2 rRNAs. All 13 proteins encoded by mtDNA are components of 4 of the 5 complexes of the oxidative phosphorylation system. During electron transport through the respiratory chain of the inner mitochondrial membrane, molecular oxygen can be monoelectronically reduced, generating reactive oxygen species, or ROS. These species are highly reactive with biomolecules and, in the intracellular environment, can attack nucleic acids, proteins, and lipids **[6-8]**.

Because mtDNA is located near sites of ROS generation, mtDNA accumulates high levels of oxidative modifications, such as oxidized bases and single-strand breaks. Therefore, the integrity of the mitochondrial genome is essential for maintaining cellular homeostasis **[8-11]**. Mitochondrial damage may be central to the impairment of cellular regulatory systems, such as the nervous, endocrine, and immune systems, and to communication between them **[12-14]**. Therefore, type 2 diabetes mellitus, obesity, hyperglycemia, hyperlipidemia, and atherosclerosis may be related to mitochondrial dysfunction **[15]**.

In this context, ILIB can be used in peripheral nervous system injuries by stimulating microcirculation by paralyzing precapillary sphincters, causing vasodilation of arterioles and capillaries, and vascular neoformation, thus leading to increased blood flow in the irradiated area. It is also used for healing various tissues by stimulating an increase in cellular ATP production, causing an acceleration of cellular mitotic activity **[15]**.

In addition, regarding the formation of rouleaux, which is caused by an increase in cathodic proteins, such as immunoglobulins and fibrinogen, resulting in the stacking of four or more red blood cells. Red blood cell membranes have a negative charge that causes these cells to repel each other, thus establishing a "bulk" state (stable distancing) **[16]**, with increased zeta potential. Zeta potential is an indicator of the stability of a dispersion. Higher zeta potentials predict more stable dispersion. Zeta potential, also known as electrokinetic potential, is measured in millivolts (mV) **[17]**.

In colloidal components such as blood, zeta potential is the electrical potential difference across the ionic layer surrounding a charged colloid ion. The higher the zeta potential, the more stable the colloid. Thus, a zeta potential less negative than -15 mV generally represents the beginnings of red blood cell clumping. When the zeta potential is zero, the colloid will precipitate into a solid **[17]**.

As a corollary, the increase in immunoglobulins and fibrinogen decreases the density of negative charges on the surface of red blood cells, allowing them to attract each other through electrostatic interactions, van der Waals interactions, and even covalent bonding (Schiff base formation). In this way, ILIB can break these binding forces between red blood cells, enabling hemorrheolysis and consequent blood tissue homeostasis **[16]**.

In this scenario, blood's constituents, such as plasma proteins, some electrolytes, red blood cells, leukocytes, and platelets, are negatively charged. Because they have similar charges, they move apart, meaning the solid elements remain close to the center of the vessel. This charge can be measured and is called Specific Conductance (SC), which in human blood averages 12,000 SC. This is the state of dispersion of the blood's formed elements that ensures optimal vascular function **[17]**.

Human blood contains 19 electrolytes, eight of which are essential (must be obtained from food) and 11 of which are non-essential. Of the eight essential electrolytes, four are cationic and four are anionic. Of the eleven non-essential electrolytes, also called trace minerals, eight are cationic and three are anionic. The main anions in blood plasma are chlorides (Cl^-), carbonates (HCO^{3-}), phosphates (HPO^{4-}), and sulfates ($S3O^{4-}$). They are primarily responsible for maintaining the dispersion forces of the elements in the blood. The main cations are sodium (Na^+), potassium (K^+), calcium (Ca^{++}), and magnesium (Mg^{++}) **[17]**.

The total dissolved electrolytes in plasma are equivalent to 9 g per liter of plasma (approximately 1 tablespoon), including essential and non-essential electrolytes, so that the average does not exceed 12,000 SC. Sodium, calcium, potassium, and magnesium are all cationic, totaling approximately 3.5 grams. Chlorides, carbonates, phosphates, and sulfates are anionic, totaling 5.5 g in an ideal combination **[18]**.

The normal blood pH is balanced between 7.35 and 7.40. Whether above or below normal, amino acids play a key role in maintaining balance, as they can be converted into anions or cations as needed. If the environment is alkaline, anions are produced; if it is acidic, cations are released. This mechanism is called the Alkaline Reserve. Fluids are divided into three compartments: intravascular (plasma), extracellular (interstitial), and intracellular space. Plasma and interstitial space can exchange ions rapidly, while ions in the intracellular space are not easily exchanged **[18]**.

If the plasma ion concentration increases, half of the cations migrate to the extracellular space, where they are stored to balance the environment. When the plasma concentration returns to normal, the electrolytes return to the plasma to be later eliminated by the kidneys. However, if the ion concentration remains high, cation migration will continue until the extracellular fluid itself becomes hypertonic. At this point, the body will have to produce water in an attempt to dilute the high concentration at the site. Edema, for example, is the accumulation of interstitial fluid resulting from high ion concentration **[18]**.

For this filtration to occur properly, the blood must be in constant motion. Therefore, it is essential to preserve its fluidity, which is only possible if there is no clotting **[18]**. In this regard, ILIB can restore blood fluidity, as the greater the number of ions present, the greater the chance of decreasing the Zeta Potential, reducing dispersion forces, and increasing the possibility of clotting.

Considering this, the present study aimed to conduct a systematic review to present the main clinical outcomes of ILIB use in restoring blood fluidity and reducing inflammatory processes.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: May 18, 2025. The AMSTAR-2 (Assessing the Methodological Quality of Systematic Reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: May 18, 2025.

Data Sources and Search Strategy

The literature search process was conducted from April to May 2025 and based on Web of Science, Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors (DeCS/MeSH Terms) were used: Obesity, Comorbidities, Hematological diseases. Intravenous Laser Irradiation of Blood (ILIB, Inflammatory processes), and using the Boolean expression "and" between MeSH terms and "or" between historical findings.

Study Quality and Risk of Bias

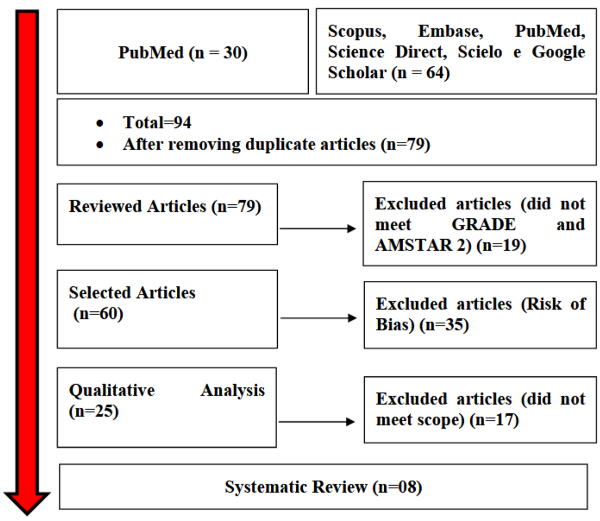
Quality was classified as high, moderate, low, or very low based on risk of bias, clarity of comparisons, precision, and consistency of analyses. The most prominent articles were systematic reviews or meta-analyses of randomized controlled trials, followed by randomized clinical trials. Low-quality evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. Risk of bias was analyzed according to the Cochrane tool by analyzing the funnel plot (sample size versus effect size), using Cohen's d test.

Results and Discussion

Summary of Findings

As a corollary to the literature search system, a total of 94 articles were found and submitted to eligibility analysis. Eight studies were subsequently selected to comprise the results of this systematic review. The selected studies were of medium to high quality (Figure 1), considering the level of scientific evidence of studies in meta-analysis, consensus, randomized clinical trials, prospective, and observational studies. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with $X^2 = 87.2\% > 50\%$. Using the Cochrane risk of bias tool, the overall assessment resulted in 35 studies with a high risk of bias and 19 studies that did not meet the GRADE criteria.

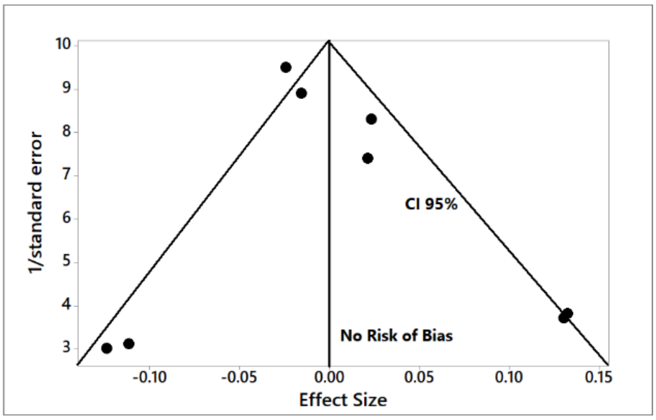
Figure 1. Flowchart showing the article selection process.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's d Test. Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph showed symmetrical behavior, suggesting no significant risk of bias, either among studies with small sample sizes (lower precision), which are shown at the bottom of the graph, or among studies with large sample sizes, which are shown at the top.

Figure 2. The symmetrical funnel plot suggests no risk of bias among the small sample size studies shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=08 studies).



Source: Own authorship.

Major Clinical Findings

Low-level laser therapy, or photobiomodulation, can induce a photobiological response within cells, activate the production of adenosine triphosphate (ATP), NO, and reactive oxygen species, and alter sodium-potassium pumps and calcium channels in cell membranes. It has also proven to be an efficient, non-invasive, low-cost, and safe tool. Among the various photobiomodulation methods, ILIB has been shown to produce systemic effects. ILIB has been studied since 1981 by Soviet scientists; it was developed for the treatment of cardiovascular diseases, with evidence of improvements in blood rheological properties and microcirculation, as well as a reduction in infarction area, cardiac arrhythmias, and sudden death **[19]**.

Knee osteoarthritis (OA) is a globally prevalent degenerative joint disease that causes pain, stiffness, and disability. Intravascular laser irradiation of blood (ILIB) has been used for chronic pain and musculoskeletal disorders. However, evidence regarding the clinical benefits and serum biomarkers after ILIB therapy in knee OA is insufficient. We designed a double-blind, randomized clinical trial to evaluate the clinical and biological outcomes of ILIB therapy for knee OA. Seventeen patients with knee OA were randomly assigned to the ILIB and control groups. Outcomes included the Western Ontario and McMaster Universities Osteoarthritis Scale (WOMAC), visual analog scale, and biomarker analysis of interleukin (IL)-6, IL-13, IL-1β, epidermal growth factor, macrophage inflammatory protein-1β, and eotaxin. Measurements were performed at baseline and three days, one month, and three months after the intervention. The ILIB group showed a significant improvement in the WOMAC-pain score at one-month follow-up compared to the control group. IL-1β levels significantly decreased at day 3, 1 month, and 3 months, and IL-13 levels decreased at day 3 and 3 months during followup in the ILIB group. ILIB therapy reduced knee OA pain for 1 month and significantly reduced serum IL-1β and IL-13 levels, suggesting potential for pain management **[20]**.

A study investigated the clinical effects of intravascular laser blood irradiation (ILIB) therapy on oxidative stress and mitochondrial dysfunction in individuals with chronic spinal cord injury (SCI) resulting from trauma. Twenty-four individuals with SCI (assigned to a sham group and a study group) and 12 normal individuals (sham) were recruited. The study group underwent 1 hour of ILIB daily for 15 days over 3 weeks. The sham group underwent ILIB without laser power. Baseline measurements established greater oxidative stress and mitochondrial dysfunction in individuals with CML than in normal individuals. On day 15 of therapy, the study group demonstrated significantly higher mitochondrial DNA (mtDNA) copy number, white blood cell adenosine triphosphate (WBC ATP) synthesis, and total antioxidant capacity (TAC), with significantly reduced malondialdehyde (MDA), than the sham group. Intragroup comparison of the study group revealed significantly increased mtDNA copy number, WBC ATP synthesis, and TAC, with significantly reduced MDA, compared to their baseline measurements. Intragroup comparisons of the sham group demonstrated no statistical differences. Low-density lipoprotein (LDL) cholesterol in the study group was significantly reduced on days 10 and 15, with high-density lipoprotein (HDL) cholesterol significantly increased on day 45. Therefore, this study demonstrated the efficacy of ILIB in alleviating oxidative stress and mitochondrial dysfunction in CML patients **[15]**.

A study evaluated the effects of ILIB on blood metabolites in type 2 diabetic patients using metabolomics. Blood samples from nine type 2 diabetic patients were compared using metabolomics before and after ILIB. The results showed a significant decrease in glucose, glucose-6-phosphate, dehydroascorbic acid, R-3-hydroxybutyric acid, L-histidine, and L-alanine, and a significant increase in blood L-arginine levels ($p<0.05$). These findings support the therapeutic potential of ILIB in diabetic patients **[21]**. Furthermore, the verification of the effects of systemic photobiomodulation on blood pressure (BP) control in humans is a current, relevant, and promising area of study, as it has contributed to the reduction and control of BP **[22]**.

Another study investigated the clinical effects of ILIB therapy on crossed cerebellar diaschisis (CCD) and evaluated the therapeutic effect in the subacute poststroke phase. A 77-year-old man with cerebral infarction in the right anterior cerebral artery territory underwent only conservative treatment, including hydration and aspirin, in the acute post-stroke phase. Once the patient was in stable condition, he underwent daily one-hour ILIB (He-Ne laser) therapy for ten consecutive days during the subacute post-stroke stage. Single-photon emission computed tomography (SPECT) was used before and after intravascular laser irradiation to detect changes in cerebral and cerebellar perfusion. The two images were then compared. CCD was detected using the first SPECT. After ILIB intervention, the second SPECT showed increased perfusion in the affected cerebellar hemisphere. Stroke patients can therefore benefit greatly from ILIB **[23]**.

A study was conducted to elucidate the specific characteristics of immunological disorders in patients with chronic endometritis and correct them using ILIB in combination with standard treatment. The study included 30 women of reproductive age with a confirmed diagnosis of chronic endometritis in partial remission. The patients were divided into two groups. Patients in group 1 (control) were treated with pharmacotherapy alone, while those in the main group (group 2) received standard therapy supplemented by intravascular laser blood irradiation in daily 25-minute sessions for 7 days using the "Mulato" device with an output power of 2 MW at a wavelength of 0.63 microns. Additionally, a third comparison group was formed, for which healthy, age-matched women were recruited. Levels of cytokines, complement components, and immunoglobulins were determined in blood plasma. The most reliable correction of immune disorders was achieved with the use of low-level laser blood irradiation compared to drug therapy alone **[24]**.

An integrative literature review included non-randomized and randomized controlled trials that specifically evaluated the therapeutic effect of ILIB in chronic systemic diseases. After applying the inclusion and exclusion criteria, 13 articles were selected, primarily randomized controlled trials. Coronary heart disease was the most prevalent, followed by type 2 diabetes mellitus, with the coronary artery being the most commonly used access route for ILIB application. Despite the varied parameters and protocols for the use of this type of therapy, all studies have shown satisfactory results in the clinical presentation of patients. ILIB is effective in all organ systems, with some positive results. However, studies on the effect of this therapy on various diseases are still scarce in the literature, and better-designed clinical trials are needed to better understand the role of ILIB in various systemic diseases **[25]**.

Conclusion

It was concluded that ILIB produces systemic effects, with improvements in blood rheological properties and microcirculation, as well as a reduction in infarction area, cardiac arrhythmias, and sudden death. ILIB can reduce low-density lipoprotein (LDL) and increase high-density lipoprotein (HDL), and is also effective in alleviating oxidative stress and mitochondrial dysfunction in patients with comorbidities or injuries. ILIB has shown an important role in reducing and controlling blood pressure in humans. Furthermore, stroke patients may benefit from ILIB. Pro-inflammatory cytokine levels can be reduced, and immune disorders have been corrected with ILIB compared to drug therapy alone.

CRediT

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The authors declare no conflict of interest.

Similarity Check

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Application of Artificial Intelligence (AI)

Not applicable.

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